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DRC 2024
Desk Research Conference
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DRC 2024

PROCEEDINGS OF
MULTIDISCIPLINARY DESK RESEARCH CONFERENCE

OCTOBER 25, 2024

MEDICINE AND SCIENCE

The Library
University of Kelaniya
Sri Lanka

PROCEEDINGS

Second Desk Research Conference
of the Library
of the University of Kelaniya

"Mining Treasures from Secondary Information Sources"

25th October 2024

University of Kelaniya

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Proceeding of the Second Desk Research Conference of the Library of the University of Kelaniya

(DRC 2024)

ISBN: 978-624-5507-87-0
eISBN: 978-624-5507-88-7

Published by the University of Kelaniya

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MESSAGE FROM THE CHIEF GUEST

SENIOR PROF. NILANTHI DE SILVA

Vice-Chancellor,

University of Kelaniya

Sri Lanka

I am delighted to extend my congratulations as we celebrate a significant milestone in our ongoing commitment to advancing high-quality research within our institution. I congratulate the Library for its outstanding efforts in organizing the upcoming Multidisciplinary Desk Research Conference, a trailblazing event in South Asia and a pioneering platform for desk-based research.

The importance of this conference is immense. It provides a unique platform for scholars from various disciplines to come together and exchange insights based on secondary data sources. As academics, we extend our influence beyond traditional teaching by engaging in applied research that meets the highest international standards, fulfilling our societal responsibilities. This event highlights the growing need for collaboration and multidisciplinary approaches to achieve remarkable research outcomes. The united efforts of all faculties and disciplines within our university in organizing this conference demonstrate our strong capability for collaboration within the academic community.

We are fortunate to have keynote speakers who, despite their busy schedules, have shown exceptional enthusiasm and commitment to contributing to the success of the conference. I sincerely thank the Librarian and the library staff for their relentless dedication and efforts, which have been crucial in bringing this academic gathering to fruition. I also congratulate the organizing committee for their unwavering dedication and meticulous planning of this event. I trust that all participants will benefit substantially from the discussions and interactions that await. May this conference serve as a catalyst for intellectual exchange, learning, and the generation of innovative ideas that will drive the future of research in our nation.

MESSAGE FROM THE RESEARCH COUNCIL CHAIRMAN

PROF. SACHITH METTANANDA

Chairman

Research Council

University of Kelaniya

Sri Lanka

It is with great pleasure that I write this message to the proceedings of the International Multidisciplinary Desk Research Conference 2024, organized by the Library of the University of Kelaniya. Following the resounding success of the DRC 2023, the Desk Research Conference has established itself as an integral part of the University of Kelaniya Research Calendar.

Desk and secondary research are receiving increasing recognition in the international research landscape. It provides an opportunity for a deeper understanding of many academic disciplines, not limited to Science and Technology but extending to Arts, Humanities, Social Sciences and Business and Management Studies.

This year's theme, "Exploring Boundless Horizons: Unveiling Insights Through Secondary Sources", clearly explains the vast scope of Desk Research. I am confident that the DRC 2024 would be an excellent platform for all multidisciplinary researchers to disseminate their important secondary research findings and provide insights into many research questions.

I congratulate the organizing committee for completing a daunting task and look forward to a successful meeting.

MESSAGE FROM THE CONFERENCE ADVISOR

DR. C.C. JAYASUNDARA

Conference Advisor

The Librarian

University of Kelaniya

Sri Lanka

With great pride and enthusiasm, I extend my heartfelt congratulations to the organizers, participants, and contributors of the 2nd Desk Research Conference hosted by the University of Kelaniya Library. This event has grown into a prestigious gathering, representing the vast intellectual diversity of our university system, covering a broad spectrum of disciplines, including technology, medicine, and beyond.

The sheer scale of this year's conference is a testament to its significance. With over 100 full research papers submitted, the conference stands as a shining pillar of scholarly rigour and innovation. Notably, a selection of some outstanding papers will be published in the Desk Research Analysis and Review Journal, further amplifying the impact of this conference on academic discourse both locally and internationally.

What makes this year particularly remarkable is the impressive participation of nearly 1,200 registered attendees, underscoring the growing interest and value placed on research dissemination through this platform. This growth is not only a reflection of the hard work and dedication of the organizers but also a promising indicator that this conference is on track to becoming one of the most impactful academic events within the Sri Lankan university sector.
As we look ahead, I am confident that the Desk Research Conference will continue to flourish, setting new benchmarks for research excellence and collaboration. It is an event poised to profoundly impact academic research in Sri Lanka and beyond.

Once again, my sincerest congratulations to all involved in making this conference a resounding success.

MESSAGE FROM THE CHAIR

DR. (MS.) R.A.A.S. RANAWEERA

Conference Chair

The Library

University of Kelaniya

Sri Lanka

With great pride and excitement, we present the second Desk Research Conference of the Library of the University of Kelaniya, a testament to our commitment to promoting research excellence through the use of secondary Data and information sources. This year conference theme, " Exploring Boundless Horizons: Unveiling Insights through Secondary Information" has brought together brilliant minds from diverse backgrounds, united by a shared passion for research and collaboration. We are privileged to host more than 100 thought-provoking research papers across diverse subject areas, including Science & Technology and Medicine, presented through multiple parallel sessions. The Conference will also feature keynote addresses by eminent academics and researchers in Sri Lanka, ensuring a rich exchange of knowledge and perspectives.

I extend my heartfelt appreciation to the Vice-Chancellor of the University of Kelaniya, Senior Professor Nilanthi de Silva, for her unwavering support and leadership. I also thank Professor Sachith Mettananda, Chairman of the Research Council, for his generous financial support and Dr. Chamli Pushpakumara, Dean of the Faculty of Computing and Technology, for his cooperation in facilitating this event.

A special note of thanks is due to Dr. C.C. Jayasundara, Librarian at the University of Kelaniya, the Conference Advisor, whose guidance has been instrumental in shaping this event. I also sincerely thank the Keynote Speakers, Session Chairs, lead paper presenters, co-authors, and reviewers for their invaluable contributions to a successful conference. My sincere gratitude goes to the editorial committee and the organizing committee for their dedication and teamwork in ensuring the success of this conference.

Finally, I wish all participants and presenters a fruitful and rewarding conference experience.

CITATIONS OF THE KEYNOTE SPEAKERS

Dr. Chandrika N Wijeyaratne

Former Vice Chancellor, University of Colombo

Outgoing Senior Professor in Reproductive Medicine

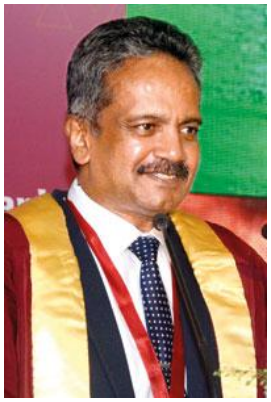
Faculty of Medicine, University of Colombo

Sri Lanka

Dr. Chandrika N Wijeyaratne is former Vice-chancellor and outgoing Senior Professor of Reproductive Medicine of the University of Colombo. She earned her MBBS degree with Honors from the Faculty of Medicine at the University of Colombo in 1983. In 1999, she completed her M.D. with a specialization in Internal Medicine, followed by Doctor of Medicine in Research focusing on Polycystic Ovary Syndrome (PCOS) and Insulin Resistance in South Asians in 2003 from the University of Colombo. She was the first endocrinologist in Sri Lanka, selected for an academic position in 1993, and distinguished herself as a pioneer women's health physician in the South Asian region. Her contributions to the field of Endocrinology were celebrated internationally with the prestigious Laureate Award for International Excellence in 2017 by the Endocrine Society of USA – in its centenary year. This award, in particular, recognized Dr Wijeyaratne's internationally pioneering work on the ethnic variations of Polycystic Ovary Syndrome (PCOS) and her successful efforts to transform diabetes management in pregnancy in a resource-limited setting. She is dedicated to preventing and controlling chronic Non-Communicable Diseases (NCDs) in Sri Lanka and South Asia. Her efforts focus on fostering multi-sectoral collaboration to help achieve the United Nations Sustainable Development Goals (SDGs) for Sri Lanka. With over 35 years of teaching experience, she has made a significant impact on both medical and postgraduate education. She played a key role in developing an innovative medical school curriculum, promoting self-directed learning and a holistic approach among Sri Lankan students. Her research interests include Polycystic Ovary Syndrome (PCOS) and insulin resistance, fetal programming and the intergenerational impacts of metabolic risks, gestational diabetes, and other complex medical conditions in pregnancy. She has also contributed to evidence-based practice guidelines for PCOS and gestational diabetes mellitus (GDM). As a mentor, she has inspired many trainees to pursue careers in Endocrinology, serving as the primary supervisor for over 13 research theses. She has over 100 publications in peer-reviewed journals, including high-impact factor journals such as the New England Journal of Medicine, The Lancet, and PLoS. She has delivered numerous orations and keynote lectures to prestigious institutions, including the Faculty Oration to her Alma Mater, Sir Nicholas Attygalle, Sir Marcus Fernando and Dr Murugesu Sinnettamby Oration of the SLMA, the inaugural Henry Rajaratnam Oration of the College of Endocrinologists and Commonwealth Medical Association.

Dr Wijeratne has had a distinguished leadership career nationally and internationally. She served as Chair of the South Asia Region Committee for the Association of Commonwealth Universities from 2020 to 2022, demonstrating her regional influence in academic leadership. She has held several prestigious positions, including being the Past President of the Sri Lanka Medical Association in 2017, the Ceylon College of Physicians in 2007, and the Endocrine Society of Sri Lanka (2004-2007). In the academic sphere, she has played pivotal roles at the University of Colombo. She was UGC nominee on the Board of Management of the Postgraduate Institute of Medicine (PGIM) and chair the Specialty Board in Endocrinology from 2007 to 2015. Dr. Wijeyaratne represented Sri Lanka in the International Society for Obstetric Medicine and led initiatives focused on public health, including the Diabetes Prevention Task Force, which she convened for 12 years starting in 2004, and the Nirogi Lanka Project, where she continues to serve as an advisor. Additionally, she chaired committees addressing non-communicable diseases and women's health through the Sri Lanka Medical Association from 2006 to 2014.

CITATIONS OF THE KEYNOTE SPEAKERS



Professor Buddhi Marambe

Department of Crop Science

Faculty of Agriculture

University of Peradeniya

Sri Lanka

Professor Buddhi Marambe obtained his B.Sc. degree in Agriculture from the University of Peradeniya (UOP), Sri Lanka, and M.Agr. & D.Agr. from the Hiroshima University, Japan. Being an academic at the Department of Crop Science of Faculty of Agriculture, UOP for more than 38 years, Professor Marambe is extensively involved in teaching, research and outreach in Weed Science, Climate Change Adaptation, and Climate-Smart Agriculture programmes conducted in Sri Lanka, especially focusing on the total food system.

With more than 150 research publications, Prof. Marambe won the "Lifetime Achievement Award" from the International Weed Science Society (IWSS) in 2022, and Presidential Awards and National Research Council (NRC) Merit Awards in Sri Lanka for scientific research related to Agriculture and Food Security in several years.

He was the Chairman and currently a member of the National Experts Committee on Climate Change Adaptation (NECCCA) and is the Chairman of the National Invasive Species Specialist Group (NISSG) of the Ministry of Environment. Professor Marambe has been the Lead Negotiator in the field of agriculture representing the Government of Sri Lanka at the Conference of Parties in the United Nations Framework Convention on Climate Change, for the past 11 years.

While being an academic, he has served as a non-executive member in the Boards of several private sector organizations to provide technical advocacies on agricultural development, and in Councils/Executive Committee of many professional associations. Professor Marambe has provided his services as a consultant to the World Bank, ADB, EU, UNDP, FAO, WFP, UNEP, ICRAF, and CIAT on issues related to agriculture and climate change at national and international levels.

CITATIONS OF THE KEYNOTE SPEAKERS

Professor Liyanage Amarakerthi
Department of Sinhala
University of Peradeniya
Sri Lanka

Liyanage Amarakeerthi is a professor in the Department of Sinhala at the University of Peradeniya. He graduated from the Faculty of Arts at the University of Colombo in 1994, earning the prestigious Prof. M.B. Ariyapala Award for "Most Competent Student of the Year" in the Special Degree Program in Sinhala. After joining the University of Colombo as an Assistant Lecturer in 1995, he was awarded a Fulbright Fellowship to study at the University of Wisconsin from 1998 to 2000, where he earned a master's degree in Languages and Cultures of Asia. He continued at the University of Wisconsin-Madison, completing his PhD in Comparative Literary Studies in 2004. His dissertation, titled *Narrative Methods of Sinhala Prose: A Historical and Theoretical Analysis of Sinhala Prose Narratives from the Twelfth Century to Post-Realist Fiction*, highlighted his expertise in Sinhala literature. He received a Dissertation Fellowship in 2003 and a Tuition Fellowship from Cornell's School of Criticism and Theory in 2005. He also received Harvard University Fellowship in 2010 and an Erasmus Mundus Fellowship at the University of Santiago de Compostela in 2013.

As a prominent Sri Lankan writer, Prof. Amarakeerthi has made significant contributions to literature, first gaining acclaim by winning the All-Island Short Story Competition in 1988 and 1991. His numerous awards include the Best Collection of Short Stories and Novels at various festivals. For the Best Short Stories Collections, he won the Vidyodaya Award in 2013, the Godage Award in 2018, and was shortlisted for the Rajatha Pusthaka Award. He won the Best Novel award at the National Literary Festival in 2008, followed by the prestigious Swarna Pustaka Award for Best Novel in 2014 and 2016, awarded by the Publishers' Association of Sri Lanka. He was shortlisted again in 2017 for the Fairway Literary Award for Best Novel. Recognizing his contributions to Sri Lankan literature, he received the Bunka Cultural Award for Literature from the Japan-Sri Lanka Friendship Cultural Fund.

Prof. Amarakeerthi's literary achievements encompass both original works and translations. In 1997, he won the Best Translation award at the State Literary Festival for translating *Maha Purushayekuta Birindakawa*. In 2020, he received the Best Translation Award at the National Literary Award Festival for his Sinhala adaptation of *Inherit the Wind*, titled *Rala Nagana Minissu*. He was also recognized in 2021 for his translation of *Itihasayak Thula Sahitya: The Translation of Works and Persons in Sinhala Literary Culture* by Charles Hallisey. Most recently, in 2023, he was honored again for his monograph *Vishwa Vidyalaya yanu Kumakda?*, which explores the significance of the humanities and liberal arts in university education.

CITATION OF THE KEYNOTE SPEAKERS

Mr. Ravibandhu Vidyapathy

Professional Dancer & Choreographer

Vice Chairman

State Ballet and Puppetry Advisory Board

Veteran Kandyan dancer, choreographer, percussionist and teacher Ravibandhu Vidyapathy hails from a family of traditional dancers and temple painters both in his paternal and maternal lineages. His father, Somabandhu Vidyapathy was a pioneering artiste who introduced the modern dance and ballet costume grammar and style to the dance theatre in Sri Lanka. His mother, dancer Malathi was the daughter of traditional dance guru Algama Kiriganitha, who groomed Sri Lanka's pioneering dancers, Chitrasena, Panibharatha, Vasantha Kumara, Chandralekha and others. Ravibandhu had his formal education at Dharmapala Vidyapala, Pannipitiya and Thurstan College, Colombo. He learnt the art of dance under legendary guru's Chitrasena and Vajira and drumming under Guru Piyasara Shilpadipathi. He also studied the classical Indian dance form Kathakali at Kerala Kalamandalam, India. Ravibandhu's ground breaking ballets and other choreographies, inspired by literal works such as Shakespeare's Romeo and Juliet, Macbeth, Othello, Greek drama, traditional Asian literature such as Ramayana, Mahabharata and Japanese Noh plays have been acclaimed nationally and internationally. He is also an accomplished percussionist and music composer. He has represented Sri Lanka at international music festivals such as the WOMAD music festival in England, Australia and Singapore, Seoul Drum Festival, Korea, Thailand Drum Festival and has toured and performed in over 30 countries, where he performed at prestigious venues such as the Smithsonian museum and Kennedy Center, America, Saddler's Wells Theater, England, the UN General Assembly Hall Geneva, President's House India, European Parliament Belgium, Opera City Hall Japan, to name a few. His artistic collaborations with international legends like Ustad Zakir Hussain, Billy Cobham, and young stars like Ambi and Bindu Subramanium have won critical acclaim, internationally.

Ravibandhu has held positions such as Chairman of National Dance and Ballet Panel of the Art Council, Member of Cultural subcommittee of UNESCO Sri Lanka, Member of Asia Dance Committee in Korea and advisory positions to cultural minister and as the director of State Dance Ensemble. Currently he works as the course director of National Diploma in Choreography at Sri Lanka Foundation and visiting lecturer and examiner at the University of Visual and Performing Arts and the University of Sri Jayawardenapura. He is the artistic director of Ravibandhu-Samanthi Dance Ensemble and Academy. In 1996, he was awarded the Bunka award by the embassy of Japan, the Derana Sri Lankan of the year award in 2017 and Kalakeerthi National Honors in 2019 respectively. In 2021, the University of the Visual and Performing Arts conferred him with an Honorary Doctorate.

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MEDICINE

A SYSTEMATIC REVIEW OF AI-BASED IMAGE PROCESSING MODELS FOR PERSONALIZED DIAGNOSIS AND SEVERITY ASSESSMENT OF SKIN DISEASES

NS Wijerama[1] PPGD Asanka[2] and T Mahanama[3]

Abstract

This systematic review provides a thorough analysis of the current state of AI-based image-processing models used in diagnosing and assessing the severity of skin diseases. The review synthesizes recent advancements in deep learning models, exploring various methodologies employed in dermatological image analysis. While significant progress has been made in developing AI tools for skin disease diagnosis, the review identifies critical challenges that hinder the clinical adoption of these technologies. Among the most pressing issues are the lack of data diversity, insufficient integration of patient-specific information, and limited generalizability of models across different skin types and conditions. The review also highlights a major gap in current research: the frequent omission of demographic and clinical data, which are essential for creating personalized diagnostic tools. Furthermore, there is a notable absence of models that can accurately assess disease severity—a crucial component for effective treatment planning and management. These shortcomings underline the necessity for more comprehensive data collection strategies, including the incorporation of multi-modal datasets that encompass diverse patient populations. In addition to data improvements, the review emphasizes the need for the development of more robust and generalizable AI frameworks. Such frameworks would enhance the accuracy and reliability of AI diagnostics in dermatology, making them more applicable in real-world clinical settings. By addressing these gaps, the review offers valuable insights and practical recommendations for future research. Ultimately, this work aims to contribute to the advancement of equitable, personalized, and effective dermatological care through the integration of cutting-edge AI technologies.

Keywords: Classification, Deep Learning, Detection, Skin, Skin Disease, Skin Cancer

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Introduction

Skin diseases represent a significant global health concern, affecting millions of people worldwide and impacting their quality of life (Chen et al., 2023). The complexity and heterogeneity of these conditions, coupled with the lack of standardized diagnostic reference points, pose substantial challenges for accurate and efficient diagnosis. In recent years, artificial intelligence (AI), particularly machine learning and deep learning techniques, has emerged as a promising tool to address these challenges in dermatology (Talukdar et al., 2023). This systematic review aims to evaluate the current state of AI applications in skin disease diagnosis and severity assessment, with a focus on research published between 2017 and 2024. Our objective is to analyze existing studies, identify research gaps, and suggest directions for future work in this rapidly evolving field.

Diagnosing skin conditions, particularly in maternity patients, presents several challenges despite being potentially rapid and accurate (Janoria et al., 2020). Accurate diagnosis aids in identifying disorders and ensuring appropriate treatment, thereby improving the well-being and quality of life of affected individuals. The complexity and heterogeneity of skin diseases, along with the lack of standardized diagnostic reference points, pose significant challenges to efficient diagnosis. Therefore, more research and the development of advanced diagnostic techniques are necessary to improve treatment methods and survival rates. Machine learning, especially deep learning, has revolutionized many aspects of medicine and offers significant benefits. These methods handle large, detailed data sets, identifying patterns and connections that contribute to creating diagnostic models (Rimi et al., 2020).

AI in healthcare involves using machine learning algorithms to enhance diagnoses and predict clinical outcomes (Jiang et al., 2017). Advances in computing power and extensive data collection within health systems have led to the development of algorithms that assist healthcare providers as clinical decision-support tools. Healthcare has seen a wide array of AI applications, such as leveraging electronic health record data for risk assessment (Juhn & Liu, 2020; Lauritsen et al., 2020), predicting and diagnosing diseases early, including sepsis (Goh et al., 2021; Komorowski et al., 2018), and utilizing wearable devices for continuous disease monitoring. Efforts to compile large medical image datasets, either within institutions or for public use, such as Deep Lesion, containing 32,000 computed tomography images for scientific studies (Yan et al., 2018), or the National Institutes of Health Chest X-Ray Dataset (Wang et al., 2017), are ongoing.

Computer vision, a branch of AI that teaches systems to interpret visual images, has greatly improved medical image evaluation accuracy and efficiency (Voulodimos et al., 2018). Convolutional neural networks (CNNs), a type of artificial neural network, have transformed image analysis by eliminating the need for traditional handcrafted features such as colors, intensity values, topological structures, and texture information (Carin and Pencina, 2018). Researchers have created deep learning models using millions of images for various tasks such as image classification, object detection, and image recognition.

Convolutional Neural Networks (CNNs) have become the leading deep learning framework for classifying skin diseases. Their research found that DenseNet201 outperformed other architectures, achieving an average accuracy of 73.52% ± 7.88 across 10 randomly split datasets. In contrast, DenseNet121 achieved an average accuracy of 69.47% ± 8.78 (Gairola et al., 2023). This study highlights the potential of densely connected networks in capturing intricate features of skin lesions. Transfer learning has proven to be a powerful technique in improving model performance, especially

when dealing with limited datasets. Researchers have utilized pre-trained models on large-scale datasets like ImageNet and fine-tuned them for skin disease classification.

The integration of machine learning techniques with deep learning models has shown promise in enhancing classification accuracy. Anand et al. (2022) proposed a hybrid approach combining CNN feature extraction with Random Forest classification. This method demonstrated improved accuracy in identifying various skin conditions, including Rosacea, Sunburn, Eczema, Acne, and Ringworm (Yashu et al., 2023).

Despite these progressions, incorporating AI into dermatological practice continues to be a significant challenge. Variability in data quality, model performance, and clinical applicability poses significant obstacles. Furthermore, the necessity for personalized diagnostic approaches, considering patient-specific factors, complicates implementation. Addressing these challenges requires models that integrate multi-modal data, including patient demographics and clinical history, to enhance diagnostic accuracy and personalization. Data sharing could accelerate data collection, but ethical and privacy concerns often hinder institutional data sharing. Skin diseases are challenging due to their complexity and the subtle differences in their manifestation among patients. Conditions like eczema, psoriasis, and melanoma can appear very similar to both untrained and trained eyes, making it difficult for algorithms to detect these subtle differences. The integration of AI into clinical workflows presents another challenge. Jaradat et al. (2023) highlighted the critical need for interpretability and clinical validation in their review. They noted that while AI models can achieve high accuracy in controlled settings, only 23% of dermatologists felt confident in integrating AI predictions into their clinical decision-making process (Ramezanpour et al., 2023). The integration of multi-modal data and advanced architectures offers a path forward for more accurate and clinically relevant AI-assisted dermatological diagnosis.

Contribution of This Systematic Literature Review

This systematic review provides a comprehensive analysis and offers key insights and recommendations for researchers in the field.

- The study consolidates research findings from articles published between 2017 and 2024, offering critical perspectives on the methodologies used for the detection, segmentation, and classification of skin lesions.
- The review identifies significant unmet needs in the current research, highlighting areas where further investigation and innovation are necessary to improve the effectiveness of AI models in dermatology.
- The report underscores the increasing accuracy of machine learning techniques in skin image analysis, which has evolved into a complementary tool for clinical evaluation, thus contributing to more precise and reliable diagnostics.

Results

The integration of multi-modal data for personalized diagnosis was examined in 15 studies. These studies underscored the importance of considering patient demographics, clinical history, and skin type to improve diagnostic accuracy. Anand et al. (2022) reported a 5% increase in accuracy when incorporating clinical history with image analysis for conditions like Rosacea and Eczema. This improvement underscores the value of a holistic approach to skin disease diagnosis. Advanced models that included these variables demonstrated better performance in disease detection and severity assessment.

Performance metrics varied across the studies, with classification task accuracy ranging from 80% to 95%. Studies utilizing deep learning models like ResNet and Inception achieved higher precision and recall rates, demonstrating their robustness in handling various dermatological conditions. For example, a study using ResNet for melanoma detection reported an accuracy of 92%, with a sensitivity of 89% and a specificity of 94% (Esteva et al., 2017). Another study using InceptionV3 for psoriasis severity assessment showed an accuracy of 88%, highlighting its clinical potential (Haenssle et al., 2020). Table 1 summarizes the performance of key architectures across different studies,

Table 1-Performance of Deep Learning Models in Skin Disease Classification

Model	Dataset	Accuracy	Sensitivity	Specificity
ResNet50	ISIC 2019	85.7%	87.3%	86.8%
VGG16	HAM10000	83.7%	84.5%	82.9%
InceptionV3	Custom (10 diseases)	82.1%	83.2%	81.0%
MobileNet	Middle East Disorders	95.7%	94.8%	96.6%

Common challenges included data diversity, imbalance, and integration with clinical workflows. Strategies such as data augmentation, transfer learning, and multi-modal integration were beneficial in addressing these issues. For instance, studies employing transfer learning from large datasets like ImageNet and ISIC exhibited significant improvements in model performance due to enhanced feature extraction capabilities (Codella et al., 2018). Transfer learning from large-scale datasets like ImageNet proved effective in improving model performance, especially for datasets with limited samples. (Riaz et al., 2023) demonstrated that pre-training on ImageNet followed by fine-tuning on dermatological images improved accuracy by 7-10% across various skin conditions. This approach is particularly valuable in dermatology, where large, diverse datasets can be challenging to obtain. Data augmentation techniques, particularly Generative Adversarial Networks (GANs), showed promise in addressing dataset imbalances. Kumar, Prashanti, and Jagadeesh (2023) reported that a modified LeNet architecture combined with CycleGAN augmentation achieved 95.03% accuracy in multi-class skin disease classification.

Novel Approaches and Emerging Techniques

Several studies explored innovative approaches to skin disease diagnosis:

1. **Federated Learning**: Riaz et al. (2023) implemented a federated learning-based deep learning method on a dataset comprising 10 distinct skin diseases. Their research found that InceptionNet performed best in this distributed learning scenario, achieving an accuracy of 98.89% while preserving patient privacy.
2. **Hybrid Models**: Anand et al. (2022) proposed a hybrid approach combining CNN feature extraction with Random Forest classification. This method demonstrated improved accuracy in identifying various skin conditions, including Rosacea, Sunburn, Eczema, Acne, and Ringworm.

while deep learning models have shown promising results in skin disease diagnosis, significant work remains in addressing dataset biases, improving model interpretability, and validating performance in diverse clinical settings.

Methodology

This study is structured as a systematic review of existing literature on AI-based image processing models for skin disease diagnosis and severity assessment. The foundation of this study is a systematic review of academic literature sourced from various databases (SCOPUS, Google Scholar, etc.),

encompassing a broad range of medical and image-processing publications. The systematic review methodology for machine learning-based skin disease detection and classification defined the study questions, search methodologies, and paper selection criteria. This work established three primary aims to examine current research on detecting and classifying skin conditions using deep learning, hybrid, and traditional machine learning methods: (1) to investigate the benefits and drawbacks of the most advanced techniques currently in use, and (2) to provide an overview of unresolved issues related to the detection and classification of skin diseases and cancer.

Table 2-Research Questions And Objectives

Research Question	Objectives
RQ1→To what extent do the suggested machine learning approaches help diagnose skin diseases?	RO1→to assess and compare the proposed machine learning techniques for diagnosing skin conditions.
RQ2→What obstacles will machine learning algorithms for diagnosing skin diseases face in the future?	RO2→to look into the unanswered issues around the use of machine learning techniques in the diagnosis of skin diseases.

To facilitate a comprehensive and unbiased comprehension of skin lesion detection and categorization, we have formulated a rigorous research question in this systematic review that may summarize the existing literature. To ensure that the study was effective and conformed to its original objective, a number of procedures and approaches were employed. With an emphasis on 2 pre-established research questions, search strings, five inclusion, and six exclusion criteria, and five search engines or databases, we thoroughly explained the components of a systematic review or survey.

Research questions: The foundation of any systematic review or study should be a set of specified research questions. As seen in Table 2, there were already 2 study subjects identified in this instance. These questions were designed to be brief, targeted at the specific objectives of the review, and precise in order to serve as a roadmap for the methodical collection and analysis of relevant data.

One of the most important steps in the systematic review process is coming up with search strings, or keywords. These well-crafted search terms are used to find scientific papers in a range of databases and search engines. They should be designed with all relevant information about the study's questions in mind. Combining truncation symbols, Boolean operators, and synonyms in search strings ensures that no significant research is missed and that the review is comprehensive. The combination of search phrases to find relevant scientific papers related to the predetermined topic is shown in Table 3.

Table 3-Pseudocode Algorithm For Establishing The Search String

Algorithm: Pseudocode for establishing the search string
The search string is composed of the following: [("Skin disease" || "Skin lesion" AND ("Machine Learning Methods" || "Machine Learning Techniques" || "Deep Learning Methods" AND ("Detection" || "Classification" || "Segmentation")]

Pre-established inclusion and exclusion criteria were created, as shown in Table 4, in order to maintain the standard and relevance of the papers that were included in the review. In this example, there were five established inclusion criteria and six established exclusion criteria. For a paper to be considered for review, it had to meet certain requirements outlined in the inclusion criteria. These included the length

of time between publications, the type of study that was relevant to the topic, the credibility of the journals that published the scientific papers, and the language used in the study. Conversely, the exclusion criteria delineated the conditions in which an article would be overlooked, including publications written in languages other than English or studies that present a notable possibility of bias, such as theses for master's and doctoral degrees, seminars, posters, case studies, and publications prior to 2020. By following these criteria, it was possible to make sure that the review focused on the most important and well-researched papers.

Table 4- Criteria for Including and Excluding Papers.

Inclusion Criteria	*Exclusion Criteria*
The articles must focus on the detection, segmentation, or classification of skin diseases or cancer.	Articles not specifically devoted to the identification, categorization, or segmentation of skin diseases and cancers.
English should be used when writing the studies.	Scientific reports; book reviews; editorial letters; abstracts; and publications are not subjected to peer review.
A study article must have been published between 2020 and 2023 in order for it to be included in the systematic review.	Studies published before 2020 with the exception of Sections 1 and 4.

Databases or search engines: Selecting the right database or search engine is also essential for systematic reviews. Making use of many databases enhances the likelihood of discovering a diverse range of relevant papers. The analysis minimized the possibility of missing significant discoveries by utilizing multiple search engines.

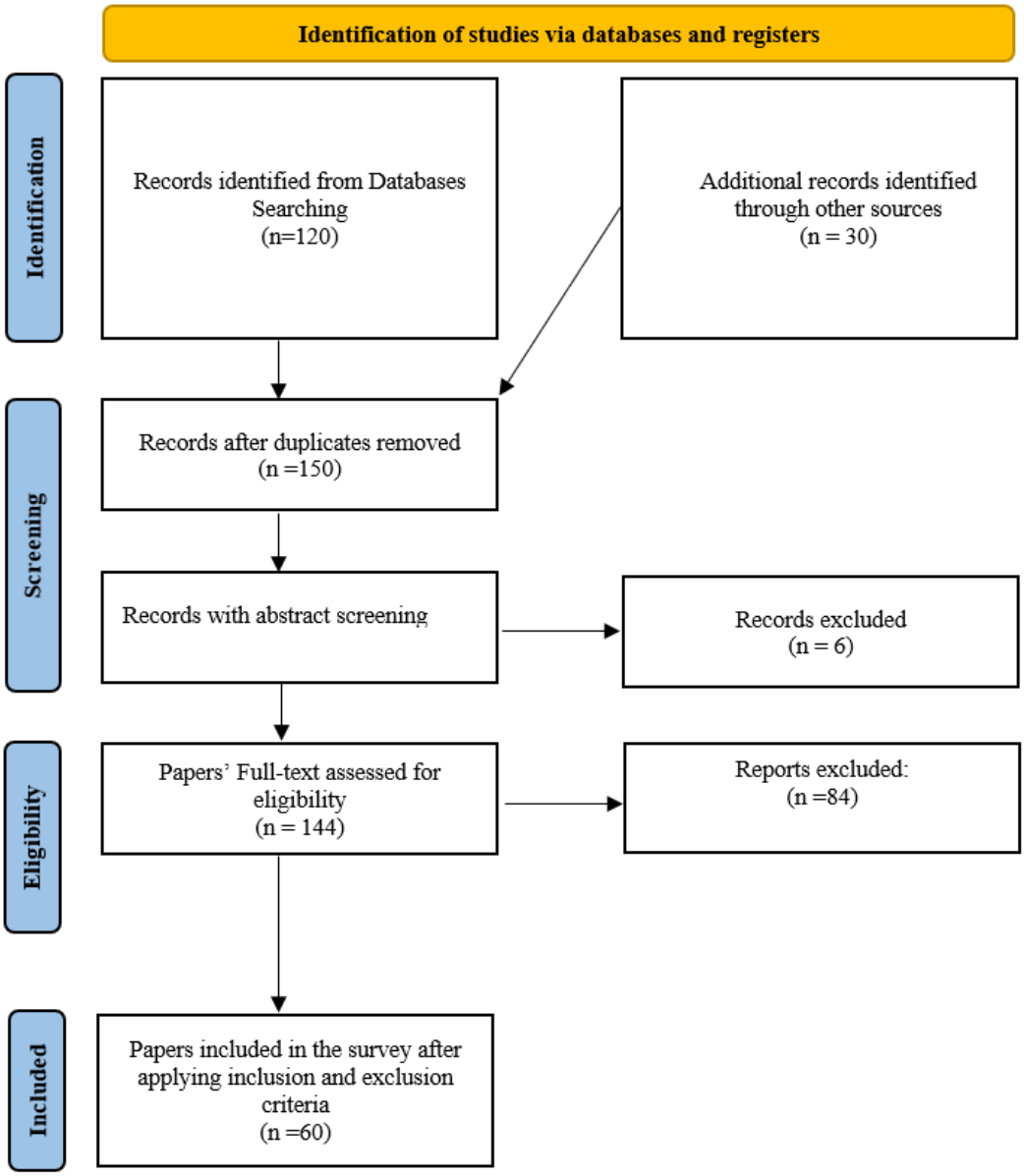

Figure 1-The Flow Diagram Of The Process Used To Seek And Choose Study Papers From Various Databases.

Discussion

Diagnostic Challenges in Dermatology

There is a critical need to address diagnostic challenges commonly faced in dermatological practice, especially where visual differentiation between conditions is difficult. One such example is the differentiation between eczema and psoriasis (Fig.2). Both conditions often manifest as red, itchy skin patches, making them challenging to distinguish with the naked eye. However, they differ significantly in several aspects, including the nature of the scaling, typical locations on the body, and the thickness of the skin patches.

Eczema and Psoriasis:

- Eczema: The scaling tends to be finer, and the affected areas are usually found in the folds of the arms and legs, on the face, and behind the ears.

- Psoriasis: Characterized by thicker, silver-white scales on top of red patches, with the scales being more pronounced and tightly adhered to the skin.

Utilizing advanced image analysis techniques to distinguish between these nuances can significantly enhance diagnostic accuracy. Image analysis allows for detailed examination of skin texture, scale characteristics, and lesion distribution, providing a more objective and precise diagnosis compared to visual inspection alone.

Figure 2-Difference Between Eczema And Psoriasis

Datasets In Dermatology

Large amounts of high-quality data are required to build a deep-learning model that performs better than others. The possibility that models will learn to produce correct predictions is greatly increased by the abundance of high-quality datasets. In order to involve the dermatological and machine learning (ML) communities in the development and improvement of algorithms, a number of publicly accessible skin image datasets have been established.

An internationally recognized public image dataset for skin cancer is the International Skin Imaging Collaboration (ISIC) archive. Due to its algorithmic challenges—which include lesion segmentation, visual dermoscopic feature detection and localization, and illness classification—the ISIC archive has garnered remarkable recognition since 2016 (Codella et al., 2018, 2017; Tschandl et al., 2018).

More than 13,000 dermoscopic pictures from top clinical facilities worldwide are featured in the archive. Furthermore, atlases of dermatology that were originally developed for instructional purposes have lately been repurposed as digital image databases for algorithm development. Certain databases, like the Dermofit Image Library, need institutional or ethical committee clearance, while others are available for a price and require a license agreement.

A variety of public datasets on skin conditions are also available. Many clinical institutes have assembled their own datasets for conditions like psoriasis, rosacea, and lip disorders in addition to these public archives. (Han et al., 2020; Papadakis et al., 2021; Webster et al., 2017).

Problems With Image Datasets And Data.

Duplicate data.

A technique to exclude duplicate images was suggested by Cassidy et al. (2022) in response to their observation that some scripts utilizing the ISIC dataset contained the same or similar images in both the training and test sets, which introduced bias into the CNN model. It should be noted that a rich source of nonduplicated data must be used for training CNNs in order to prevent bias and overestimation of model performance. This is because the model predictions improve in accuracy by extracting a higher

number of unique features rather than by simply enriching the data by sourcing a large number of images.

Data quality and imbalance

Concerns about image quality can arise since clinical image quality varies depending on the technology and the person taking the pictures, particularly with nonpublic institutional datasets. Since a specific instrument is used to obtain demographic images, there may not be as much variation in the quality. This problem is exacerbated by dermatology's general shortage of significant picture repositories; future model development will require solutions such as diversifying the images in datasets by incorporating multi-modal data, including patient demographics, and clinical history.

Generalizability of Models

Although numerous studies highlight the potential use of AI models in dermatology, it is important to note that the majority of these papers are largely proof-of-concept, trained, and tested on retrospective datasets. The limitation in generalizability can be categorized into three main issues: lack of datasets in general, lack of diversity in datasets, and lack of patient-specific information. These barriers to generalizability include data imbalance across age, sex, ethnicity, skin tone, disease type, and disease prevalence. If not adequately addressed, these issues could lead to poor performance of the models when applied outside their training and test populations.

For instance, publicly available datasets like the ISIC challenge archive have been predominantly collected from fair-skinned patients in the United States, Europe, and Australia, which poses a significant limitation. Similarly, Han et al. (2020) and Winkler et al. (2019) acknowledged that their validation was limited to one race in one region, such as Asian populations in South Korea and Caucasian populations in Germany. Haenssle et al. (2020) also stated that their dataset lacked certain benign, malignant, or inflammatory skin lesions and consisted predominantly of images from Caucasian backgrounds.

These findings suggest that AI models are likely to struggle with generalizing across nonwhite skin types and populations with skin lesion types not included in the training datasets. To address these challenges, there is a need for studies deploying models for prospective validation in real-world settings where these models will be used.

Impact Of Skin Type Variability On Diagnostics

Previous studies have generally not accounted for the impact of skin type variability on the accuracy of skin disease diagnostics. Skin diseases manifest differently across various skin types, significantly influencing the effectiveness of image-based diagnostic systems. For instance, research by Adamson and Smith (2018) highlighted that machine learning models may underperform on images from patients with darker skin tones due to the lack of diversity in training datasets. This indicates a significant gap in current AI models' ability to generalize across diverse populations. Therefore, there is a critical need for developing algorithms that recognize skin diseases while being sensitive to variations in skin type to ensure higher accuracy and applicability across diverse populations.

Assessment Of Disease Severity

Another critical area often neglected in existing research is the assessment of disease severity from images. Understanding the severity of a skin condition is crucial for determining the appropriate treatment strategy. Esteva et al. (2017) and Haenssle et al. (2020) demonstrated the potential of deep learning models in diagnosing skin conditions but highlighted the lack of models that can accurately assess the severity of these conditions. Advanced machine learning algorithms capable of evaluating

the severity of skin conditions can significantly impact medical intervention strategies, potentially reducing complications and improving patient management. Therefore, incorporating severity assessment into AI models for dermatology is essential for developing comprehensive diagnostic tools.

Integration Of Multi-Modal Data

Most existing diagnostic systems rely exclusively on image data, neglecting other relevant patient information that could influence diagnostic outcomes. Han et al. (2020) and Winkler et al. (2019) noted that integrating patient demographic data, clinical symptoms, and other health metrics with image data can enhance the personalization of diagnostics. This multi-modal approach tailors diagnostics to individual patient profiles, significantly improving the accuracy and relevance of the diagnostics. Thus, there is a need for developing multi-modal diagnostic models that analyze dermatological images in conjunction with patient-specific data to provide more personalized and accurate diagnostics.

Early and precise diagnosis not only improves patient outcomes but also offers considerable cost savings within the healthcare sector. By decreasing the need for multiple diagnostic tests and reducing the incidence of misdiagnosis, AI models can lower the long-term treatment costs associated with advanced skin diseases. The development and implementation of these models can contribute valuable insights into the interplay between different types of skin data and disease manifestations, spurring further innovations in dermatological research and leading to improved clinical protocols and guidelines.

Conclusions

This systematic review provides a comprehensive analysis of AI-based image processing models used in the diagnosis and severity assessment of skin diseases, shedding light on both the advancements made and the substantial challenges that remain. While AI has demonstrated considerable potential in dermatology, especially in enhancing diagnostic accuracy and streamlining clinical workflows, several critical gaps hinder its full integration into clinical practice.

A primary contribution of this review is the identification of significant limitations within the current body of research. One such gap is the pervasive lack of diversity in training datasets. Most existing models are trained on datasets that predominantly represent lighter skin tones, leading to reduced accuracy and reliability when applied to patients with darker skin types. This lack of diversity not only limits the generalizability of AI models but also risks perpetuating healthcare disparities, making it crucial to develop datasets that encompass a broader range of skin tones and conditions.

Another gap identified is the limited integration of multi-modal data, such as demographic information, clinical history, and genetic factors, into AI models. Current approaches largely focus on image data alone, neglecting other relevant patient-specific information that could significantly enhance diagnostic accuracy and personalization. The incorporation of multi-modal data is essential for developing AI models that can provide more nuanced and tailored diagnoses, which are critical for effective treatment planning and improving patient outcomes.

Moreover, the review highlights the inadequacy of existing models in assessing the severity of skin diseases. While some models are capable of identifying conditions, few are designed to evaluate the severity, which is vital for determining appropriate treatment strategies and monitoring disease progression. This gap underscores the need for developing AI models that not only diagnose but also assess the severity of skin conditions, thus enabling more informed clinical decision-making.

The review also addresses the challenges of model interpretability and clinical integration. Despite high accuracy rates in controlled settings, many AI models remain "black boxes," offering little transparency into their decision-making processes. This lack of interpretability hinders their acceptance and use in clinical practice, as healthcare providers are often hesitant to rely on tools they do not fully understand. Future research should prioritize the development of explainable AI models that provide clear and actionable insights, fostering greater trust and adoption among clinicians.

Furthermore, the review calls attention to the ethical and privacy concerns related to data sharing, which often hinder the collection of high-quality, diverse datasets. Addressing these concerns through the development of secure data-sharing frameworks will be crucial for advancing AI research in dermatology.

This review not only synthesizes existing knowledge but also provides a critical roadmap for future research. By identifying these gaps and proposing strategic directions, it aims to guide the development of more robust, inclusive, and clinically relevant AI models. Such advancements are essential for realizing the full potential of AI in dermatology, ensuring that it serves as a tool for equitable and personalized healthcare that benefits all patients, regardless of their demographic background. The insights provided by this review are instrumental in paving the way for the next generation of AI-driven dermatological care, with the ultimate goal of improving patient outcomes globally.

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IMPROVING CARDIOVASCULAR RISK PREDICTION OF SRI LANKANS USING ARTIFICIAL INTELLIGENCE

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Abstract

There are no CV risk prediction models derived from Sri Lankan cohorts. Therefore, the World Health Organization(WHO) risk charts developed for the Southeast Asia Region are being used to risk stratify Sri Lankans. However, Sri Lankans are quite different to some Southeast Asian countries and may not agree with Sri Lankans. Therefore, we aimed to develop a CV risk prediction model specific to a cohort of Sri Lankans. Using supervised machine learning of 10-year follow-up data of a randomly selected, population-based cohort of Sri Lankans, we developed a model to predict the 10-year risk of developing a cardiovascular event. We compared predictions of the new model at baseline in 2007 with the observed events in 2017 following a 10-year follow-up using receiver operating characteristic curves(ROC) to find the predictive performance. We compared the predictions of the new model and the currently used WHO risk charts. We selected 2596 Sri Lankans between 40 and 65 years old with no history of previous CV diseases (CVD) at recruitment and who had completed 10-year follow-ups. There were 179 hard CVDs recorded over the ten years. CVD included all cardiovascular deaths confirmed or presumed cases as mentioned in death certificates, non-fatal strokes, and physician-diagnosed non-fatal acute coronary syndromes, including elective percutaneous coronary interventions and coronary artery bypass grafts done on patients with symptomatic unstable angina. Any cardiac presentation except those mentioned here was excluded. Of 179 events, the ML-based model predicted 124; only 33 were predicted by the new model, while only 33 were predicted by 2019 WHO risk charts. The new ML-based model had 0.93 accuracy with an AUC-ROC of 0.74 ± 0.06. Machine learning of individual data of a Sri Lankan cohort improved CV risk prediction of Sri Lankans than using risk charts developed for an epidemiological region using a modelling approach.

Keywords: Cardiovascular Risk, Prediction, Machine Learning, Artificial Intelligence, Sri Lanka

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IMPACT OF CHILLY CLIMATE ON FEMALE ACADEMICS AND STUDENTS IN STEM FIELDS IN HIGHER EDUCATION SETTINGS

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Abstract

In the context of academia, the term “chilly climate” is used to describe a subtle, often unnoticed environment of discrimination and marginalisation, particularly hostile towards certain groups, such as women, minorities, or those with non-dominant identities. In numerous societies, deep-seated gender norms and stereotypes frequently sustain inequalities in educational achievements, career paths, and academic involvement, particularly in Science, Technology, Engineering, and Mathematics (STEM) disciplines where women continue to be significantly underrepresented. This review article examines the impact of the chilly climate on female academics and students in STEM fields within higher education settings through a systematic and comprehensive literature search. A broad search was conducted using major academic databases and research platforms including Google Scholar, PubMed, ResearchGate, ScienceDirect and Scopus. Keywords such as "chilly climate," "STEM academics," "women in STEM," "impact of chilly climate," and "gender biases in academia" were employed. Articles, book chapters, and conference papers published from 1982 to 2024 were included. This data was analyzed thematically to identify key patterns and themes related to the impact of the chilly climate. The thematic analysis highlighted recurring issues related to Academic Performance and Participation, Career Progression and Retention, Psychological and Emotional Well-Being, Broader Educational Environment. Addressing the chilly climate requires a multifaceted approach. By making changes, institutions can work towards reducing the impact of the chilly climate and enhancing the success and wellbeing of all individuals. Implementation of social coping programs to provide emotional and psychological support for women, increasing interaction in learning, providing quality advising, encouraging families to support females and improving gender diversity in academic and work environments can have a positive impact on making the chilly climate warmer so that female representation in STEM field could be further uplifted.

Keywords: Chilly Climate, Gender Biases In Academia, Impact Of Chilly Climate, STEM Academics, Women In STEM.

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Introduction

In the context of academia, the term “chilly climate” is used to describe a subtle, often unnoticed environment of discrimination and marginalization. This climate can be particularly hostile towards certain groups, such as women, minorities, or those with non-dominant identities. Unlike blatant acts of discrimination, a chilly climate is characterized by its covert nature. It manifests in the form of microaggressions, stereotypes, exclusionary practices, and a general lack of acknowledgment or appreciation for the contributions of those who are marginalized. The term “chilly climate” encapsulates the often unseen but pervasive barriers that can prevent individuals from fully participating in, belonging to, and succeeding within the institution. For students, dealing with a chilly climate can be very unpleasant. It can lower their self-belief, lessen their drive, and hinder their active engagement in both studies and other activities (Lee & Mccabe, 2021).

In numerous societies, deep-seated gender norms and stereotypes frequently sustain inequalities in educational achievements, career paths, and academic involvement (Biggs et al., 2018). This disparity is particularly pronounced in Science, Technology, Engineering, and Mathematics (STEM) disciplines where women continue to be significantly underrepresented. Despite efforts to promote gender diversity and inclusion, barriers such as societal expectations, implicit biases, low sense of belonging and limited access to resources persist, hindering women's active involvement and advancement in STEM fields (Blackburn, 2017).

The findings from the 15-month fieldwork at the University of Kelaniya, Sri Lanka (Ruwanpura, 2011) revealed that social and cultural expectations heavily constrain female students, particularly from working-class backgrounds, impacting their ability to express autonomy and sexuality. These constraints, reinforced by class and nationalism, align with the concept of a chilly climate in STEM settings, where traditional gender roles and societal pressures create a hostile environment for women. The study highlights the dual role of higher education as both a path to better opportunities and a source of further constraints, with women engaging in self-surveillance to maintain respectability. These insights contribute to understanding how intersectional factors shape student experiences and perpetuate gender inequities in STEM fields.

In the landscape of higher education, fostering an inclusive and equitable environment that promotes active engagement among all students is essential for academic success and personal development.

Given these considerations, it is crucial to examine the specific impacts of the chilly climate on female academics and students in STEM fields within higher education settings. This review aims to address the research question ‘what are the impacts of the "chilly climate" on female participation, career progression, and psychological well-being in STEM disciplines?’ The objective is to comprehensively review and analyse existing literature to identify recurring themes and patterns related to the impacts of the chilly climate on women in STEM. Additionally, this review seeks to propose evidence-based strategies that higher education institutions can adopt to create a more inclusive and supportive academic environment. By examining these factors, this review aims to contribute to the understanding of gender biases in academia and to inform policies and practices that promote gender equity in STEM education and careers.

Methodology

This review article examines the impact of the chilly climate on female academics and students in STEM fields within higher education settings through a systematic and comprehensive literature search. To gather relevant studies, a broad search was conducted using major academic databases and

research platforms including Google Scholar, PubMed, ResearchGate, ScienceDirect and Scopus. These platforms were chosen for their extensive coverage of scholarly articles and their capacity to provide both historical and current research insights.

The search utilized specific keywords to ensure the inclusion of relevant literature. Terms such as "chilly climate," "STEM academics," "women in STEM," "impact of chilly climate," and "gender biases in academia" were employed to capture a wide array of studies related to the topic. The search focused on identifying research that addresses the chilly climate's effects on female students and academics in STEM disciplines. The inclusion criteria were designed to ensure the relevance and quality of the studies reviewed. Articles, book chapters, and conference papers published from 1982 to 2024 were included. Data extraction involved systematically capturing information on study objectives, methodologies, findings, and conclusions.

This data was analysed thematically to identify key patterns and themes related to the impact of the chilly climate. The thematic analysis highlighted recurring issues such as reduced academic participation, career progression barriers, psychological effects, and broader educational implications. The quality of the studies was assessed based on the relevance to the research questions. To ensure quality assurance and rigour in the thematic analysis process, three researchers independently engaged in the analysis. They began by thoroughly immersing themselves in the identified literature, reviewing the material multiple times to identify recurring patterns. The data was then systematically coded by each researcher independently, ensuring that personal biases were minimized. Afterward, the individual coding results were amalgamated to create a consistent and comprehensive coding framework. The identified themes were subsequently reviewed and validated by the supervisor, providing an additional layer of scrutiny. This multi-step process of independent coding, cross-verification, and supervisory review ensured rigour in the thematic analysis.

Results

This review encompasses a total of 26 articles, with the majority originating from the United States of America followed by studies based on Sri Lanka, United Kingdom, Sweden, and South Korea, highlighting a global range of perspective and reflection on the topic.

Causes of the Chilly Climate

The concept of the chilly climate, especially in educational settings, was significantly brought to light by Hall and Sandler in their seminal works from the early 1980s. They identified various systemic issues contributing to an environment less conducive for women's academic and professional growth. Differential treatment by instructors and peers created a less supportive and more hostile environment for female students (Hall & Sandler, 1982, 1984). This initial identification of the chilly climate set the stage for numerous subsequent studies exploring its multifaceted nature and impacts.

Institutional and structural factors play a crucial role in perpetuating the chilly climate. Organizational culture and policies within higher education institutions can sustain a chilly climate for women faculty, as highlighted by the lack of support for work life balance, gender biased evaluation criteria, and insufficient mentoring opportunities (Maranto & Griffin, 2011). These institutional barriers create an environment where women feel less valued and supported, impacting their career advancement and overall job satisfaction.

Classroom dynamics also significantly contribute to the chilly climate. Unequal participation opportunities and gender-based biases from instructors reinforced a chilly environment, where female

students often received less encouragement and fewer opportunities to participate actively in class discussions (Crawford & MacLeod, 1990). Decades later, it was confirmed that women are still less heard and their contributions are often undervalued, perpetuating the chilly climate (Lee & McCabe, 2021). This undervaluation discourages active participation and affects female students' confidence and academic performance.

Field specific challenges further exacerbate the chilly climate. Mostly in Sri Lanka, cultural and institutional norms and gender specific expectations significantly contribute to the chilly climate (Jayaratne et al., 2020). Deeply ingrained cultural attitudes towards gender roles can impact female students' experiences in male-dominated fields. Comparisons of perceptions of the chilly climate in traditional and non-traditional majors showed that women in male dominated fields faced more significant challenges (Morris & Daniel, 2008). This highlights the additional barriers women encounter in pursuing careers in STEM and other traditionally male dominated fields.

Social and cultural influences also play a crucial role in shaping the chilly climate. Broader social and cultural norms about gender roles significantly influence women's experiences in academia (Britton, 2017). Societal expectations and stereotypes about gender often dictate women's behaviour and opportunities, further entrenching the chilly climate in educational and professional settings.

Instances where females are judged based on stereotypes made it uneasy for them to perform well in STEM fields due to the tendency of underestimating their abilities, having concerns about fitting in, having perceptions about STEM being male-dominated, lack of confidence and being considered unfit for STEM based on their appearance and behaviour. Moreover, faculties having low expectations for female students, providing less inspiration and opportunities, favouring male students over females, their contribution not being adequately valued, hostility towards feminism and prejudice of women were also linked with chilly climate (Seifried, 2000; Kim & Kim, 2023).

Schemas of inequality frame the way individuals interpret their day-to-day work environments, sharpening or distorting their ability to recognize unfair circumstances. Those using meritocratic schemas are less likely than those using structural schemas to recognize chilly departmental climates and chilly professional cultures (Cech et al., 2018).

Doctoral degrees in most graduate science programs require that graduate students spend large amounts of time conducting research in science laboratories. As a result, the environment in the research lab is key to the success or failure of graduate students, particularly women. Analyses of the data indicated that the social climate in the research lab, shaped by the attitudes and behaviours of the women's male colleagues and/or research advisors, created a "chilly place" for the female graduate students (Ferreira, 2002).

Research studies suggest that aspects such as various social factors, institutional structures, poor advising, lack of opportunities, being from different socioeconomic backgrounds, having to face harassment, discrimination and biases were found to be closely linked with the environment being chilly for females (Blackburn, 2017). Lack of female professors who could be considered as role models for female students was also found to be a major concern in the academic environment being chilly for females (Schulze & Tomal, 2006).

Impact of the Chilly Climate

The chilly climate in educational and professional settings has extensive and multifaceted impacts,

affecting various aspects of women's academic and professional lives. The consequences of this environment are significant, spanning academic performance, career progression, psychological well-being, and the broader educational landscape. Furthermore, as women are subjected to a variety of negative impacts of chilly climate under different aspects including academic performance, career development and retention, psychological health and emotional well-being, it depicts the importance of addressing such issues for making the environment more comfortable for females to work in and perform.

Academic Performance and Participation

The chilly climate has a considerable impact on women's academic performance and participation. Women in fields traditionally dominated by men, such as engineering, face challenges that negatively influence their academic success. These challenges often include subtle biases and a lack of institutional support, which can undermine women's engagement and performance (Walton, et al., 2015). Additionally, women frequently encounter undervaluation of their contributions in academic settings, which can lead to reduced self-confidence and lower levels of engagement (Lee & McCabe, 2021). This cycle of diminished visibility and participation adversely affects their overall academic outcomes.

Furthermore, women's ability to participate fully in academic activities can be hindered by the chilly climate. Research has shown that women in college classrooms often receive less encouragement compared to their male peers, which contributes to lower academic involvement (Crawford & MacLeod, 1990). This reflects broader systemic issues within educational institutions that fail to adequately support and promote women's academic interests (Morris & Daniel, 2008).

Feeling intimidated, a sense of being less competent than the male counterparts, doubting their own capabilities and hesitation in participating in academic activities could hinder the academic performance of the female students. Self-silencing was also found to be common among women in STEM fields which may negatively impact on their engagement in academic work (Kim & Kim, 2023).

Career Progression and Retention

The impact of the chilly climate extends to career progression and retention. Gender biases in evaluation and promotion processes create significant barriers for women faculty, limiting their advancement opportunities. These biases manifest as differential treatment and less favourable evaluations, contributing to lower promotion rates and higher attrition among women in academia (Maranto & Griffin, 2011). Such systemic disadvantages affect not only immediate career prospects but also long-term career satisfaction (Britton, 2017).

The barriers to career advancement can result in higher turnover rates among women faculty, exacerbating the gender imbalance in academic positions. Women who experience a chilly climate may feel unsupported and less motivated to pursue long term academic careers, leading to a loss of talent and diversity within the field (Maranto & Griffin, 2011). These systemic barriers reinforce a cycle where women remain underrepresented in higher academic ranks, perpetuating gender disparities in academia.

A study shows that junior women STEM faculty reported greater experiences of ostracism and incivility compared to junior men STEM faculty, leading to more negative occupational well-being outcomes (heightened turnover intentions and lowered affective organizational commitment) for

women. It was found that early-career women in STEM experienced more ostracism and incivility from their male colleagues than from their female colleagues. Experiences of ostracism (and to a lesser extent, incivility) from male colleagues related to more negative occupational (lowered academic self-efficacy and positive future career perceptions) and psychological (greater psychological distress) well-being outcomes (Miner et al., 2019).

It was revealed that junior women faculty in STEM experience an interpersonally chillier climate compared to junior men faculty in STEM and that working in such a climate has consequences for junior women's well-being especially when they have chilly interpersonal experiences with male colleagues. These findings suggest that exposure to a chilly climate and its effects may be an important explanation for the lack and withdrawal of women in STEM academic fields (Miner et al., 2019).

Banerjee & Pawley, 2013 proposed an alternative metaphor of a "foggy climate" to represent the experiences of 4 faculty members in a STEM college: within their academic careers, these four faculty members encountered a foggy climate of inadequate information regarding P&T policies, and developed "fog lights" of formal and informal resources to light their way.

The study findings reveal that only women who participate in redefinition strategies (negotiating her own personal identity with that of the Science and Engineering (SE) departmental culture of which she was a part) related to their marginalized status are able to persist; those who cannot redefine their marginality in relation to the dominant discourse of SE begin to lose interest or doubt their competence in the field, resulting in their departure from SE (Hughes, 2012).

In terms of employment, a chilly climate may result in low confidence in pursuing STEM-related careers, diminished professional aspirations, low job satisfaction, difficulties in job retention and promotion for females (Wuhib & Dotger, 2014; Kim & Kim, 2023). Employer discrimination, perception that women may prioritize their families over their careers, lack of role models and gendered expectations may also influence negatively on women's career aspirations in the STEM field (Sassler et al., 2017).

Psychological and Emotional Well-Being

The chilly climate also has significant effects on women's psychological and emotional wellbeing. Women in environments characterized by a chilly climate often experience increased stress and feelings of isolation due to pervasive sexism and lack of representation (Biggs et al., 2018). These experiences can result in mental health challenges such as anxiety and burnout, further impacting their academic and professional performance.

In STEM fields, the chilly climate has been linked to lower levels of social support and capital for female students. This lack of support aggravates feelings of isolation and anxiety, making it more difficult for women to persist and succeed in these fields (Jorstad et al., 2017). The psychological side of these experiences undermines women's confidence and overall wellbeing, affecting their academic achievements and career satisfaction.

A chillier climate related to more emotional exhaustion and cynicism. Furthermore, a positive relation was found between women–scientist interference and cynicism when the chilly climate was low or moderate. When interference was high, chilly climate did not have a relation with cynicism. When women experienced many threats (i.e., high chilly climate, high interference), they reached a threshold

where additional emotional cost did not matter (Jensen & Deemer, 2019).

When considering the psychological and emotional impacts, a chilly climate could be responsible for stress, anxiety, frustration, lack of self-esteem, depression, alienation and self-doubt among females. These may eventually cause females to develop low interest in STEM fields (Kim & Kim, 2023).

Broader Educational Environment

The broader educational environment is also affected by the chilly climate. Research conducted in a chiropractic training institution has found that a chilly climate contributes to a less inclusive and supportive educational atmosphere (Palmgren et al., 2013). This effect highlights that the chilly climate impacts not only individual experiences but also the overall quality and inclusiveness of the educational setting. A less supportive environment diminishes the educational experiences of all students, creating a less collaborative and equitable learning atmosphere.

Discussion

The impact of the chilly climate in educational and professional environments has deeply influenced various dimensions of women's experiences and outcomes. This climate, marked by both subtle and overt biases, creates significant barriers to women's full participation and success. Foundational work by Hall and Sandler (1982, 1984) established that these biases foster environments that are less supportive and more challenging for women. Subsequent research has further elaborated on how these systemic biases affect academic and professional settings, illustrating the pervasive nature of the chilly climate.

Academically, the chilly climate contributes to diminished participation and performance among female students. Women in fields like engineering often face unique challenges, including reduced engagement and support, which negatively impact their academic success (Walton et al., 2015). Furthermore, the undervaluation of women's contributions in classrooms has been shown to reduce their confidence and hinder their academic performance. This dynamic creates a cycle of decreased visibility and engagement for female students (Lee & McCabe, 2021). A sense of being less competent than the male counterparts, was also found to be common among women in STEM fields which may negatively impact on their engagement in academic work (Kim & Kim, 2023).

Career progression is similarly impeded by the chilly climate. Gender biases in evaluation and promotion processes, low confidence in pursuing STEM-related careers, low job satisfaction, present significant barriers for women faculty leading to lower career advancement opportunities and higher attrition rates (Maranto & Griffin, 2011; Wuhib & Dotger, 2014; Kim & Kim, 2023). Employer discrimination, perception that women may prioritize their families over their careers, lack of role models and gendered expectations may also influence negatively on women's career aspirations (Sassler et al., 2017). These systemic issues contribute to reduced representation in higher academic ranks and affect women's immediate career satisfaction and long-term aspirations (Britton, 2017). The barriers encountered not only impact current career trajectories but also influence future career plans and success.

The psychological and emotional impact of the chilly climate is substantial. Women who experience pervasive sexism and exclusion often report increased stress, anxiety, frustration, lack of self-esteem, depression, feelings of isolation, self-doubt which can adversely affect their mental health, interest, overall career satisfaction (Biggs et al., 2018; Kim & Kim, 2023).

In STEM fields, the chilly climate is associated with lower levels of social support and capital, which exacerbates feelings of anxiety and discouragement among female students (Jorstad et al., 2017). This psychological toll can undermine women's confidence and hinder their academic and professional achievements.

The broader educational environment is also affected by the chilly climate. Evidence from studies in various academic settings indicates that the presence of a chilly climate results in a less inclusive and supportive atmosphere. This effect impacts the overall quality of education for all students, highlighting the need for systemic reforms to address these pervasive biases and improve the educational environment (Palmgren et al., 2013). By addressing these issues, institutions can work towards creating a more equitable and supportive educational setting.

Despite decades of intervention and research, the question remains: *"How can the chilly climate be mitigated"*. A feminist, women-centred faculty writing program at a US university that offered relief from the frigid temperatures by fostering a sanctioned space for women faculty to set aside their care work and to experience psychological safety, in turn, encouraged them to feel positive emotions regarding their writing and research. In addition to being impactful, the writing program is a feasible and easily adaptable intervention (Sharp & Messuri, 2023).

A US research-intensive university introduced an approach, to provide administrators with the tools and motivation to increase women's representation in STEM fields. Pre and post training questionnaires that were conducted, demonstrated that training can shift administrator attitudes. In addition, interviews with participants and surveys of faculty indicated the extent to which this approach altered departmental culture beyond policy and procedure. The results demonstrate the importance of empowered unit administrators, deans and chairs for the formation of a welcoming and inclusive departmental culture (Bystydzienski et al., 2016).

In a randomized controlled trial, 2 brief interventions designed and tested to mitigate the effects of a "chilly climate" for female engineering students. The social belonging intervention aimed to protect students' sense of belonging in engineering by providing a nonthreatening narrative with which to interpret instances of adversity. This helped women integrate into engineering, for instance, increasing friendships with male engineers. The affirmation training intervention aimed to help students manage stress that can arise from social marginalization by incorporating diverse aspects of their self-identity in their daily academic lives. This also helped women develop external resources, and deepening their identification with their gender group. These interventions raised women's school-reported engineering GPA over the full academic year, eliminating gender differences. They also led women to view daily adversities as more manageable and improved women's academic attitudes (Walton, et al., 2015).

Conclusions

Literature suggests that a chilly climate can undermine engagement and performance of both female students and faculty members, diminishing the educational experiences of students in STEM fields in higher education settings. Furthermore, a chilly climate lowers promotion rates and higher attrition among women in academia, affecting not only immediate career prospects but also long-term career satisfaction, leading to higher turnover rates among women faculty.

As women in academia are less motivated to pursue long term academic careers, there is a loss of talent and diversity within the field. Eventually a cycle where women remain underrepresented in

higher academic ranks is created, perpetuating gender imbalances in academia. Female academics who are unable to adopt redefinition strategies (negotiating her own personal identity with that of the departmental culture) related to their marginalized status are able to persist; those who are unable to begin to lose interest or doubt their competence in the field, resulting in their departure. They are forced to develop "fog lights" of formal and informal resources to light their way due to inequitable access to supportive resources. Female academics experience increased stress, feelings of isolation, and mental health challenges such as anxiety and burnout, and decreased confidence, impacting their academic and professional performance and satisfaction., making it difficult for women to persist and succeed in STEM fields.

Addressing the chilly climate requires a multifaceted approach. Institutional reforms are needed to combat gender biases and foster a supportive environment. Implementing targeted interventions, such as confidence building workshops and mentorship programs, has shown promise in relieving some of the negative impacts of the chilly climate. Additionally, fostering a cultural shift towards greater inclusivity and recognition of women's contributions is essential for creating a more equitable academic and professional landscape.

By making these changes, institutions can work towards reducing the impact of the chilly climate and enhancing the success and wellbeing of all individuals. Furthermore, implementation of social coping programs to provide emotional and psychological support for women, increasing interaction in learning, providing quality advising, encouraging families to support females and improving gender diversity in academic and work environments can have a positive impact on making the chilly climate warmer so that female representation in STEM field could be further uplifted.

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THE RELATIONSHIP BETWEEN SMARTPHONE USE AND SLEEP DISTURBANCES IN ADOLESCENTS: A REVIEW OF THE SELECTED LITERATURES

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Abstract

In recent years, the rapid development and wide spread of smartphone technology of has transformed the daily life of adolescents. The smartphone is a multi-purpose device and is especially important for the education of young people. While technological advancements offer many benefits, the increase in smartphone use has a significant impact on adolescent health, especially sleep. Adequate sleep is very important for the physical, emotional and cognitive development of adolescents. Adequate sleep in adolescence supports academic performance, mental health and well-being. The research problem of this study is to investigate whether there is a connection between smartphone use and sleep disturbances in adolescents. The main purpose of this research is to study the relationship between smartphone use and sleep disturbances in adolescents. Thematic analysis was used as the qualitative research methodology, with previous research papers serving as secondary data sources in data collection. The research revealed that adolescents use smartphones more than four hours a day. Mostly used in the evening and at night before going to bed. In particular, the time spent sleeping by adolescents is directed towards activities such as using social media, sending text messages, and playing video games. Also, spending a lot of time with smartphones tends to go to bed later and wake up earlier, resulting in less sleep time. Adolescents report poor sleep quality due to smartphone addiction. Research has also revealed that blue light from smartphone screens inhibits the production of melatonin, a hormone essential for regulating sleep-wake cycles. Disruption of melatonin production leads to difficulty initiating and maintaining sleep. Adolescence is a period of emotional development. There they continue to be tempted to use the mobile phone at night. Further research is needed to assess the effectiveness of different intervention strategies to reduce the negative impact of smartphone use on adolescent sleep quality.

Keywords: Adolescents, Mental Health, Sleep Disturbances, Smartphone, Technology

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Introduction

Technology encompasses a broad range of tools, systems and devices designed to solve problems and improve efficiency. These innovations enhance quality of life. From the invention of wheel to development of the internet, technological advancements have profoundly shaped human civilization. In the modern era technology manifests in various forms. This includes information and communication technologies (ICTs). Medical technologies, transportation systems and industrial machinery are also significant. These technologies have revolutionized how people communicate. They access information more easily and perform tasks efficiently. Furthermore, they interact with the world in transformative ways.

The rapid development of digital technology particularly since the late 20th century, has led to proliferation of personal electronic devices such as computers. Tablets and smartphones. These devices have become integral to daily life. They offer unprecedented connectivity. They provide access to vast amounts of information. Users can perform a wide range of functions remotely.

The internet, a cornerstone of modern technology, has facilitated global connectivity. It enables the sharing of information at unprecedented scale. This transformation affects industries. It also impacts economies and social structures. However, the integration of technology into daily life presents challenges. Issues related to privacy and security are significant concerns. There is also potential for negative health impacts. These include problems associated with excessive screen time and digital addiction (Owens et al, 2013)

Smartphones, a subset of personal electronic devices, are handheld devices that combine functionalities of a mobile phone with those of computer. Over time smartphones have rapidly evolved. These devices have become multifunctional tools essential in modern life. They enable users to make calls. Users can also send text messages. Additionally, users can access the internet use social media and take photographs. Smartphones also allow the utilization of myriad applications. These applications serve various purposes. These purposes include productivity, entertainment and education. The integration of advanced features such as high-resolution cameras and GPS navigation has enhanced usability. Biometric security and powerful processors have made smartphones indispensable for many users.

With the development of technology, the smart phone plays a special role in communication. They facilitate instant communication. Call texts and messaging apps constitute powerful tools in this regard. Social media platforms enable users to connect. They share experiences with global audiences. Smartphones also serve as primary sources of information. They allow users to access news, weather updates and educational resources on the go. Additionally, they offer numerous entertainment options. These include music videos, games and eBooks.

Despite their numerous benefits, smartphones also pose certain risks. Particularly when it comes to health and well-being. Excessive use of smartphones especially before bedtime. Linked to various negative outcomes. Sleep disruption. Eye strain and increased stress levels are also concerns. The convenience and constant connectivity offered by smartphones can lead to addictive behaviors where individuals feel compelled to check their devices frequently even at expense of their sleep and overall health. Understanding the impact of smartphone use on health and developing strategies to mitigate these risks is essential for maintaining a balanced and healthy relationship with technology (Fuller et al, 2017).

The widespread integration of smartphones into everyday life has significantly transformed the way adolescents communicate, access information and be entertained. While these devices provide many benefits, including educational resources and social connections, recent experts have suggested that excessive smartphone use has a negative impact on adolescent health, particularly sleep. According to Straker (2022), a smartphone is defined as a "portable device with a touch screen interface that can be used with stylus or finger touch". Adequate sleep is critical during adolescence, a period characterized by rapid physical, emotional, and cognitive growth.

Sleep disturbances, including delayed sleep onset, reduced sleep duration, and poor sleep quality, have been consistently linked to excessive smartphone use, particularly when devices are used before bedtime (Twenge et al., 2017). Prior research has shown that engaging and stimulating content accessed through smartphones can increase cognitive and emotional arousal, making it difficult for teenagers to relax and sleep. While these findings have established a correlation between smartphone use and sleep disturbances, they primarily focus on general smartphone use or screen time.

However, there remains a significant gap in the literature regarding the specific smartphone usage patterns (e.g., the type of content accessed, the duration and timing of use, and the role of individual differences such as gender or sleep habits) that may contribute to sleep disturbances. Furthermore, much of the existing research does not explore how cultural and social factors influence adolescents' smartphone use and its impact on sleep quality. Additionally, strategies to mitigate the negative effects of smartphone use on sleep have been underexplored in empirical studies, leaving a practical gap in understanding how to address these sleep disturbances in adolescents effectively.

Therefore, this study aims to investigate the relationship between specific patterns of smartphone use and sleep disturbances in adolescents, with the goal of identifying both psychological and behavioral factors contributing to these disruptions. By doing so, this research seeks to provide a more nuanced understanding of how smartphone usage affects adolescent sleep and propose targeted interventions to mitigate its adverse effects. Although existing research has established a link between smartphone use and sleep disturbances in adolescents, several critical gaps remain. Most studies focus on general correlations without delving into the specific patterns of smartphone use that most significantly impact sleep. Additionally, there is limited research on how these disturbances affect various aspects of adolescent health, such as cognitive performance, emotional regulation, and academic achievement. Understanding these nuances is crucial for developing effective interventions. This study aims to fill these gaps by providing a comprehensive analysis of how different smartphone usage patterns-such as timing, frequency, and content-affect sleep quality, onset, and duration. By addressing these gaps, the research seeks to offer insights that can inform targeted strategies to mitigate negative sleep outcomes and promote healthier smartphone habits among adolescents.
Smartphone addiction can be understood through various psychological theories. The behaviorist theory posits that behaviors are learned by the environment. Smartphone addiction is a learned behavior resulting from the stimulus-response-consequence principle. According to psychodynamic theory, smartphone addiction can be seen as a way to avoid frustration or seek pleasure and forgetfulness (Aljomaa et al., 2016).

The theory of optimal flow (Csikszentmihalyi, 1990) suggests that people repeatedly engage in activities that provide satisfaction or joy. Thus, smartphone addiction can be viewed as an activity that offers satisfaction and joy, leading to addiction (Csikszentmihalyi, 1990). Social identity theory emphasizes the influence of group norms on addiction. This theory proposes that "when and to the extent that people define themselves in terms of shared social identity, they will be more likely to

influence each other" (Haslam et al., 2018). In this context, smartphone addiction can be seen as a phenomenon shaped by group norms.

Research Problem

The growing popularity of smartphone use among teenagers is worrying for their sleeping patterns. Although there is increasing evidence linking excessive smartphone use with sleep problems, the specific nature of this relationship and the underlying factors are not yet clear. Therefore, this research seeks to bridge the gap in understanding how different dimensions of smartphone usage (such as screen time, content type and usage patterns) lead to adolescent sleep disturbances.

Main Objective

The major aim of this review will be to analyze and synthesize related existing literature focusing on smartphone usage with respect to adolescent sleep disorders in relation to key patterns contributing factors along potential mechanisms involved. In addition, it intends to identify gaps from present day studies while advising on more studies about combating sleeping problems associated with mobile phones among teenagers.

Research Methodology

This study adopts a mixed-methods systematic literature review to investigate the impact of smartphone use on sleep disturbances in adolescents, synthesizing both qualitative and quantitative research. A comprehensive search was conducted using databases like PubMed, PsycINFO, and Google Scholar with terms such as “smartphone use,” “sleep disturbances,” and “adolescents.” Inclusion criteria focused on studies involving adolescents aged 12-18, addressing the relationship between smartphone use and sleep issues. Both qualitative and quantitative studies were included to provide a broader understanding of the topic. The data was analyzed using thematic analysis, which allowed for identifying key themes like sleep onset delay and reduced sleep duration. This mixed-methods approach ensures a more nuanced and holistic view of how different smartphone usage patterns influence sleep problems, making it an appropriate methodology for addressing the complex relationship between technology use and adolescent sleep.

Findings/ Discussion

The impact of smartphone use on adolescent sleep is multifaceted, involving both physiological and behavioral factors. The emission of blue light from smartphones disrupts melatonin production, leading to delayed sleep and poorer sleep quality. Additionally, the engaging nature of smartphone activities, such as social media use and gaming, can result in bedtime procrastination and increased cognitive arousal, further contributing to sleep disturbances. This study reviewed 25 research papers on the topic, analyzed through thematic analysis, to provide a comprehensive understanding of the complex relationship between smartphone use and sleep. The findings underscore the need for targeted interventions to effectively address these issues.

The Effect of Blue Light on Sleep

A primary mechanism by which smartphone use disrupts sleep is through the emission of blue light. Research has found that blue light, which has a wavelength of 450-495 nanometers, suppresses melatonin production more than any other wavelength of light. Melatonin is a hormone produced by the pineal gland in the brain it helps regulate sleep-wake cycles. Normally, melatonin levels rise in the evening, promoting feelings of sleepiness and signaling the body that it's time to sleep. However, exposure to blue light from smartphones and other electronic devices can inhibit melatonin production, which delays sleep and reduces sleep quality.

A number of studies have investigated the effects of blue light on sleep. A study by Chang (2015) et al. found that participants who used light-emitting e-Readers before bed took longer to fall asleep, experienced less evening sleepiness, and had lower melatonin levels compared to those who read printed books. Similarly, a study by Figueiro (2017) et al, showed that exposure to blue light from tablets and smartphones significantly suppresses melatonin levels and delays sleep time.

Aspects of Smartphone Use and Sleep Behavior

In addition to the physiological effects of blue light, behavioral aspects of smartphone use also influence sleep disruption. Excessive use of smartphone leads to sleep disorders. The phenomenon of "sleep delay" is also a significant factor in sleep disruption. This happens when people delay going to sleep because they engage in activities on their smartphones. Research by Kroese et al (2014), found that individuals who engaged in sleep delay reported poorer sleep quality and shorter sleep duration. Moreover, the interactive nature of smartphones, which often involves responding to notifications and engaging in conversations, can increase cognitive arousal and make it difficult for individuals to relax and fall asleep.

Sleep Quality and Duration

There is a significant relationship between the effect of smartphone use on sleep quality and duration. Many studies have shown that excessive smartphone use is associated with poorer sleep outcomes. A meta-analysis by Exelmans and Van den Bulck (2016), found that higher levels of smartphone use were consistently associated with shorter sleep duration, longer sleep onset latency, and poorer sleep quality. Similarly, a study by Arora et al (2014) reported that adolescents who use their smartphones for more than two hours a day are more likely to experience sleep disturbances and difficulty waking up in the morning.

The quality of sleep is also affected by the content consumed on smartphones. Watching videos, playing games, and engaging in emotional conversations increase arousal and make it difficult to fall asleep. Furthermore, constant exposure to social media can lead to feelings of anxiety and stress, which can further exacerbate sleep problems. A study by Levenson et al. (2017), found that greater social media use was associated with increased risk of developing sleep disturbance and insomnia symptoms.

Mental Health and Sleep

The relationship between smartphone use, sleep and mental health is complex and bidirectional. Poor sleep quality and duration can have a significant impact on mental health, increasing the risk of depression, anxiety and other mood disorders. In contrast, people with mental health problems are more likely to use their smartphone excessively, especially at night, as a coping mechanism. A study by Twenge et al. (2017), found that adolescents who spend more time on electronic devices, including smartphones, are more likely to report symptoms of depression and suicidality. The study also revealed that these teenagers are more likely to not get enough sleep. Similarly, a study by Lin et al. (2016), reported that problematic smartphone use was associated with poorer sleep quality and higher levels of anxiety and depression among college students.

Experimental Studies on Smartphone Use and Sleep

The pervasive use of smartphones in modern society has led to growing concerns about their impact on various aspects of health, particularly sleep. Numerous experimental studies have sought to understand how smartphone use affects sleep patterns, quality, and overall health. This paper will review key

experimental studies that explore the relationship between smartphone use and sleep disruption, focusing on the mechanisms involved and potential interventions.

One of the critical studies in this area was conducted by Chang et al. (2015), which investigated the effects of light-emitting e-Readers on sleep. The study involved 12 healthy young adults who were exposed to either an e-Reader or a printed book before bedtime over two weeks. The e-Reader emitted blue light, while the printed book did not. Participants read on either the e-Reader or a printed book for four hours before bedtime in a controlled laboratory setting. The results showed that those who used the e-Reader took significantly longer to fall asleep, had reduced evening sleepiness, and lower melatonin levels compared to those who read the printed book. The study concluded that blue light from electronic devices can delay sleep onset and disrupt sleep quality by suppressing melatonin production.

Another notable study by Levenson et al. (2017) examined the relationship between social media use and sleep disturbance among young adults. The study involved 1,788 young adults aged 19-32 who completed an online survey assessing social media use and sleep disturbances. Participants reported their frequency of social media use and sleep patterns. The study has found a significant association between high social media use and increased sleep disturbances. Participants who checked social media frequently throughout the day and particularly before bedtime were more likely to report difficulties falling asleep and maintaining sleep.

Research by Kroese et al. (2014) explored the concept of bedtime procrastination and its impact on sleep duration. The study involved 177 participants who completed an online survey measuring bedtime procrastination, self-regulation, and sleep habits. Participants reported their typical bedtime, wake-up time, and the extent to which they engaged in activities on their smartphones before bed. The results indicated that individuals who frequently engaged in bedtime procrastination by using their smartphones reported shorter sleep duration and poorer sleep quality. The study highlighted that the engaging nature of smartphone activities can delay bedtime and reduce overall sleep duration.

Figueiro et al. (2011) examined the possibility of reducing the negative sleep-related effects from blue light exposure by using blue light filters in their study. The investigators, at the end of two hours before bedtime, had 20 college students exposed to a tablet screen with and without blue light filters. Measurements for melatonin and sleep parameters were taken using polysomnography. The melatonin suppression relative to that of unfiltered blue light was significantly reduced using a blue light filter, and its sleep onset latency and sleep quality improved. Therefore, it is suggested that blue light filters can be one of the effective interventions to minimize adverse influences of smartphone use on sleep.

A study by Kalmbach et al. (2020) examined the effectiveness of Cognitive Behavioral Therapy for Insomnia (CBT-I) in improving sleep among individuals with high smartphone use. The study involved 60 participants who reported insomnia symptoms and high smartphone use before bedtime. Participants were randomly assigned to receive either CBT-I or a control intervention. The CBT-I group received six weekly sessions focused on sleep hygiene, stimulus control, and cognitive restructuring. The results showed that participants who received CBT-I reported significant improvements in sleep quality, sleep duration, and reduced smartphone use before bed compared to the control group. This study demonstrated that CBT-I could effectively address sleep problems associated with excessive smartphone use.

Jean et al. (2017) reported that the use of electronic devices, exposure to social media, and reading news online increased the odds of short sleep duration, with clear exposure-response relationships observed

for electronic devices after 2 or more hours of use each day. Other activities related to short sleep duration, such as homework time, working for pay, and TV watching, were relatively stable or decreased over this time period, making it unlikely.

The study, according to Scott (2019), offers a new normative profile of UK adolescent social media use and sleep. Results strongly support there being statistically and practically significant associations between use and sleep patterns, with a particular potential for a later pattern of sleep onset. Sleep education and interventions are recommended to center around supporting young people in the balancing of online interactions with an appropriate and adequate sleep on school nights.

The study, according to Hale (2015), This work was conducted systematically, searching and updating the scientific literature on the association between screen time (e.g., television, computers, video games, mobile devices) and sleep outcomes in school-aged children and adolescents. We reviewed 67 papers published from 1999 until early 2014. They found that in 90% of these, screen time is adversely associated with sleep outcomes, primarily duration and timing. However, some of the results are partially driven by screen type, participant age and gender, and day of the week.

Conclusion

Based on the findings discussed, it is evident that both physiological and behavioral factors contribute to sleep disturbances related to smartphone use in adolescents. The emission of blue light from smartphones significantly impacts melatonin production, leading to delayed sleep onset and reduced sleep quality. Behavioral aspects, such as bedtime procrastination and increased cognitive arousal from engaging with smartphones before bed, further exacerbate sleep issues. The studies reviewed highlight a consistent relationship between excessive smartphone use and negative sleep outcomes, including shorter sleep duration and poorer sleep quality. Additionally, the content consumed on smartphones, such as social media and gaming, can increase emotional arousal and stress, which negatively impacts sleep. This comprehensive understanding of the relationship between smartphone use and sleep disturbances underscores the need for effective intervention strategies, such as the use of blue light filters and cognitive-behavioral therapy, to mitigate the adverse effects on adolescent sleep health.

The proliferation of smartphones has revolutionized modern society and provides unparalleled convenience and connectivity. However, adolescents are facing sleep quality problems due to these technological advancements as they resort to the use of cell phones.

Experimental studies show that excessive smartphone use and sleep latency are associated with decreased sleep duration and poorer sleep quality. Research has revealed that teenagers experience these symptoms due to excessive smartphone use. The link between smartphone use and sleep extends to mental health. Poor sleep increases the risk of depression, anxiety and other mood disorders.

Adolescents should be educated to reduce the harmful effects of overuse of mobile phones. Therapeutic approaches such as cognitive behavioral therapy have the potential to improve sleep quality and reduce late-night smartphone use. Despite significant progress in understanding the impact of smartphone use on sleep, there are areas of research that need further investigation. Future research should explore the long-term effects of smartphone use on sleep across different populations and identify more effective strategies for reducing sleep disruption. Conditions arising due to the rapid evolution of technology should be explored.

Finally, there are two main areas of positive and negative effects through the smartphone, and as negative effects, it is essential to identify and address the negative effects on sleep. By adopting appropriate interventions and promoting awareness of healthy smartphone usage practices, adolescents can enjoy the benefits of technology without compromising their sleep, physical health, and mental health. It enables to build overall well-being.

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THE PERSISTENCE ADAPTATION OF AND IDEAS OF HUMOURAL THEORY: FROM GREEK MEDICINE TO THE EARLY MODERN PERIOD AND BEYOND

RMDS Randiwela[1] and W Subasinghe[2]

Abstract

This research analyses the persistence and adaptation of Humoural ideas, from Hippocratic medicine to the early modern period of 1500-1800, culminating in the comparison of it with modern medicine. From each time period, drawing on primary sources and using thematic analysis set within a historical framework, the research investigates how physicians engaged with new discoveries and adapted Humoural concepts into their practice. The English translations of key texts of Greek medicine, like the *Corpus Hippocraticum and De Materia Medica*, are interpreted for the constitution of Humoural theory. English translations of early modern sources, such as *De Fabrica Corporis Humani* and *Exercitatio Anatomica de Motu Cordis et Sanguinis in animilibus*, are analyzed in respect to their suggestions regarding the manner by which anatomical and physiological discoveries challenged and possibly reshaped the concepts of the humours. Secondary literature with valuable insights on the practical use, adaptations, and eventual decline of the theory will also be considered. According to the findings of the research, despite the appearance of new medical knowledge, Humoural ideas persisted, and the physicians of early modernity adapted the theory for new discoveries by the reinterpretation of functions and coexisting with emerging diagnostic methods. The flaws in Humoural theory, however, became more obvious as the concept of disease etiology changed. Although the residue of its influence may persist in contemporary medical terminology, Humoural theory ultimately yielded to more scientifically based theories of health and disease. Thus, the persistence of Humoural theory emphasizes that even with new knowledge, firmly held traditional medical theories are difficult to dismiss. The integration of the two provided a nuanced perspective of disease and cure ultimately. It also proves the vitality of the role of physicians, inventions of medical field and leading medical movements in reshaping the existing medical practices.

Keywords : adaptation, Humoural ideas, medicine, persistence, thought

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Introduction

The Humoural theory can be recognized as a fundamental but major concept in science of healing from Greece signifying the West. In Greek medicine health is interpreted as the maintenance of balance among the four bodily liquids identified as 'Chymoi' or Humours of blood, phlegm, yellow bile and black bile. All these four liquids were present in the body, but their levels changed with disease either to be excessive or deficient. The main role of a physician according to Greek medicine was to detect the 'Chymos' or Humour which was imbalanced and try to restore balance through diet, physical exercises, sleep and medicine. Its earliest roots in the west can be detected in Greek medicine in the medical cult practices of Asclepius in Asclepeions (700 BCE) and later in Hippocrates who was an Asclepiad (460 – 377BCE).

The Humoural theory was then adapted by Galen (129 CE- 216 CE) a Greek physician and philosopher who moved to Rome in 162 CE and rose to dominance in Roman medicine. From Galen the theory of Humours was transmitted to Avicenna, the Persian Physician in his 'Canon of Medicine' (1025 CE) which is identified as a translation of Galen's Commentary on Hippocrates' 'On the nature of man' in Arabic. From Avicenna, the theory of Humours reached India under Islamic- Arabic invasions as Unani system of Medicine which is also identified as Hikmat/ Unani - Tibb while another branch remained among the Arabic- Muslims and reached the West again and became the base of Modern medicine where Hippocrates is identified as its founder for his rational and scientific approach to medicine.

The Humoural theory made an enormous impact on the course of medical practices throughout the pre-modern period[1]. This era was characterized by limited scientific understanding of disease and its causes, and by reliance on traditional healing methods often based on superstition and folklore. Physicians during this time, relied on pulse diagnosis, which consisted of the examination of qualities of the pulse to establish the balance of humors. Treatment was adjusted to the restoration of balance, often by techniques such as bloodletting, purging, or dietary changes. Humoural theory not only guided medical practice but also saturated social views of health and personality by using temperaments to explain individual differences.

Although dominated for centuries, the Humoural theory began to encounter numerous challenges during the late Renaissance[2] and Early Modern period[3], 1500-1800. For instance, while Humoural theory enjoyed centuries of dominance, its explanatory power began to wane in the face of historical events. Recurring epidemics, such as the Black Death[4] and cholera outbreaks, exposed the limitations of Humoural explanations for disease causation and transmission. These events, coupled with the increasing frequency of diseases unfamiliar to the Humoural framework, eroded public and medical trust in the theory. The inability of Humoural theory to effectively explain, prevent, or treat a growing number of diseases contributed to its decline.

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[1] *The period before the advent of modern medicine, which is generally considered to have begun in the 19th century*

[2] *The Late Renaissance is a period of the Renaissance characterized by a shift in artistic and intellectual focus from the Classical world to contemporary issues and themes. It occurred roughly from the late 15th century to the early 17th century.*

[3] *The Early Modern period is a historical era that spans from the late 15th century to the late 18th century. It is characterized by significant shifts in European society, culture, and politics, including the Renaissance, the Reformation, the Age of Exploration, and the Enlightenment*.

[4] *The Black Death was a devastating pandemic that swept across Europe and Asia in the mid-14th century. It is estimated to have killed between 30% and 60% of Europe's population.*

It was during this time that new anatomical and physiological discoveries were crucial to the reshaping of the contemporary understanding of the human body. The rise of anatomical dissection in the 16th century played a significant role in the advancement of medical knowledge. For instance, the Flemish anatomist Andreas Vesalius published his major work De Fabrica Humani Corporis (On the Fabric of the Human Body) in 1543. His detailed illustrations, along with highly accurate dissections, revealed mistakes in Galen's anatomical descriptions that were based on animal, not human, dissections. These discrepancies challenged the very foundations of Humoural theory, which is so firmly based on Galenic anatomy.

Another influential figure was the British physician William Harvey, from 1578 to 1657. Harvey himself made an innovation in the circulatory system of blood in 1628, which challenged a central planks of the Humoural theory. The latter specified that blood was constantly being produced and consumed in the liver, not pumped around the body as Harvey showed. Harvey's discovery represented a significant blow to the Humoural account of the role of blood in health and disease.

The invention of the microscope in the 17th century opened up a new window into the invisible world of cells. Pioneer microscopists like Antonie van Leeuwenhoek (1632-1723), upon seeing microorganisms for the first time, felt the inchoate stirrings of evidence against the then-current Humoural explanation of illness through bodily fluid imbalances. Even though the full formulation of a germ theory[5] of disease did not appear until the 19th century, these observations on microorganisms formed an important underpinning for a new theory of infectious diseases.

The humoral theory declined gradually and not all of a sudden. Sure enough, early modern physicians continued the practice of most of the concepts of Humoural theory while readily admitting new discoveries. Gradually, then, physicians adapted and reinterpreted Humoural ideas in light of emerging knowledge. It is evident from the consideration of these seminal figures and discoveries that the rise of anatomical dissection, the discovery of the circulatory system, and the fledgling science of microscopic observation all contributed to the decline of the Humoural theory.

Research Problem

Although the Humoural theory had increasingly encountered challenges from the emerging anatomical and physiological knowledge in the early modern period (1500-1800), there is considerable evidence that suggests the Humoural concepts continued to have survived and persisted in medical practice. This paper investigates the nature and extent of such persistence.

How did physicians adapt, reinterpret or even disguise Humoural ideas in the face of new discoveries? What sorts of features of the Humoural theory persisted and continued to strengthen medical theory and practice and treatment techniques?

Research questions

- How did early modern physicians alter the principles of Humoural theory to include new knowledge about anatomy and physiology?
- In what ways did the notion of temperaments survive into the early modern period in the influence it had on medical diagnosis?

[5] *Germ theory is the scientific theory that microorganisms, such as bacteria and viruses, are the cause of infectious diseases. This theory marked a significant breakthrough in medicine and public health, revolutionizing our understanding of disease prevention and treatment.*

- How different in actuality from pre-modern methods were early modern medical practices in their use of Humoural concepts?
- How did the persistence of Humoural ideas interact with ideas that were merging in medical theory in the early modern period?

Methodology:
The Qualitative research methodology was employed in this research. The historic and thematic analysis were also utilized because the study had to read, analyze, and interpret historical material in English translations as its main device for gathering and analyzing information. The below mentioned Primary Sources were used in this research.

Primary Sources:

- **Greek Medicine:**
    - *Corpus Hippocraticum* (Collection of Hippocratic Writings): This foundational collection, compiled between the 5th and 3rd centuries BCE, is central to understanding the origins and core tenets of Humoural theory. Thematic analysis will focus on key texts like *On the Nature of Man* and *On Regimen in Acute Diseases*, examining how these works establish the four humors, temperaments, and their connection to health and disease.
    - *De Materia Medica* (On Medical Material) by Pedanius Dioscorides (1st century CE): This influential pharmacopoeia details medicinal plants and their properties. Thematic analysis will explore how Dioscorides connects the therapeutic effects of these plants to balancing Humoural imbalances.

- **Early Modern Medicine:**
    - **De Fabrica Corporis Humani* (On the Fabric of the Human Body, 1543) by Andreas Vesalius: This groundbreaking anatomical treatise challenged Galenic understandings of the human body. Thematic analysis will focus on how Vesalius' work, while potentially unsettling the Humoural framework, might have also prompted reinterpretations of Humoural functions to accommodate new anatomical discoveries.

- **Early Modern Medical Practice:**
    - **Exercitatio Anatomica de Motu Cordis et Sanguinis* (An Anatomical Exercise on the Motion of the Heart and Blood, 1628) by William Harvey: This revolutionary work established the circulatory system, posing a significant challenge to the Humoural explanation of blood flow. Thematic analysis will explore how Harvey's work influenced physicians' understanding and potential adaptations of Humoural concepts related to blood.

    - **Physician's Manuals and Practice Texts:** Manuals like Georgius Agricola's *De Re Metallica* (On the Nature of Metals, 1556) and Nicolas Culpeper's *The English Physitian* (1653) will be analyzed thematically. The focus will be on how these manuals incorporate Humoural concepts into treatment recommendations and diagnosis, revealing practical applications of the theory in early modern medicine.

    - **Medical Case Studies:** Case studies by physicians like Giovanni Lancisi (De Motu Cordis et Aneurismatibus, On the Motion of the Heart and Aneurysms, 1708) offer

valuable insights into the real-world application of Humoural diagnosis and treatment. Thematic analysis will explore how these case studies utilize (or struggle with) Humoural concepts alongside other emerging diagnostic methods, potentially revealing limitations of the theory for specific conditions.

- **Modern Medicine:**
    - **Medical textbooks:** Modern medical textbooks on pathology or physiology will be analyzed thematically to identify any lingering influences of Humoural concepts in contemporary medical terminology or frameworks. For instance, the concept of "Humoural immunity" will be explored to see if it represents a direct continuation of the historical theory or simply shares a similar term.

Other than that, secondary sources on academic databases—JSTOR, PubMed, Google Scholar—with such keywords as "Humoral theory," "history of medicine," "early modern medicine," and "Greek medicine" along with books, articles, and dissertations from medical historians were used whenever necessary as they include a wider historical background and also put forward a theoretical framework for the analysis.

Each of the sources was considered in detail with regard to their authorship, audience, era, and possible biases. For instance, the Greek medical texts may take on a more theoretical and philosophical approach to the concept of humors compared to the early modern case studies that are firmly based on experience with patients. It thereby organizes different sources of knowledge critically reviewed and triangulated in providing depth to the persistence, adaptation, and eventual decline of the Humoural ideas throughout history.

Results and Discussion:

Adaptation of Humoural Concepts

While Humoural theory encountered numerous challenges in the early modern period, some physicians did not abandon these concepts completely. For instance, the circulation of the humours that was discovered in 1628 by William Harvey seriously threatened the humoral explanation of blood. On the one hand is the former understanding that blood was thought to be constantly produced and consumed in the liver. On the other hand, Harvey's work on the circulation of the blood throughout the body. Nonetheless, some physicians attempted to reconcile these ideas by asserting that blood, comprising the circulatory system, changed in such a way within the body, as the Humoural theory would dictate in its idea of the "cooking[6]" of the humors. This redefined framework permitted the maintenance of the connection between blood and the Humoural system.

Focus on the Qualities over location:

The invention of anatomical dissection proved a difficult challenge to Galen's specific localization of humors in the body. Physicians such as Georg Ernst Stahl (1660-1734) shifted attention from the site of humors to their qualities. Stahl suggested that the four humors represented different "forces" in the body- not material fluids. In this way, the theory of Humoural balance could be retained without specific anatomical site for the humours themselves .

[6] *How the Humours were produced through the digestion of food.*

Temperament and Diagnosis:
The theory of temperaments[7], related to the four humors, remained in effect during the early modern period on diagnosis. Physicians would observe their patients' features and behaviors to determine which temperaments they were dominated by all in an effort to provide clues regarding possible health issues that they might have. For example, a melancholic temperament related to black bile is associated with a tendency to depression or digestive disorders. Although new diagnostic techniques appeared, the concept of temperaments remained a familiar construct for understanding the individual's health.

Limitations in Adaptation
Inevitably, one has to acknowledge the limitations of such adaptations. As knowledge of anatomy and physiology advanced, the Humoural explanations became increasingly strained. For instance, the discovery of microorganisms by Antonie van Leeuwenhoek in 1676 weakened the Humoural explanation of disease based on imbalances of bodily fluids. Consequently, obvious signs began to demonstrate that the limitations of this adapted framework of Humoralism were starting to show, thus opening space for a more complete shift toward germ theory in the 19th century.

Physicians of the early modern time modified concepts of Humour in a variety of ways to suit new discoveries. Among other examples, they reappraised what the humors did, shifted the focus from location to qualities, and retained the use of temperaments in diagnosis. Adaptations such as these are evidence of persistence across the face of challenge from new scientific knowledge. These adaptations also underline the weakness of the theory and prefigure its eventual decline in favor of more comprehensive explanations of health and disease.

Temperament and diagnosis in early modern medicine
Although the Humoural theory was numerously challenged, its developed concept of temperaments remained influential and significant in medical diagnosis during the early modern period, 1500-1800.

Temperaments as a Diagnostic Framework:
Early modern physicians relied on the notion of temperaments—sanguine, choleric, melancholic, and phlegmatic—through which they classified patients based on their physical features and behaviors. The temperaments were related to the four humors and helped physicians understand each person's predisposition toward illness. For example, the physician would classify the patient with the choleric temperament, related to yellow bile, as having a predisposition toward anger and fever. This can then influence treatment decisions, such as recommending a cooling diet or purging to rebalance the Humours.

However, the limitations of the Humoural framework for diagnosis became increasingly apparent as the understanding of specific diseases progressed. For example, the discovery of microorganisms by Antonie van Leeuwenhoek (1676) challenged the ability of temperaments to explain infectious diseases.

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[7] The theory of temperaments is an ancient Greek concept that classified individuals based on their personality traits and disposition. It proposed that there were four primary temperaments, each associated with a specific balance of bodily fluids, i.e. Sanguine: Associated with blood, this temperament is characterized by optimism, cheerfulness, and a love of life, Choleric: Associated with yellow bile, this temperament is characterized by impulsiveness, ambition, and a fiery temper, Melancholic: Associated with black bile, this temperament is characterized by sadness, pessimism, and introspection, Phlegmatic: Associated with phlegm, this temperament is characterized by calmness, apathy, and a slow and deliberate nature.

As scientific knowledge advanced, the use of temperaments in diagnosis gradually declined in the later part of the early modern period. The notion of temperaments remained a significant influence in medical diagnosis during the early modern period. Physicians used this framework to categorize patients, explain symptoms, and guide treatment decisions. However, the rise of new diagnostic methods and a growing understanding of specific diseases eventually led to a decline in its dominance. This highlights the way medical knowledge builds upon, and sometimes challenges, existing frameworks as new discoveries were invented.

Symptoms explained through Humoural concepts.
Physicians also used Humoural concepts to account for particular symptoms. Headaches, for instance, could be blamed either on too much blood or on an excess of phlegm depending on the other symptoms experienced. Treatment in this model was thus dictated by the Humoural etiology, which in the case of suspected blood excess would involve bloodletting.

Coexistence with novel approaches.
With the discovery of new diagnostic modalities, like the pulse diagnosis, based on the qualities of the pulse, the application of temperaments was not abandoned altogether. Many physicians combined the above-mentioned methods in their practice. For example, a physician would feel the pulse of a patient and consider the patient's temperament afterward in order to reach a diagnosis, considering both of these methods. This combined approach gave a more complete depiction about the condition of the patient.

However, the inadequacies of the Humoural framework for diagnosis were gradually realized as understanding of specific diseases evolved. For example, Antonie van Leeuwenhoek's discovery of microorganisms in 1676 completely undermined the authority of temperaments in explaining infectious diseases[8]. As science progressed, the application of temperaments in diagnosis gradually fell out of favor in the latter part of the early modern period. One of the major influences on medical diagnosis during early modern times is the humoral theory of temperaments. That was how the medical personnels classified patients, explained symptoms, and guided treatment judgments. It remained dominant until its decline with the rise of modern diagnostic methods and a growing knowledge of some diseases. It characterizes how medical knowledge builds upon, and sometimes challenges, existing frameworks as new discoveries come to light.

Persistence of Humoural Ideas in Treatment Practices
Treatment:
The Humoural theory continued to influence specific treatment strategies in the early modern period (1500-1800), even as new approaches emerged.

- ***Bloodletting:*** The discovery of the circulatory system by William Harvey (1628) challenged the rationale behind bloodletting, a common practice based on the idea of removing excess blood to restore Humoural balance[9]. However, the practice persisted, though with some adaptations. Physicians might now target specific veins based on the suspected location of the

[8] *Infectious diseases are caused by the invasion of the body by harmful microorganisms, such as bacteria, viruses, fungi, and parasites. These microorganisms can spread from person to person or from animals to humans.*
[9] *The idea that Humoural imbalance was caused due to an excess or deficient Humour*

imbalanced humor, or they might use bloodletting as a more general "cleansing" technique[10]. The decline of bloodletting was gradual, and it wasn't entirely abandoned until the 19th century.

- **Purging and Cathartics:** Similarly, purging practices aimed at eliminating excess phlegm or other humors continued. Physicians might prescribe laxatives or enemas based on their Humoural diagnosis[11]. While new understandings of the digestive system emerged, the concept of purging retained some relevance in early modern medical practice.
- **The Rise of Chemical Medicines:** The early modern period also saw the rise of "chemical medicines" – complex herbal concoctions or mineral compounds. These medicines were sometimes linked to Humoural theory, with their ingredients chosen to address specific imbalances[12]. However, the development of these medicines also reflected a growing interest in the active properties of substances, paving the way for a more pharmacological approach to treatment.

Diet and Lifestyle:

The Humoural emphasis on diet and lifestyle modifications continued to play a role in early modern medical practices. Physicians often recommended specific foods or activities based on their perceived effects on the humors. For example, a patient with a choleric temperament (associated with yellow bile and hot temperament) might be advised to avoid spicy foods and engage in cooling activities like baths.

- **Focus on Digestion:** Humoural theory placed a strong emphasis on proper digestion, as it was believed to be essential for maintaining a balance of humors. Physicians might prescribe specific dietary regimens to promote good digestion and prevent the buildup of "impurities" that could contribute to disease[13].
- **Preventative Measures:** Humoural concepts also informed preventative measures. Physicians might recommend regular exercise, bloodletting (in some cases), or seasonal adjustments in diet to maintain overall Humoural balance and prevent illness.

Limitations and Evolution:

It's important to note that these practices were not solely based on Humoural theory. Other factors like cultural beliefs and empirical observations also played a role. As the understanding of nutrition and physiology progressed, dietary recommendations became more nuanced and less reliant on Humoural concepts. Humoural ideas continued to inform treatment practices and approaches to diet and lifestyle in the early modern period. While practices like bloodletting evolved and new approaches emerged, the emphasis on maintaining a healthy balance and addressing imbalances through various means resonated

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[10] Bloodletting was a common medical practice in ancient and medieval times, often used as a means of cleansing the body and restoring balance. It involved the removal of blood from the body, usually by making an incision or using leeches. While bloodletting was once widely believed to be beneficial for health, it is now considered a dangerous and ineffective practice.

[11]For example, if a patient was believed to have an excess of phlegm, which was associated with a cold and wet temperament, a laxative might be prescribed to help expel the excess phlegm.

[12]For example, if a patient was believed to have an excess of phlegm, a physician might prescribe a laxative made from herbs like rhubarb or senna. If a patient was believed to have an excess of bile, a cooling medicine made from herbs like mint or chamomile might be prescribed. These "chemical medicines" were often based on empirical knowledge and traditional remedies

[13]According to the Humoral theory, imbalances in these humors could lead to the buildup of impurities, which were thought to cause various health problems. Some examples of impurities that were believed to contribute to disease include: Excess mucus, excess bile, toxins, waste materials

with the Humoural framework. Over time, however, a more scientific understanding of disease and treatment would lead to a decline in the reliance on Humoural concepts.

Continuity and Comparison in Humoural Practices

Early modern medical practices occupying Humoural concepts showed both continuities and divergences from pre-modern approaches .

• Similarity: The main ideas of Humoural theory – the four humours, temperaments, and the centrality of balance – remained to be important in medical practice in both periods. Practices such as bloodletting, purging and dietary alterations based on Humoural imbalance continued to be used.

• Divergences. On the other hand, however, some major changes happened in the early modern era. The Theories of Humours were increasingly being questioned and adjusted by physicians in view of new discoveries, anatomical, or physiological. On this note, the discovery by William Harvey of the circulatory system in 1628 really brought criticism on the rationale of bloodletting and hence more qualification to its practice.

• Selective Use: Early modern physicians would retain some of the ancient practices that were associated with the Humoural theory, while being under no illusions that this was by any means the full extent of advanced medical insight in their day. For example, a physician could still bleed a patient due to the apparent benefit of "cooling the blood" to reduce inflammation but cancel the lowering of the Humoural at high levels argument.

Comparisons with Novel Conceptions:

The developing ideas of medicine and the staying power of previous Humoural theory during early modern times worked in many respects against each other :

- Reconciliation Attempts: Some tried to reconcile new discoveries with humoral concepts. A good example was Giovanni Lancisi, who from 1622-1700, redesigned the role of blood in circulation and made it fit within a humoral framework.
- Parallel Frameworks: In many instances, however, concepts of Humoural working alongside new ideas such as germ theory existed in somewhat parallel frameworks. Physicians might be using Humoural theory for diagnosis and treatment while acknowledging the role of microorganisms in specific diseases.
- Gradual Shift: That is, the demise of the theory of Humours was not sudden. The realization of disease etiology as being due to germs and pathologies specific for a particular disease became full-bodied, slowly, which exposed the limitations of the Humoural explanations. This, as a gradual shift, led to laying the way for a fuller break from the theory in the later centuries.

Much of early modern medical practice, informed by concepts of Humoural theory, would both continue premodern approaches whilst adapting to new discoveries. In that process, physicians would sometimes try to square Humoural ideas with emerging theories but just as often coexisted in parallel. The gradual accretion of new knowledge slowly undermined the dominance of the Humoural theory.

Conclusions and Recommendations:

The paper traced the persistence and accommodation of Humoural ideas within early modern medicine from 1500 to 1800. Physicians did not simply abandon the concepts from the theory of humors while challenged with new anatomical and physiological discoveries. It is in the adjustments, such as

reinterpretation of functions, shifting from location to qualities, and continuation of the use of temperaments in diagnosis, that the physicians were able to retain their application of the Humoural ideas, thereby fitting them to exist alongside rising practices and theories of medicine. Physicians could combine the use of Humoural diagnosis with new forms of diagnosis like pulse diagnosis but give credence to microorganisms in known diseases. The decline of Humoural theory was gradual. Adaptations endured for some time, yet the limitations of the theory became increasingly clear as the etiology of disease came into understanding. This research points out the importance of persistence and adaptation studies of established medical theories, notwithstanding the new knowledge. It further illustrates how doctors wrestled with new discoveries and the process of reconciling them within the existing framework. The understanding of this process adds essence to the historical transition of medical thought during the early modern period. Moreover, it denotes that very only a few medical transitions are clear breaks. It is quite common for many old and new ideas to coexist in a time period. As with reinterpretation, adapting occurs before a complete paradigm shift as it was evident in the medical field.

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SYSTEMATIC LITERATURE REVIEW ON AI CHATBOT SOLUTION FOR MEDICAL PRACTITIONER ADOPTION AND ENGAGEMENT WITH THE HEALTHCARE SYSTEM IN SRI LANKA

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Abstract

This study examines the impact of adopting digital health technologies, specifically AI-driven solution chatbots, on healthcare systems in Sri Lanka. Despite the global proliferation of digital health tools, Sri Lanka faces unique challenges and opportunities in integrating these technologies. This research addresses key barriers, facilitators, and the potential role of AI chatbots in transforming healthcare delivery in the region. A systematic literature review was conducted, analyzing 52 relevant studies from 2016 to 2023, sourced from Google Scholar, ResearchGate, arXiv, and Sci-Hub. The review focused on global trends in health technology adoption, barriers specific to Sri Lanka, and strategies for the successful implementation of AI-driven healthcare solutions. The findings indicate that inadequate infrastructure, socio-economic factors, and cultural resistance are significant barriers to the adoption of digital health technologies in Sri Lanka. However, lessons from global best practices and case studies from similar contexts highlight the potential strategies to overcome these challenges. AI chatbots, in particular, demonstrate significant potential in improving healthcare efficiency and patient engagement but require robust infrastructure and supportive policies for successful implementation.Effective strategies such as improving infrastructure, providing financial incentives, and comprehensive training programs are crucial for overcoming the identified barriers. The role of AI chatbots is underscored as a transformative tool in healthcare, capable of reducing workload for healthcare professionals and enhancing patient management. However, challenges related to data privacy, accuracy, and reliability necessitate continuous human oversight and adaptive regulatory frameworks.Integrating AI-driven solutions like chatbots into Sri Lanka's healthcare system could lead to more efficient healthcare delivery, reduced workload for medical practitioners, and ultimately, better patient care and management across the country. While these technologies offer promising improvements, addressing their limitations through better infrastructure, supportive policies, and ongoing human involvement is essential. Future research should focus on practical applications and the long-term impact of these technologies in healthcare settings.

Keywords: AI chatbots, digital health technologies, healthcare system, implementation strategies

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Introduction

In the rapidly changing field of healthcare, artificial intelligence (AI) is becoming a key player in improving patient care and operational efficiency. One promising application of AI is the use of chatbots to enhance patient engagement and streamline administrative tasks. This research focuses on the adoption of AI-driven chatbots by medical practitioners in Sri Lanka, a country facing unique challenges in healthcare delivery.

Globally, AI technologies have been adopted more rapidly in developed countries due to better infrastructure and supportive policies. For instance, the Health Information Technology for Economic and Clinical Health (HITECH) Act in the United States significantly boosted the adoption of Electronic Health Records (EHRs) (Smith et al., 2019). Similarly, the UK's NHS Global Digital Exemplar (GDE) program has facilitated digital transformation in healthcare (NHS Digital, 2020).

However, in Sri Lanka, adoption has been slower due to factors like poor infrastructure and lack of training. Studies highlight that inadequate infrastructure and resistance to change are major barriers to telemedicine adoption in Sri Lanka (Jayasinghe et al., 2016). AI-driven chatbots could help address these issues by providing scalable and efficient solutions for patient management and clinical support. However, the successful implementation of AI chatbots in healthcare requires addressing several critical factors. Trust, usability, and integration into existing workflows are key determinants of technology adoption among healthcare professionals (Ford et al., 2021). Concerns about data privacy and security, the accuracy of chatbot responses, and the need for comprehensive training programs also significantly influence the acceptance of AI chatbots (Wilson et al., 2021; Au Yeung et al., 2023).

This research aims to systematically analyze the adoption of AI-driven chatbots in Sri Lanka's healthcare system, identify the barriers and facilitators influencing their integration, and explore global best practices to provide actionable insights for enhancing healthcare delivery and patient management in the region.

The study addresses the following four research questions:

RQ1: What are the key barriers and facilitators affecting medical practitioners' adoption and engagement of healthcare technologies in Sri Lanka’s healthcare system?

RQ2: How can AI-driven chatbots improve healthcare delivery and patient management in Sri Lanka, and what are the potential challenges in integrating these technologies into existing healthcare workflows?

RQ3: How do the adoption patterns of AI-driven chatbots in Sri Lanka compare to global best practices in digital health technology, and what lessons can be drawn to enhance implementation strategies in developing countries?

The objectives of this review are to:

1. To Identify and analyze the key factors affecting the adoption and engagement of healthcare technologies among medical practitioners in Sri Lanka.
2. To analyze the existing systems and technologies preferred by medical practitioners in Sri Lanka.
3. To assess the potential impact of AI chatbots on improving healthcare efficiency and patient management in Sri Lanka.
4. To explore best global practices of successful AI chatbot implementations in healthcare systems and their applicability to the Sri Lankan context.

By examining the current barriers and facilitators to technology adoption, analyzing existing healthcare technologies, and evaluating AI chatbot solutions, this study seeks to provide actionable insights for enhancing healthcare delivery in Sri Lanka. The findings from this research will contribute to the broader understanding of how AI-driven solutions can be effectively integrated into healthcare systems in developing countries, ultimately leading to improved patient outcomes and more efficient healthcare services.

Methodology

This study employs a systematic literature review to investigate the adoption and engagement of AI chatbots in the healthcare system of Sri Lanka, focusing on their impact on healthcare delivery, practitioner engagement, and patient outcomes. The review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a comprehensive and robust research process. Relevant papers were sourced from multiple databases, including Google Scholar, PubMed, IEEE Xplore, and Scopus, using key search terms such as "AI chatbots in healthcare," "digital health technology adoption," "telemedicine adoption barriers," "healthcare practitioner engagement with AI," and "AI in healthcare systems." The initial search yielded 8,215 records.

To refine the dataset, specific inclusion and exclusion criteria were applied. Papers were included if they focused on the adoption of digital health technologies or AI chatbots in healthcare, employed qualitative, quantitative, or mixed research methodologies, were published between 2019 and 2024, were available in full text, and were published in English. Studies were excluded if they did not pertain to healthcare or AI-driven chatbots, were not peer-reviewed, or relied solely on theoretical models without empirical evidence. After applying these criteria, 51 papers were selected for the final evaluation. Data extraction focused on key search terms included "AI chatbots in healthcare" "digital health technology adoption" "telemedicine adoption barriers" "healthcare practitioner engagement with AI" and "AI in healthcare systems.". The extracted data was synthesized to identify common themes, trends, and gaps in the current literature.

This systematic review aims to provide a comprehensive understanding of the current state of AI chatbot adoption in healthcare, with a particular focus on developing countries like Sri Lanka. The findings will contribute to the broader understanding of AI technology adoption in healthcare and provide insights for policymakers and healthcare practitioners in Sri Lanka and similar contexts.

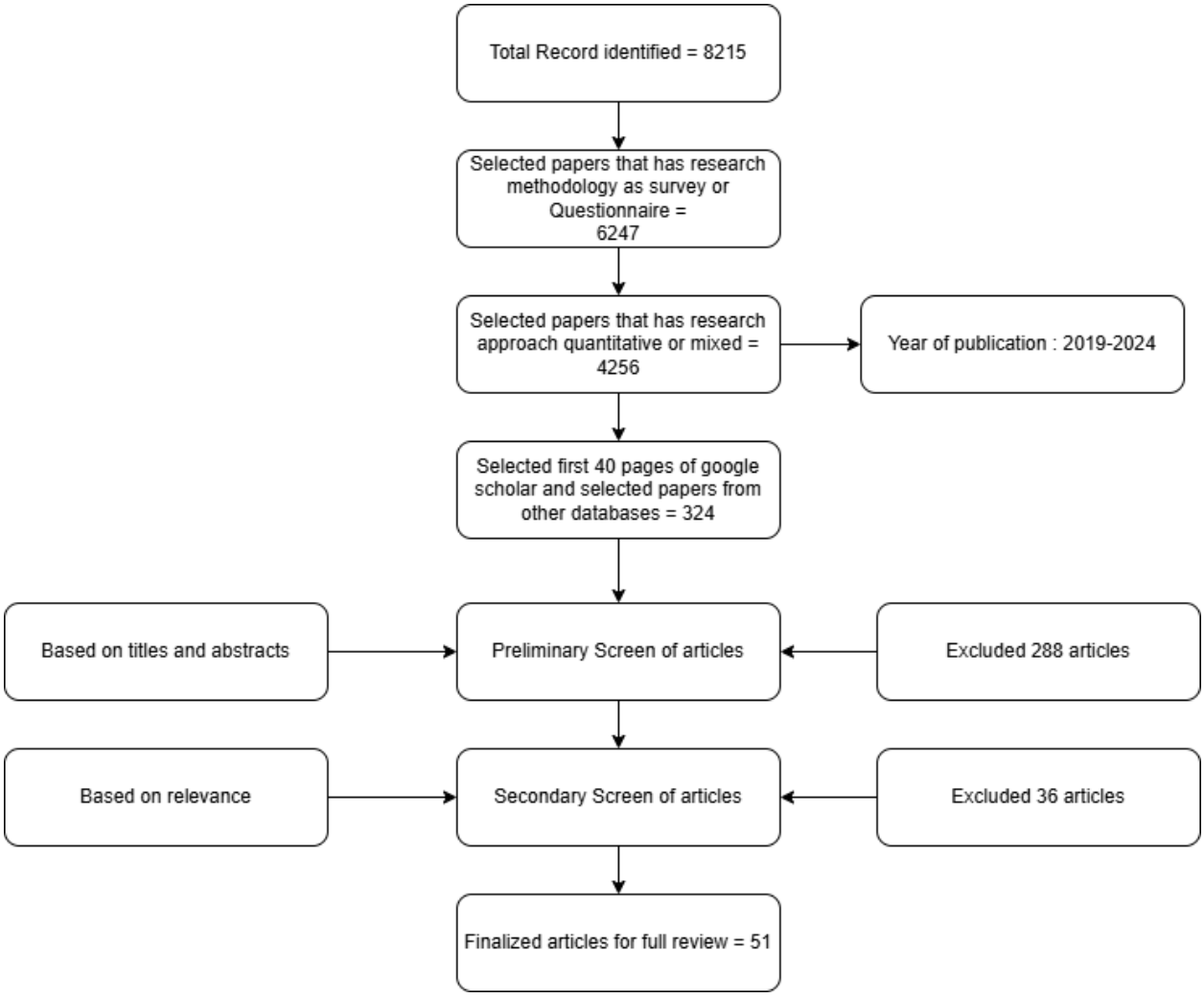

Figure 3 - PRISMA Flow Diagram

Results and Discussion

Global Trends in Health Technology Adoption and Engagement

Globally, the adoption of digital health technologies has varied significantly, with developed countries leading due to robust infrastructure, supportive policies, and substantial investments. The transformative potential of digital health technologies, especially in telemedicine and AI-driven diagnostic tools, has enhanced healthcare delivery by improving accessibility and efficiency (Mitchell & Kan, 2019). This transformation was particularly evident during the COVID-19 pandemic, which saw widespread use of telemedicine due to the necessity of physical distancing and remote healthcare services. For example, digital health technologies have improved healthcare workers' competencies and workplace environments by enhancing decision-making, efficiency, and productivity (Borges do Nascimento et al., 2023).

Current Trends and Technology Adoptions

In developed countries, the integration of Electronic Health Records (EHRs) has been pivotal. The Health Information Technology for Economic and Clinical Health (HITECH) Act in the United States incentivized EHR adoption, significantly improving clinical documentation and patient care (Smith et al., 2019). Similarly, the United Kingdom’s Global Digital Exemplar (GDE) program has facilitated digital transformation in the National Health Service (NHS), creating blueprints for other healthcare providers to follow (NHS Digital, 2020). Artificial intelligence (AI) has also been impactful, enhancing

diagnosis, risk prediction, and treatment in specialties such as radiology, pathology, and ophthalmology (Rajpurkar et al., 2022). AI tools in clinical laboratory medicine have improved medical education and clinical inquiries, despite challenges like ensuring accuracy and managing misinformation (Yang et al., 2023).

Successful adoption in developed countries is often driven by comprehensive governmental policies and financial incentives. For example, the HITECH Act mandated meaningful use standards to ensure effective EHR utilization, leading to improved clinical outcomes and reduced medical errors (Smith et al., 2019). The UK's GDE program has promoted digital health innovation by supporting NHS organizations that exemplify digital excellence, creating replicable models of best practice (NHS Digital, 2020).

AI integration in healthcare involves addressing explainability and ethical concerns. Explainability in AI applications is crucial for regulatory compliance and building trust among healthcare providers and patients (Amann et al., 2020). Strategic investments in AI technologies and supportive regulatory frameworks have driven innovation while ensuring AI applications in healthcare are safe, effective, and equitable (Secinaro et al., 2021).

The Impact of Government Policies and Incentives on Technology Adoption

Government policies and incentives are crucial in accelerating health technology adoption. During the COVID-19 pandemic, countries that implemented supportive policies for telehealth saw rapid growth in these services. For instance, there is a need for comprehensive regulations and guidelines to maximize telehealth benefits in Sri Lanka (Kulatunga et al., 2020). Supportive policies also address data privacy, security, and ethical considerations, which are essential for building trust in AI-driven healthcare solutions (Amann et al., 2020).

Studies show that social influence, facilitating conditions, and personal innovativeness significantly influence EHR adoption (Hossain et al., 2019). Enhancing social strategies, technical sufficiency, and training programs can increase EHR adoption, emphasizing the need for supportive policies and incentives. Telemedicine has been shown to reduce travel costs and time, particularly in rural areas, enhancing healthcare delivery efficiency (Haleem et al., 2021). However, barriers to telemedicine adoption include privacy concerns, lack of interoperability, technical difficulties, and resistance from both patients and healthcare providers.

Lessons from Global Best Practices

Insights from global best practices offer valuable lessons for enhancing technology adoption. For example, targeted education and training are essential to bridge the digital knowledge gap and address data security concerns (Wernhart et al., 2019). Comprehensive factors—technological, social, and organizational must be considered for successfully implementing mobile health (mHealth) tools (Jacob et al., 2020).

Addressing infrastructural and financial barriers is crucial to enhancing telehealth adoption, particularly in rural areas (Chen et al., 2021). Leadership, comprehensive training, and technology use are critical for implementing clinical practice guidelines (Correa et al., 2020). Contextual factors like healthcare infrastructure and social values should inform mHealth adoption strategies (Han et al., 2017).

Examining case studies from similar contexts provides practical insights into successful technology adoption. AI-driven chatbots have the potential to improve healthcare delivery by handling simple

consultations and enhancing patient engagement (Bhirud et al., 2019). AI chatbots have also been shown to significantly outperform medical students in direct and scenario-based questions, proving effective in public health education (Baglivo et al., 2023). Additionally, healthcare chatbots play a significant role in delivering remote health services and providing administrative assistance, though they also face challenges such as ethical issues and technical difficulties (Laymouna et al., 2024).

Barriers to Adoption in Sri Lanka

The adoption of digital health technologies in Sri Lanka is confronted with numerous challenges, including technological, socio-economic, cultural, and organizational barriers. Despite the potential benefits of integrating AI-driven solutions and other digital health technologies, these barriers significantly hinder their widespread adoption and effective use. Understanding and addressing these barriers is crucial for developing strategies that can enhance healthcare delivery and improve patient outcomes in Sri Lanka. This section explores the various obstacles to the adoption of digital health technologies in the Sri Lankan healthcare system, drawing on insights from existing research, government reports, and local studies.

Technological and Socio-Economic Barriers

Technological barriers, such as inadequate infrastructure and poor connectivity, significantly impede the adoption of digital health technologies in Sri Lanka. Poor infrastructure and lack of technological skills among healthcare workers have been identified as major challenges in implementing telemedicine in rural areas (Jayasinghe et al., 2016). Similarly, addressing infrastructural deficiencies is critical for enhancing telehealth adoption in rural areas (Chen et al., 2021).

Socio-economic barriers, including limited financial resources and socio-cultural resistance, further hinder technology adoption. Social influence and facilitating conditions significantly impact EHR adoption in Bangladesh, which can be paralleled to the Sri Lankan context (Hossain et al., 2019). Comprehensive regulations and guidelines are needed to maximize telehealth benefits during the COVID-19 pandemic in Sri Lanka (Kulatunga et al., 2020).

Cultural and Organizational Barriers

Cultural resistance to change and organizational inertia also pose significant challenges. Addressing cultural and organizational barriers is crucial for enhancing m-health adoption in Sri Lanka (Han et al., 2017). Involving end-users in the design of e-health programs is important to overcome resistance and improve usability (Wilson et al., 2021).

Insights from existing research and local studies provide valuable context-specific information. Infrastructural deficits, enhancing digital literacy, and implementing supportive policies are necessary to improve healthcare accessibility (Jayasinghe et al., 2016). AI chatbots have proven effective in public health education, emphasizing the need for structured implementation and regulatory support (Baglivo et al., 2023).

Facilitators for Adoption

Successfully adopting digital health technologies in Sri Lanka requires more than just addressing the barriers; it involves actively fostering an environment conducive to technological integration and innovation. Facilitators for adoption encompass a range of strategies, including enhancing technological infrastructure, providing financial incentives, implementing comprehensive training programs, and drawing lessons from global best practices. These facilitators are crucial for overcoming existing challenges and ensuring that digital health technologies are effectively integrated into the healthcare

system, leading to improved patient care and operational efficiency. This section explores the potential strategies and supportive measures that can facilitate the adoption of digital health technologies in Sri Lanka.

Potential Strategies to Overcome Technological and Socio-Economic Barriers

Overcoming the technological and socio-economic barriers to the adoption of digital health technologies in Sri Lanka requires a multifaceted approach. One of the primary strategies is to improve the technological infrastructure. This includes enhancing internet connectivity, particularly in rural areas, and ensuring the availability of necessary technological devices. Significant investments in technological infrastructure are crucial for the successful implementation of telemedicine in rural Sri Lanka (Jayasinghe, Crowder, & Wills, 2016). This involves not only upgrading existing infrastructure but also providing healthcare facilities with the latest technological tools and resources (Jayasinghe, Crowder, & Wills, 2016).

Providing financial incentives is another critical strategy. These incentives can help offset the costs associated with adopting new technologies, making them more accessible to healthcare providers, particularly those in under-resourced areas. The importance of facilitating conditions and financial support in encouraging technology adoption has been highlighted in EHR adoption studies (Hossain, Quaresma, & Rahman, 2019). Similar strategies can be applied in Sri Lanka to motivate healthcare providers to adopt and integrate digital health technologies (Hossain, Quaresma, & Rahman, 2019).

Comprehensive training programs are essential to equip healthcare providers with the necessary skills and knowledge to use new technologies effectively. Well-structured training programs can significantly enhance the readiness and confidence of healthcare professionals in using digital health tools. These programs should be continuous and tailored to the specific needs of different healthcare settings to ensure that all users are adequately prepared to adopt new technologies (Gagnon et al., 2015).

Lessons Learned from Global Best Practices

Global best practices provide valuable insights that can be applied to enhance the adoption of digital health technologies in Sri Lanka. One key lesson is the importance of ensuring data quality, ethical standards, and multidisciplinary collaboration. High-quality data is crucial for the effective implementation of AI in healthcare. Ensuring that data is accurate, comprehensive, and regularly updated can improve the performance and reliability of AI-driven solutions. Ethical standards are also paramount, as they help protect patient privacy and ensure that AI technologies are used responsibly (Secinaro et al., 2021).

Multidisciplinary collaboration involves engaging stakeholders from various fields, including healthcare providers, technologists, policymakers, and patients. This collaborative approach ensures that the development and implementation of digital health technologies are well-rounded and address the needs and concerns of all stakeholders. The positive impact of digital health technologies on healthcare workers' competencies and workplace environments can be enhanced through collaborative efforts (Borges do Nascimento et al., 2023).

The Role of Supportive Policies, Robust Infrastructure, and Comprehensive Training Programs

Supportive policies are critical for the successful adoption of digital health technologies. These policies can provide a regulatory framework that ensures the safe and effective use of new technologies. The importance of adaptive regulatory frameworks that can keep pace with the rapid advancements in AI

technology has been discussed, emphasizing the need to address issues related to data privacy, security, and ethical use of AI to build trust among healthcare providers and patients (Romagnoli et al., 2024).

Robust infrastructure is equally important. This includes not only technological infrastructure but also the physical and organizational infrastructure necessary to support the implementation and use of digital health technologies. Ensuring that healthcare facilities have reliable internet connectivity, adequate power supply, and the necessary hardware and software is crucial. Addressing privacy concerns, technical difficulties, and interoperability is key to improving telemedicine adoption (Haleem et al., 2021).

Comprehensive training programs are vital for equipping healthcare providers with the skills and knowledge needed to effectively use new technologies. These programs should be ongoing and updated regularly to keep pace with technological advancements. The importance of comprehensive training for the successful adoption of electronic clinical decision support systems (CDSSs) among UK general practitioners has been highlighted (Ford et al., 2021). Similar training programs can be implemented in Sri Lanka to enhance the adoption of AI-driven healthcare solutions (Ford et al., 2021).

Studies of Successful Technology Adoption in Similar Contexts

Examining studies from similar contexts can provide practical insights into successful technology adoption. One such example is the study on AI-driven chatbots in healthcare, which highlights the potential of chatbots to improve healthcare delivery by handling simple consultations and enhancing patient engagement (Bhirud et al., 2019). The integration of Natural Language Understanding (NLU), Natural Language Generation (NLG), and Machine Learning (ML) techniques can make chatbots more effective in providing personalized healthcare counseling. This approach can be applied in Sri Lanka to develop chatbots that address specific healthcare needs and improve accessibility (Bhirud et al., 2019).

Another relevant case study is research on the use of AI chatbots in public health education, which demonstrated their effectiveness in answering complex medical questions and providing valuable educational support. The findings showed that AI chatbots outperformed medical students in direct and scenario-based questions, highlighting their potential to enhance medical education and training in Sri Lanka (Baglivo et al., 2023).

Additionally, a study on healthcare chatbots provides insights into the roles, user groups, benefits, and limitations of chatbots in healthcare. The study categorizes chatbot roles into delivering remote health services and providing administrative assistance, highlighting their potential to improve healthcare quality, efficiency, and accessibility. However, significant limitations such as ethical challenges, medicolegal and safety concerns, technical difficulties, and overreliance must be addressed to ensure the optimal, safe, and equitable use of chatbots in healthcare (Laymouna et al., 2024).

The Role and Impact of AI Healthcare Chatbots

AI healthcare chatbots represent a significant advancement in digital health technology, offering a range of functionalities that can transform patient care and healthcare operations. These chatbots utilize artificial intelligence to provide real-time assistance, manage routine tasks, support clinical decision-making, and enhance patient engagement. As healthcare systems worldwide increasingly integrate AI solutions, understanding the specific role and impact of AI chatbots becomes essential, especially in developing countries like Sri Lanka. This section examines the various capabilities of AI healthcare chatbots, their benefits in improving healthcare delivery, the challenges and limitations associated with their implementation, and their potential to revolutionize healthcare in Sri Lanka.

Examination of AI Chatbot Functionalities and Capabilities

AI chatbots have emerged as powerful tools in healthcare, offering functionalities that range from answering simple medical queries to assisting in complex clinical decisions. These chatbots leverage advanced technologies such as Natural Language Processing (NLP), Machine Learning (ML), and Artificial Intelligence (AI) to interact with users in a human-like manner. The potential of AI chatbots in medical education and clinical laboratory medicine has been underscored, with AI chatbots providing timely responses to clinical inquiries, assisting in interpreting laboratory results, and supporting medical education by delivering accurate and validated information (Yang et al., 2023).

The role of AI chatbots in managing routine queries and reducing the workload on healthcare professionals is highlighted, as these chatbots can handle tasks such as symptom checking, scheduling appointments, and providing preliminary diagnoses based on symptom descriptions. This functionality not only streamlines administrative processes but also allows healthcare providers to focus on more complex cases, thereby improving overall efficiency in healthcare delivery (Bulla et al., 2020).

Chatbots like Endurance, designed to assist dementia patients, and MedWhat, which answers general healthcare inquiries, exemplify the diverse applications of AI in healthcare. Endurance helps track the cognitive status of patients, providing caregivers with valuable insights into their condition, while MedWhat offers a platform for patients to ask health-related questions and receive informed responses. However, the limitations of current chatbots in providing natural, human-like communication are noted, with the integration of Natural Language Understanding (NLU) and Natural Language Generation (NLG) techniques suggested to enhance their conversational capabilities (Bhirud et al., 2019).

Benefits of Integrating AI Chatbots in Healthcare Systems

Integrating AI chatbots into healthcare systems offers numerous benefits, including improved patient engagement, enhanced operational efficiency, and reduced workload for healthcare professionals. The potential of AI chatbots in medical education is explored, highlighting their ability to automate repetitive educational tasks, provide real-time feedback, and support personalized learning experiences. These chatbots can serve as interactive tutors, helping medical students and professionals stay updated with the latest medical knowledge and practices (Ghorashi et al., 2023).

AI chatbots also play a crucial role in patient management by offering continuous support and monitoring. A comprehensive architecture for AI-powered health chatbots integrating NLU, NLG, and deep learning techniques enables these chatbots to process user inputs accurately and generate appropriate medical responses, enhancing patient care and management. For instance, chatbots can provide medication reminders, monitor chronic conditions, and offer lifestyle advice, which helps in managing patient health more effectively (Khadija et al., 2021).

Furthermore, AI chatbots can significantly enhance access to healthcare services, especially in remote and underserved areas. By offering virtual consultations and health advice, chatbots reduce the need for in-person visits, thus overcoming geographical barriers and improving healthcare accessibility. The potential of AI to reduce travel costs and time for patients, enhancing the overall efficiency of healthcare delivery systems, is also highlighted (Haleem et al., 2021).

Challenges and Limitations of AI Chatbot Integration

Despite the numerous benefits, integrating AI chatbots into healthcare systems presents several challenges and limitations. Data privacy and security are among the most significant concerns. Chatbots

handle sensitive patient information, and ensuring the confidentiality and security of this data is paramount. The readiness of AI chatbots for clinical use requires rigorous validation and ethical considerations to safeguard patient data and ensure compliance with privacy regulations (Au Yeung et al., 2023).

Accuracy and reliability are other critical challenges. Chatbots must provide accurate and reliable medical information to be effective. However, instances of AI chatbots generating incorrect or biased outputs can undermine their utility and trustworthiness. Privacy concerns and liability issues are significant barriers to successful chatbot implementation, and for chatbots to be trusted by healthcare providers and patients, they must undergo rigorous testing and validation to ensure their accuracy and reliability (Reis et al., 2020).

Additionally, the lack of human empathy in AI interactions can be a limitation. While chatbots can provide timely and accurate information, they often lack the empathetic communication that human healthcare providers offer. This limitation is particularly significant in mental health applications, where empathetic interactions are crucial. The safety concerns of using generative AI chatbots in mental health highlight their inadequacies in recognizing and appropriately responding to mental health crises, underscoring the need for careful evaluation and domain-specific training to prevent potential harm to users (De Freitas et al., 2022).

The integration of AI chatbots into existing healthcare workflows can also be challenging. Healthcare providers may face difficulties in adapting to new technologies, especially if they are not user-friendly or well-integrated with existing systems (Ford et al., 2021). The importance of seamless integration and comprehensive training to enhance adoption and usability has been emphasized in studies on the adoption of electronic clinical decision support systems (CDSSs) among UK GPs (Ford et al., 2021). Similar strategies are necessary for the successful integration of AI chatbots in healthcare systems (Ford et al., 2021).

AI chatbots hold significant potential to transform healthcare by improving patient engagement, reducing workload, and enhancing operational efficiency, their integration poses several challenges. Addressing data privacy, accuracy, reliability, and empathy concerns, along with ensuring seamless integration and comprehensive training, are essential for the successful adoption and implementation of AI chatbots in healthcare systems. The lessons learned from global best practices and the insights from existing research can guide the development of effective and sustainable AI-driven healthcare solutions in Sri Lanka.

Conclusions and Recommendations

The integration of digital health technologies, particularly AI-driven solutions like chatbots, holds significant promise for transforming healthcare systems worldwide, including in Sri Lanka. This literature review has highlighted both the potential benefits and the substantial barriers to adoption and implementation. This paper examined the adoption and potential impact of AI-driven healthcare solutions, particularly chatbots, within the context of Sri Lanka's healthcare system. The research focused on understanding the current state of digital health technology adoption, identifying key barriers and facilitators, and exploring global best practices to inform strategies for enhancing healthcare delivery in Sri Lanka. The review highlighted that while there is a global trend towards embracing digital health technologies, Sri Lanka faces significant challenges in this area. The adoption of AI-driven solutions like chatbots is still in its nascent stages, primarily due to inadequate infrastructure, poor connectivity, and limited digital literacy among healthcare professionals. These technological

barriers are compounded by socioeconomic factors, such as limited financial resources and cultural resistance to change.

The study identified several barriers to the adoption of AI-driven healthcare solutions in Sri Lanka. Technological barriers include inadequate infrastructure and poor internet connectivity, while socio-economic barriers involve financial constraints and cultural resistance. Organizational inertia and lack of comprehensive training programs further hinder adoption efforts. To overcome these challenges, a multifaceted approach is necessary. Strategies such as improving infrastructure, providing financial incentives, and implementing comprehensive training programs are crucial to creating an environment conducive to technology adoption. Global best practices offer valuable insights for Sri Lanka. Successful adoption in developed countries is often driven by robust infrastructure, supportive policies, and financial incentives. These lessons underscore the importance of creating adaptive regulatory frameworks that address data privacy, security, and ethical considerations. Additionally, case studies from similar contexts demonstrate the effectiveness of AI chatbots in enhancing healthcare delivery and patient engagement, highlighting the potential for these technologies to transform healthcare systems in Sri Lanka.

Despite the promising potential of AI chatbots, several research gaps remain. There is a need for comprehensive studies on the long-term impacts of AI chatbots on healthcare outcomes in developing countries like Sri Lanka. Additionally, more research is needed to understand the socio-cultural dynamics influencing the acceptance and use of AI chatbots in different healthcare settings. Developing culturally sensitive implementation strategies and comprehensive ethical and legal frameworks will be crucial to addressing these gaps.

In conclusion, AI-driven healthcare solutions like chatbots hold significant promise for improving healthcare delivery in Sri Lanka. However, addressing the identified barriers and research gaps is crucial. By focusing on enhancing infrastructure, providing comprehensive training, implementing supportive policies, and conducting further research on the socio-cultural, ethical, and long-term impacts of these technologies, Sri Lanka can leverage AI to transform its healthcare system and improve health outcomes for its population. This revised conclusion aligns with your research questions and objectives, providing a clear and organized summary of your findings and their implications for the adoption of AI-driven healthcare solutions in Sri Lanka.

Acknowledgments

I would like to express my sincere gratitude to my supervisors, Prof. Janaka Wijayanayake and Dr. Kaneeka Vidanage, for their invaluable guidance and support throughout this research on " AI Chatbot Solutions for Medical Practitioner Adoption and Engagement with the Healthcare System in Sri Lanka." This study was greatly influenced by their expertise.

I also thank the academic and research communities whose work provided the foundation for this review.

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TRANSFORMATIVE IMPACT OF ARTIFICIAL INTELLIGENCE IN LABORATORY MEDICINE- TRENDS AND PITFALLS

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Abstract

By precisely analysing complicated data from laboratory tests, artificial intelligence (AI) is improving diagnostic accuracy, decreasing mistakes, and increasing reliability, all of which are dramatically changing the field of laboratory medicine. It accelerates data processing, making it possible to spot trends and abnormalities in test results more quickly. This facilitates quicker patient care decision making. AI improves patient outcomes and treatment efficacy by personalising medicine based on unique patient data. By automating repetitive procedures, it optimises laboratory workflows, freeing up healthcare personnel to concentrate on more complicated situations while also optimising productivity. AI is also vital to predictive analytics, which predicts the course and results of diseases and makes early intervention possible. Additionally, AI facilitates drug discovery by predicting possible drug candidates and effectively studying molecular interactions. In general, artificial intelligence in laboratory medicine is transforming healthcare through enhanced diagnosis, customised treatment plans, and increased operational efficiency in lab settings. The objective of the present review is to summarise the transformative impact of Artificial Intelligence in laboratory medicine.

Keywords: Artificial Intelligence, Diagnostic Accuracy, Laboratory Medicine, Personalised Medicine, Predictive Analysis

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Introduction

Laboratory medicine has been practised for centuries, and the human workforce has continued without the support of AI until recently. This raises the question: why do we need AI in laboratory medicine now? The answers lie in many perspectives. Medical laboratories in developed countries typically produce millions of test results annually. Since most subsequent medical decisions are based on laboratory test results in pathology reports, the results of medical tests are extremely important. Only when laboratory data are compared to clinical decision limits, population-specific reference ranges, or prior results from the same patient can the results be interpreted as appropriate (Sikaris, 2015). Further, significant technological improvements are being made due to the continuous explosion of new technologies and methodologies. As a result, the function of laboratories and laboratory personnel is changing. For example, the explosive expansion of "omics" testing has produced massive amounts of data, so much so that medical experts need to improve their statistical and interpretive abilities to handle this data explosion. To guarantee the calibre and standardisation of medical tests, new cooperative models involving hospitals, academic institutions, and in vitro diagnostic (IVD) businesses (such as translational medicine initiatives and campus-based firms) must be developed (Cobbaert, Smit and Gillery, 2018). Greaves *et al* predicted that the 2020s would likely see a lot of pressures and factors shape laboratory medicine. Several current and upcoming changes appear as critical to the future of laboratory medicine based on our research of the larger healthcare landscape and various parts of the field, including pre-analytical, and post-analytical components as well as linkages. They also added that, whatever the future might bring, laboratory medicine has a long history of implementing new technologies (Greaves *et al*., 2019).

Objectives

- Evaluate the impact of AI on diagnostic accuracy and efficiency
- Analyse the role of automation in modern clinical laboratories
- Examine the benefits and limitations of AI in data analysis and interpretation
- Assess the future directions and innovations in AI for laboratory medicine
- Assess the social and professional implications of AI adoption

Methods

Database Selection and Search Terms

A comprehensive search was conducted across multiple academic databases, including Google scholar, PubMed, ScienceDirect, and Web of Science. The search strategy included a combination of keywords such as "artificial intelligence," "machine learning," "laboratory medicine," "diagnostic testing," "automation," and "data interpretation". The search was limited to articles published between January 2000 and December 2023 to ensure the inclusion of recent advancements and perspectives.

Inclusion and Exclusion Criteria

Articles needed to focus on the application of AI in laboratory medicine, specifically in areas such as diagnostic testing, data analysis, and automation. Eligible studies had to provide empirical data, theoretical frameworks, case studies, or expert opinions on these topics. Additionally, only articles published in peer-reviewed journals and written in English were considered. The review excluded articles that were not directly related to laboratory medicine or AI, studies that focused solely on the technical aspects of AI without clinical relevance, as well as non-peer-reviewed articles, editorials, opinion pieces, and conference abstracts.

Data Extraction and Quality Assessment

Relevant articles were initially screened based on titles and abstracts. Full-text articles of potentially eligible studies were then retrieved and reviewed in detail. Data extraction was performed using a standardized form that captured key information, including the study's objective, methods, AI technology used, outcomes, and conclusions.

Current Trends in AI Applications

There has been a surge in significant investments in AI-based healthcare solutions in recent years. To understand the scope of this growth, it is important to examine the market size of AI within the healthcare industry (Dave, 2024)

AI in Diagnostic Testing and automation

In the evolving landscape of clinical laboratories, automation is becoming increasingly prevalent. The integration of sophisticated instruments and coordinated systems, which include advanced robotics and AI capabilities, is transforming laboratory operations. Automated equipment now allows robotic systems to efficiently execute processes that laboratory assistants or technologists once handled. This shift towards automation, encompassing everything from sample storage to assay analyses, has the potential to enhance testing volumes significantly. By leveraging modern automated systems, laboratories can achieve greater efficiency and throughput, addressing the growing demands for rapid and high-volume testing. This discussion highlights the transformative impact of automation on laboratory practices and its implications for future operations (Champman, 2003; Naugler and Church, 2019).

Automation in high-volume laboratories: adoption and impact on efficiency

High-volume chemistry, haematology, and molecular biology laboratories have traditionally been quick to adopt total laboratory automation. This trend has enabled the consolidation of testing into centralised or core laboratories, whether within healthcare systems or large reference facilities. Automation in these areas has been demonstrated to reduce overall test turnaround times, decrease the percentage of outlier results, and lower the demand for urgent short turnaround time (STAT) testing (Ialongo *et al.*, 2016; Lou *et al.*, 2016). Despite the high level of automation in contemporary clinical chemistry and haematology analysers, only a few total laboratory automation systems have been developed. The Cobas® system from Roche Diagnostics is one of the key examples, which can independently process, analyse, and store samples. When connected to a track system with additional modules, it can also perform sample sorting, decapping, quality control, aliquoting, and recapping of in vitro diagnostic specimen tubes (Mutters *et al.*, 2014; Bailey, Ledeboer and Burnham, 2019).

Artificial intelligence has been applied to medical problems for over thirty years. However, its meaningful integration into clinical laboratories is still in its early stages. Like automation, AI is poised to become a fundamentally disruptive technology in the coming decades (Naugler and Church, 2019).

AI in Data Analysis and Interpretation

Challenges in explainability of AI in healthcare

Explainability is one of the most heavily challenged issues regarding using AI in healthcare. The lack of explainability in AI-driven systems persists in provoking criticism despite evidence that they perform better than humans in specific analytical tasks. However, explainability raises a number of medical, legal, ethical, and societal issues that need careful investigation; it is not just a technology problem (Shortliffe and Sepúlveda, 2018). Amann *et al* concluded that neglecting explainability in clinical

decision support systems threatens core ethical values in medicine and could harm both individual and public health.

The need for multidisciplinary collaboration

There is a need for increased awareness among developers, healthcare professionals, and legislators about the challenges and limitations of opaque algorithms in medical AI. Fostering multidisciplinary collaboration is essential to address these issues effectively (Amann *et al.,* 2020).

Implications for Low- and Middle-Income Countries

AI technology has the potential to significantly assist healthcare systems in low- and middle-income countries (LMICs). These nations often face challenges such as limited resources, inadequate infrastructure, and a high burden of diseases. AI technologies can address these issues and enhance healthcare delivery in LMICs. For example, AI can support clinical decision-making in resource-constrained environments, improve the accuracy of disease identification, and optimise diagnostic processes (Oduoye *et al.*, 2024). Although the authors acknowledge the significant influence of AI on laboratory medicine in countries LMICs, they also highlight several obstacles, including insufficient data accessibility, inadequate digital infrastructure, and ethical concerns. For successful implementation, significant investments in digital infrastructure, the creation of data-sharing networks, and the development of regulatory frameworks are required.

AI was utilized in a Kenyan study to increase the precision of malaria diagnosis in isolated locations with low medical infrastructure. The research, headed by Paltiel *et al*. (2022), used an AI-driven diagnostic tool that examined blood samples to accurately identify malaria. Since the technology was included into neighborhood clinics, medical professionals have been able to diagnose and treat malaria patients more successfully even with little training and resources. This example shows how AI can improve diagnostic procedures and assist clinical decision making in settings with limited resources (Paltiel *et al*., 2022).

An experimental study conducted in India showed AI can enhance tuberculosis (TB) detection. An AI system was used in the Rajkomar *et al*. (2018) research to analyse chest X-rays and identify TB more accurately than with conventional techniques. Several primary health centres implemented the AI system, which greatly decreased diagnostic errors and allowed patients to receive treatment on time. This experiment demonstrates how AI may improve disease detection and streamline diagnostic procedures in low- and middle-income countries (Rajkomar *et al*., 2018).

While AI has a lot of potential in LMICs, there are a few issues that need to be resolved before it can be successfully implemented. For example, the problem of insufficient digital infrastructure in many LMICs was brought to light in a research conducted by Mugo *et al*. (2021). The study concentrated on a digital health project in rural Uganda with the goal of implementing AI technologies for tracking maternal health. Even with the potential of AI, the project ran into serious problems because of unreliable internet connectivity and limited data accessibility. To encourage the use of AI in various contexts, the authors stress the necessity of making significant investments in digital infrastructure, building data sharing networks, and developing legislative frameworks (Mugo *et al*., 2021).

Benefits of AI in Laboratory Medicine

Most laboratory IT systems are not equipped to properly model certain solutions, leading to the development of AI algorithms in recent years. Contributing to patient care individually can be impractical, making AI systems valuable for assisting in test selection and interpretation. When

provided with ground-truth data, such as information from the diagnostic work-up of a symptom or disease, including medical history, lab results, and final diagnosis, these systems can determine the most efficient and effective diagnostic pathway (Cadamuro, 2021).

Artificial intelligence and machine learning (ML) technologies can be applied to the test selection process and the interpretation of complex, multiple test outcomes. They can produce probability ratings for potential subclinical diseases a patient may have and likelihood scores to evaluate the dangers of potential diseases. The foundation of these evaluations is a comparison between the patient's lab test profile and demographics and a sizable database of verified cases (Gunčar *et al.*, 2018).

The Accelerate Pheno® is a novel advancement that provides swift antimicrobial susceptibility test results from real-time digital image analysis of bacterial cell growth. The application of AI to quantify protein biomarkers within a micro bubbling digital assay format using bright-field smartphone microscopy is recently being described. Also, researchers continue to investigate whether AI can enable measurements of nontraditional analytes, such as those found in the analysis of breath, the pupillary light reflex, or vocal patterns. These are some of the key examples of AI being used in the fields of modern laboratory medicine (Herman *et al.*, 2021).
Improved accuracy and efficiency, enhanced diagnostic capabilities, reduction in human error, accelerated research and development, and cost-effectiveness and resource optimisation are some of the key benefits of AI and ML in laboratory medicine. Therefore, the capacity to actively shape laboratory regulations must be considered a developing field within laboratory medicine. Rather than merely complying with the rules as they are, laboratory experts can share knowledge, offer experience, and influence the direction of the industry (Carobene *et al.*, 2023).

Pitfalls and Challenges
Given that the ChatGPT currently has half a billion users, it is highly probable that patients are already using it to translate their laboratory test results into understandable language. This is especially likely since many online search engines are either integrating or have already integrated AI-powered chatbots. However, ethical and legal considerations, data privacy and security concerns, risk of over-reliance on AI, bias in AI algorithms, and integration and interoperability issues are some of the significant drawbacks of AI in laboratory medicine (Amann *et al.*, 2020; Blatter *et al.*, 2022; Pennestrì and Banfi, 2022; Cadamuro *et al.*, 2023; Yang *et al.*, 2023).

For example, a 2019 study by Challen *et al*. examined the limits of AI in interpreting sophisticated medical data. The study covered how AI platforms, such as IBM Watson, found it difficult to handle complex clinical contexts in real world oncology applications. As a result, they frequently made recommendations that were inappropriate for particular patient circumstances. Watson occasionally recommended treatments that were out-of-date or not practical, illustrating the difficulties AI has when addressing complicated cases needing in depth medical expertise and pattern recognition. This instance highlights the dangers of using AI to make complicated medical decisions when human judgment is still essential (Challen *et al*., 2019).

ChatGPT is superficial, providing generic answers for complex cases where multiple dependencies among results should be considered and patterns recognised for accurate interpretation. Additionally, the chatbot is reluctant to make definitive statements about overall findings or recommend specific actions, typically advising users to consult a physician or book a visit. Despite this, ChatGPT has impressively demonstrated that AI can analyse medical data, even without specific training or fine-tuning for this purpose (Cadamuro, 2023).

The primary ethical concerns surrounding the application of AI technologies in laboratory medicine are related to the unique function that laboratory personnel perform the automatic elaboration of data, and the use of sensitive patient information. Machines cannot validate or guarantee the quality of inputs (Cabitza *et al.*, 2021; Campagner, Carobene and Cabitza, 2021). To provide accurate data analysis and interpretation throughout the entire process, laboratory professionals must actively participate. This can be facilitated by the use of a common language, such as Logical Observation Identifiers Names and Codes, to identify health measurements, observations, and documents (Cabitza and Banfi, 2018; Banfi, 2019).

AI in healthcare raises ethical questions about algorithmic bias and data privacy, among other things. The debate surrounding IBM Watson's cancer treatment recommendations is one prominent example of how AI decision making can have implications for ethics. The AI system issued incorrect treatment recommendations as a result of gaps in its training data. (Challen *et al*., 2019). The danger of depending excessively on AI was also demonstrated by a study conducted in Kenya, where high accuracy malaria detection using AI tools was followed by difficulties in successfully integrating these technologies into the country's already existing healthcare infrastructure (Paltiel *et al*., 2022).

There are several challenges to integrating AI into laboratory medicine for cardiovascular care. These include addressing regulatory and ethical issues, ensuring accountability across the AI community, from developers to users, and guaranteeing data privacy and patient safety. Fortunately, there are emerging ethical principles and legal frameworks aimed at creating trustworthy AI systems (Gruson *et al.*, 2020). Further, a survey has shown how little the medical community knows about AI specifically and how important it is to provide AI education. Using new and current AI tools in combination could be one tactic (Paranjape *et al.*, 2021).

Future Directions and Innovations

Novel technologies like artificial intelligence and machine learning offer exciting applications for enhancing laboratory medicine; the Big Data concept remains fundamental for sophisticated data analysis in large databases. To ensure laboratory medicine data is optimally usable for clinical and research purposes, it needs to be FAIR: findable, accessible, interoperable, and reusable. Achieving this involves automated recording, device connection, efficient Extract, Transform, Load (ETL) processes, careful data governance, and modern data security solutions (Blatter *et al.*, 2022).

The transformation of laboratory medicine data into “Big Data” involves many steps essential for lean, efficient, sustainable, and complete data management. This process not only enhances research capabilities but also leads to the cleansing and modernisation of laboratory data. If laboratory medicine does not embrace these developments, it risks becoming merely a number generator or disappearing as an academic subject within integrated diagnostic devices. On the other hand, the value of comprehensive, quality-assured laboratory medical data and metadata for clinical research is immense. Setting standards for openness, collaboration, and the justification of medical data is crucial. Ultimately, health data is the new lifeblood that can revitalise laboratory medicine both figuratively and literally (Dahlweid, Kämpf and Leichtle, 2018; Perakslis and Coravos, 2019).

Other than the technically oriented future of AI, the socialisation of AI technology with laboratorians and clinicians is an area of active discussion among professional organizations and researchers. AI and ML have and will continue to intensely change the way in which laboratory data are analysed and drive clinical care decisions. The ongoing development of more sophisticated ML methods, coupled with

emerging laboratory measurement technologies, should lead to further improvements in clinical efficiency and patient outcomes. It is vital that these approaches be carefully designed, evaluated, and monitored to safeguard quality, achieve effectiveness, and minimise harm (Herman *et al.*, 2021).

Lab-on-a-chip technology, that simplifies laboratory procedures to a single chip, is another exciting advancement. Point-of-care testing may now be done efficiently and accurately owing to this technology, especially in environments with limited resources. Diagnostic testing is about to change due to the potential of lab-on-a-chip technologies, which will make the tests more accessible and less dependent on centralised laboratory facilities (Wang *et al*., 2021).

Lab medicine will be significantly impacted by the combination of genetics and personalized medicine. Because of the developments in next generation sequencing (NGS), genetic data can now be analysed quickly and affordably, allowing for customized treatment regimens based on each patient's unique genetic profile. This strategy reflects a change toward more individualized healthcare since it not only increases treatment efficacy but also lowers the risk of negative drug reactions (Mardis, 2019).

Conclusion

The integration of artificial intelligence into laboratory medicine marks a crucial shift in the field, driven by the growing volume and complexity of diagnostic data and advancements in automation and computational methodologies. While traditional laboratory practices have served well for centuries, the contemporary demands for rapid and accurate diagnostics necessitate the adoption of AI technologies. These technologies offer unique opportunities for enhancing diagnostic accuracy, improving efficiency, and supporting complex decision making processes. The transformative potential of AI is particularly evident in areas such as diagnostic testing automation, data analysis, and interpretation, where it can reduce human error, streamline operations, and provide valuable clinical insights.

Despite these promising advancements, the adoption of AI in laboratory medicine is not without challenges. Issues related to explainability, data privacy, ethical considerations, and the risk of over-reliance on technology must be carefully navigated. Moreover, the disparity in AI adoption between developed and low- and middle-income countries highlights the need for equitable access to technological advancements and the development of appropriate regulatory frameworks. The successful implementation of AI in laboratory medicine will require a multidisciplinary approach involving collaboration among healthcare professionals, developers, policymakers, and researchers.

Looking forward, the future of laboratory medicine lies in the seamless integration of AI and ML technologies with traditional practices, ensuring that laboratory data is findable, accessible, interoperable, and reusable. The continuous evolution of AI, coupled with the growing socialisation of these technologies among laboratorians and clinicians, promises to enhance clinical efficiency and patient outcomes further. As the field progresses, it is essential to maintain a focus on quality assurance, ethical considerations, and patient safety, ensuring that the benefits of AI are fully realised while minimising potential risks. Finally, the embrace of AI in laboratory medicine has the potential to revolutionise the field, paving the way for more precise, efficient, and patient-centred care.

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UPDATES ON DENGUE VACCINES; CURRENT STATUS, CHALLENGES AND FUTURE PERSPECTIVES

TN Siriwardana[1] and N Gunathilaka [2]

Abstract

Dengue is a significant public health challenge worldwide. Vector management has become the prime intervention in dengue control. Although there have been various attempts to make a dengue vaccine during the last 3-4 decades, it has become a challenging task. This review focused on exploring the history of dengue vaccine development, its present status and future prospects. A literature review from 2010- 2022 covering vaccine development approaches was considered in this study. Significant advancements in vaccine development are evident, with several candidates advancing through clinical trials. The live-attenuated CYD-TDV (Dengvaxia) vaccine by Sanofi Pasteur, the first dengue vaccine approved, has shown variable efficacy and raised safety concerns, especially in dengue-naïve populations. The TAK-003(Intertypic chimera-DENVax) (Qdenga®) has been approved by the European Medicines Agency (EMA) for use in individuals aged 4 years and older, based on national guidelines. The TV003/TV005 developed by the National Institutes of Health is currently in Phase III trials. These vaccines aim to address the challenges of antibody-dependent enhancement (ADE) and provide broad, serotype-specific immunity. The live-attenuated vaccines have shown potential, but they face issues like genetic instability and adverse reactions. Non-replicating platforms, such as DNA and subunit vaccines, offer safer alternatives but may need adjuvants to enhance immunogenicity. The review highlights the necessity for ongoing research and innovation to create vaccines that induce strong, protective immune responses without ADE. Despite the approval of Dengvaxia, its limited efficacy in some populations underscores the need for next-generation vaccines that offer comprehensive protection across various demographics.

Keywords: Dengue, Dengvaxia, Vaccine Development, Virus

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BIOETHICS TEACHING AND ITS' EFFECTIVENESS IN UNDERGRADUATE MEDICAL PROGRAMMES: A NARRATIVE REVIEW

PKS Godamunne[1] and K Kodikara[2]

Abstract

Medicine is an art as much as it is a science. Patients wish to consult professional and compassionate doctors, though they rarely meet such. To cultivate professionalism in medical students, bioethics teaching have been incorporated into medical programmes in varying degrees across the world. This reports findings from a narrative synthesis of previously published literature that evaluates the evidence regarding implementation of bioethics in undergraduate medical curricula, with special attention to the Asia, Pacific region. For this purpose, Google Scholar and MEDLINE/PubMed databases were searched for articles on bioethics published between January 2000 to April 2024. Reviews or studies that were published in languages other than English were excluded from the search. The focus was placed on the development of moral competence as the intention of this review was to inform bioethics teaching. The results reveal a high degree of diversity of the curricular structure of bioethics courses and the lack of formalization of bioethics in the curricula specially in the Asia-Pacific region. Bioethics teaching resulted on lowering student indecision when faced with moral dilemmas. The call for use of local cases to enhance bioethics education is prominent, enabling more opportunities for reflection and discussion, to stimulate critical judgment of future clinicians.

Keywords: Bioethics, medical students, moral competence, review

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Introduction

While scientific and technical knowledge advances have contributed to exponential progress in medicine, clinical practice remains as much an art as science (Tooke, 2016). For thousands of years, the doctor's armamentarium consisted of the herb, the knife, and the word (Grant, 2002). As time passed, however, the 'word' has received less attention than the other two, with an evident decline in a physicians' ability to fulfill patient's expectations regarding communication, willingness, and permanent care (Coulehan & Williams, 2003). Medical ethics or 'bioethics' a term coined by Potter in 1970 (Gracia, 2001) and medical humanities have been formally introduced into the curriculum around the 1970s in the West (Shankar, 2016) to counter doctors' insufficient emotional involvement by fostering reflexive professionalism (Sheehan et al., 2015). Teaching bioethics is fundamental to good medical practice, as it combines the application of scientific knowledge with a respect for the values and preferences held by the patient, attempting to render them active participants in the care process (Tavares et al., 2022). However, bioethics and medical humanities education did not gain traction until the 1990s in the Asia-Pacific region (Shankar, 2022). Since then, bioethics has become the dominant discipline of the two, globally (Shankar, 2022). This may be because exploring ethical issues in medical practice may not challenge the traditional knowledge and power structures inherent in medicine as opposed to medical humanities. Thus, teaching bioethics was perceived as more comfortable and considered less radical than the teaching of humanities to medical fraternity. Until recently, the medical humanities have been embedded or hidden in a bioethics paradigm, the best example of which is the journal Medical Humanities being launched as a special issue of the Journal of Medical Ethics in 2000 (Greaves & Evans, 2000; Shankar, 2022).

It is being argued that bioethics may only be one among many disciplines that constitutes medical humanities. Medical humanities involves interactions between the patient and the healthcare practitioner, where ethical issues may be evident in only some of these interactions. Ethical values do not exhaustively cover the value system in medicine. Hence, a wider understanding of values is vital to explore ethical issues that arise in healthcare adequately. The burgeoning non-communicable diseases in the last few decades mean that the medical practitioners need to respond more to the emotional needs of patients. As artificial intelligence (AI) embodies healthcare and medical education, medical educationists and clinicians alike need to face ethical challenges that are inevitably associated with AI. Hence, medical humanities become an integral part of clinical medicine.

Bioethics programmes mushroomed in the United States primarily in the medical schools in the 1970s (ten Have & Neves, 2021). In a relatively short period of time almost all medical schools in America introduced bioethics education to their undergraduate degree programms. Since then, Europe and other countries have begun to incorporate bioethics education, to varying degrees. Inclusion of bioethics in the curricula has become a requirement for accreditation of the undergraduate medical programms in some countries such as the United States (Singer, 2003; Ypinazar & Margolis, 2004). Consequently, bioethics-teaching came to be offered not only in undergraduate programs but also in graduate, and postgraduate education. Asian medical schools have incorporated bioethics into their curricula in the late 20th and early 21st century, with some countries in the Asia-Pacific region such as Malaysia, Pakistan, and India lagging far behind (Ganguly et al., 2023; Ngan & Sim, 2021;Singh et al., 2017). Moreover, bioethics education is highly heterogenic, with different types of programs offered within and across countries, with varying approaches, methods and volume of teaching (ten Have & Neves, 2021), with arguments of contextualizing bioethics teaching, questioning the suitability of western approaches to the eastern cultures (Bergstresser et al., 2020). Although literature is ripe with how some countries teach bioethics, reviews of how Asia pacific region attempts to introduce bioethics concepts to its' students is scarce.

The aim of this narrative review is therefore to partially fill this gap in the literature by ascertaining how bioethics teaching is established globally, with special attention to the Asian context, and the extent to which it is effective in meeting the objectives of establishing bioethics programmes.

Methodology

This paper reports findings from a narrative synthesis of previously published literature on the topic bioethics teaching in undergraduate medical education. A narrative review is appropriate when several quantitative studies use different methodologies or have different theoretical conceptualizations (Baumeister, 2012). By evaluating and synthesizing multiple individual studies, a broader consistency can be discovered (Siddaway et al., 2019). In this way, a narrative review allows for a global vision that serves as a starting point for knowing which aspects have been studied and which need to be investigated. This narrative review followed the methodological guidelines of the SANRA tool (Baethge et al.,2019).

A broad electronic search of the Google Scholar and MEDLINE/ PubMed databases was performed to extract relevant studies published between January 2000, and April 2024. No time restrictions were imposed as a search criterion. The search strategy used both medical MeSH terms and free-text words. The search was performed using a combination of broad search terms including bioethics (i.e., bioethics OR medical ethics OR ethics) AND moral competence (i.e., (moral competence OR moral judgement OR moral reasoning) AND undergraduate medical education (i.e., (undergraduate medical curricul* OR undergraduate medical education OR medical school* OR medical student* OR medical undergrad*). Additionally, a hand search through reference lists of retrieved articles was conducted. Duplicates were eliminated by going through the abstracts. Reviews or studies that were published in languages other than English and research that involved postgraduate trainees or doctors and allied health undergraduate trainees were excluded from the search. The focus was placed on the development of moral competence as the intention of this review was to inform bioethics teaching. Based on the literature review the following important content was extracted.

Results

Moral decline

The current perception of the layman into health professionals and specially physicians, is that most are exclusively concerned with the technical side of their profession, leaving behind its relational component. Patients and their families across the globe seem frustrated with doctors' capacity to fulfill their expectations regarding communication, willingness, and permanent care (Coulehan & Williams, 2003). This scenario, also known as dehumanization of medicine, has been attributed to various causes such as organization of the healthcare system, and the relative decline of humanistic values in general (Serodio et al., 2016). Moreover, there is a widespread feeling that medical training, at undergraduate and graduate levels, somehow contributes to escalate dehumanization (Serodio et al., 2016). The classical description is that students enter medical school with a generous and empathetic attitude but, with years passing by, they become self-centered individuals, who are less-empathetic and almost inhuman (Serodio et al., 2016) with evidence of moral reasoning stagnation during medical training (Fleisher et al., 2003; Patenaude et al., 2003).

Explanations for moral regression could be found in both, the formal and the hidden curricula (Tavares et al., 2022). At the beginning of the 20th century, basic sciences and hospital practical training became the core of formal medical curriculum in many parts of the world (Hiatt & Stockton, 2003). Hence, humanistic education founded on history, philosophy, and literature received lack of much attention.

Thus, medical students learn how to behave like a doctor mainly via the hidden curriculum (Serodio et al., 2016) mostly by leaning into role models identified among professors, and clinicians. However, in the background of physicians' lack of humanistic skills demonstrated in literature, identification of negative role models may lead students astray in their relationship with patients.

When dehumanization is explored with the constructive structural theory in moral psychology, moral development can be associated with cognitive development in an invariable and irreversible sequence of stages (Serodio et al., 2016). Accordingly, individual moral reasoning development begins with a completely egocentric approach. It then passes through the recognition of different social perspectives (from close people such as family to the society as a whole) with time and reaches highest developmental stages with the employment of universal moral principles to solve moral dilemmas. Once individuals reach this higher stage, they will not employ lower stage moral reasoning when faced with moral problems. It is believed that the more the years of formal education a person undergoes, the higher the stages of moral reasoning they will employ when encountering moral problems. Thus, medical students are supposed to achieve higher moral development stages by the time they graduate from medical school. Interestingly, in addition to the cognitive part, it is widely accepted that there is an affective aspect in moral behavior. However, the cognitive structural authors such as Kohlberg and Piaget viewed affection as an 'invariable variable', and thus focused on the cognitive processes that are involved in moral decisions and actions (Serodio et al., 2016), leading to the cognitive part becoming more prominent in literature.

Bioethics

Biomedical ethics or in short, 'Bioethics' is the study of moral values and judgments applied to medicine (ten Have & Gordijn, 2013). Simply put, it enables reflection on healthcare related issues as right and wrong, with indication of what to do and what not to (Shakya et al., 2015). The West, working within their own value system, may have been able to develop a 'near consensus' on how to deal with at least some of the pressing bio-ethical questions in the western context (Sharma et al., 2016) .However, the same cannot be said for the East, with some countries are yet to deliberate upon bioethical issues in accordance with their own, unique socio-cultural and religious practices. Important to note is that studies have shown that most of the knowledge of biomedical ethics is acquired during the period of undergraduate training (Hernández González et al., 2013). Bioethics education has shown a positive impact on moral development and on making better doctors (Hariharan et al., 2006). A great initiative in bioethics education could be the UNESCO Bioethics Core Curriculum which is a highly comprehensive curriculum grounded in the UNESCO Universal Declaration of Bioethics and Human Rights (UNESCO, 2005). This bioethics curriculum is grounded in the universal humanitarian principles of human dignity, human rights, nondiscrimination, and respect for the environment and the commonwealth of life, which caters to the global community. However, the appropriateness of locating bioethics within geographic, historical, and philosophical spaces is frequently questioned throughout broader theoretical debates, extending to discussions of whether a 'global bioethics' is possible or even desirable (Fox & Swazey, 1984; Holm & Williams-Jones, 2006; Nie, 2013; Tai & Lin, 2001). Moreover, since many core bioethical principles have roots in cultural norms, rather than universal norms, clinical ethical practice is not uniform across global settings, and teaching bioethics to a diverse group of medical students poses unique challenges (Feldman et al., 1999). Additionally, despite the increased emphasis on bioethics teaching in universities in both developing and developed countries, the main goals or best methods of teaching bioethics and appropriate assessment methods of ethics curricula are still debated upon (Carrese et al., 2015).

Bioethics teaching in undergraduate medical programmes

Although bioethics teaching is incorporated into medical curricula in most countries (de la Garza et al., 2017; Ganguly et al., 2023) it is not highly impressive in terms of teaching volume, time, and commitment (Roberts et al., 2004, 2007). Although bioethics education is required in USA, it comprises only 1% of the undergraduate medical curricula (ten Have & Patrão Neves, 2021). Bioethics is a core component of all medical curricula in Australia and New Zealand (Torda & Mangos, 2020). Similar to USA, Canada and the UK, incorporation of bioethics into the undergraduate medical curricula in Australia and New Zealand is necessary for course accreditation by the AMC (GMC, 2018). Similar observations can be made in Pakistan, a South Asian low-middle income country where the accreditation body for undergraduate medical education, the Pakistan Medical and Dental Council (PMDC) recommended introduction of bioethics education as a part of undergraduate medical curricula in 2002 (Ashfaq et al., 2021; Riaz et al., 2023). While the guidelines explicitly stated that bioethics must be taught and assessed in undergraduate medical programs, the introduction of bioethics education into the curriculum was left at the discretion of medical colleges in Pakistan (Riaz et al., 2023). Bioethics is taught in almost all medical schools in Malaysia (Sim et al., 2019) and Hong Kong (Becker, 2005). Although Bioethics has come to secure a definite position within the fields of policy making, medical treatment, and research in Japan, bioethics incorporation to undergraduate medical curricula is still in its developmental stage (Akabayashi, 2009), where 60.8% of medical schools were found to offer bioethics training in the first year of the programme, with only 11.4% offering bioethics teaching during the clinical years (Kosik et al., 2014).

Most teaching and learning activities in bioethics were found to be sporadic contributed mostly by a lack of teachers well versed in bioethics (Iqbal & Khizar, 2010; ten Have & Neves, 2021; Van McCrary, 2001). Universities have a limited capacity to provide professional training of ethics and moral philosophy to sustain teaching quality (Ngan & Sim, 2021). Another common challenge is limited curriculum time to include ethics in the packed medical teaching timetable (Ravindran, 2008). In most instances bioethics was not taught as a formal part of the curricula, which made bioethics an optional course (Riaz et al., 2023).

Significant differences were observed in bioethics curricular content and objectives, methods used to teach bioethics concepts, and the period of undergraduate curricula where bioethics teaching in incorporated (i.e., first year before clinical exposure vs fifth year during clinical exposure) (Martins, Santos, Ricou, et al., 2021; Ravindran et al., 1998; Shaikh & Humayun, 2012; Sherer et al., 2017; Vaswani & Vaswani, 2015). In most medical schools in Nepal, Medical ethics, a part of bioethics is included and is being taught under Forensic medicine (Sharma et al., 2016) or behavioral sciences (Javaeed, 2019; Serodio et al., 2016; Shaikh & Humayun, 2012). Several studies conducted on both sides of the Pacific reveal a lack of consensus regarding goals/ objectives, teaching methods and assessment strategies on teaching of bioethics in undergraduate medicine (Carrese et al., 2015), with few validated bioethics curricula (de la Garza et al., 2017). Learning environments were found to be not conducive for ethical reflection by some studies (García-Mangas et al., 2016).

A study carried out in the United Kingdom in 2016 reveals the attempts of several countries towards seeking to unify the bioethics curriculum (Giubilini et al., 2016). Greenberg et al., (2016) posits the importance of understanding the relevant and common issues of a culturally diverse student body in order to define the specific high-impact topics to be addressed in bioethics education. In attempts to move away from centralizing on Western ethical issues, specific forms of bioethics for individual Asia-Pacific national contexts have been considered and attempted. Some (Alora, 2004; Alora & Lumitao,

2001b, 2001a) have described the possibility of a distinct Filipino bioethics course based on local culture and everyday life. More variations were found in evaluation of bioethics related teaching activities (ten Have & Neves, 2021).

Moral competence

Kohlberg defined moral competence as the capacity to make moral decisions and judgments (i.e., based on internal principles) and to act in accordance with such judgments (Kohlberg, 1964). Kohlberg presented six levels of development (Kohlberg, 1971), grouped in three stages of moral development. The pre-conventional stage (levels 1 and 2) is mostly observed in children, which is marked by fear of being punished. The conventional stage (levels 3 and 4) is present in most adolescents and adults, which is characterized by the perception that 'correct' moral action is based on social rules imposed by recognized authorities or institutions. The post-conventional stage (levels 5 and 6) which is the highest stage of moral competence presented by Kohlberg, is only achieved by few and for them, action is based on universal moral principles, guided by reciprocity and equality. They are not thwarted by the societal opinions and pressures. Kohlberg emphasized the importance of ensuring intellectual, social, and educational awareness to foster individual moral development (Kohlberg, 1984), where he/she develops the ability to work in groups, share decision-making and, take responsibility for their actions (Martins, Santos, Nogueira, et al., 2021). As any competence, moral competence could be developed (Lind, 2016), but contrary to moral preferences and orientations, it does regress if not properly stimulated (Bataglia, 2010). Lind (2016) developed a questionnaire, the Moral Competence Test (MCT) formerly known as Moral Judgement Test (MJT), consisting of two ethical dilemmas, that allow the subject to show his competence in applying his moral structure in adverse situations (Bataglia, 2010). In the extended version of MCT the subject is confronted with three ethical dilemmas. According to Lind, the C-score which results from the application of the MCT, reflects the individuals' ability to choose arguments against or in favor of a moral option (Lind, 2016). Accordingly, a C-scores lower than 4.9 points indicate no or little moral competence; 5 and 9.9 points reflect very low moral competence; 10 and 19.9 points, less moral competence than is necessary for choosing moral options in a dilemma; 20 to 29.9 points, sufficient moral competence to solve most ethical dilemmas; and above 30 points, a high moral competence (Lind, 2018). The is regarded as a valid and a reliable questionnaire for measuring moral competence of health professions students.

When this instrument was applied to the same cohort of medical students in at least two moments of their undergraduate education, it showed a decline of the moral competence in different countries including Germany (Lind, 2000b), Australia (Hegazi & Wilson, 2013) , Portugal (Neves Feitosa et al., 2013), and Brazil (Feitosa et al., 2013; Schillinger, 2006), cementing the concept of moral decline as a student progresses through undergraduate medical programmes. Serodio et al., (2016) explains that any educational tool based on Kohlberg's cognitive-structural theory will be affected by moral motivation. Moral motivation is strongly associated with the system of values the individual builds for him/ herself. As values are an affective investment, they suggest that teaching aimed to improve the cognitive domain be best employed with strategies aimed at the affective aspect of moral behavior.

Way forward

Self at al., (1998) suggested that bioethics teaching could lead to improved moral development leading to better ethical practice and decision making (AlMahmoud et al., 2017; Greenberg et al., 2016; Liu et al., 2018; Savitha et al., 2018). Although the aim is to improve moral competence with Bioethics teaching, the effectiveness of bioethics teaching on medical students seem inconclusive (de la Garza et al., 2017; Fernandes et al., 2012; Martins et al., 2020). The findings of such studies question the role of bioethics education in developing decision-making and the change of opinion in medical students.

Literature shows that the existing teaching methods need to be modified to achieve this goal, with curricular and organizational revision of the medical course (Lind, 2000a; Serodio et al., 2016). Some studies have shown students struggles to relate to the situations described in theory when bioethics was taught prior to starting clerkships, and their desire to learn from positive role modelling in addition to formal teaching of bioethics concepts (AlMahmoud et al., 2017; Savitha et al., 2018). Educators have emphasized that bioethics education should be integrated throughout the whole duration of medical education (Asghari et al., 2009), and should be adjusted to each real caring situation (Abma et al., 2009). Serodio e al., (2016) posits that purely expositive classes do not attract students' attention. Thus, they recommend interactive learning activities to be incorporated more into bioethics teaching. Furthermore, they suggest inclusion of pedagogical interventions aimed at the affective aspect of moral behavior, use of cultural goods (plastic arts, literature, plays and movies) to enable students' reflection on the system of values they are building and how those will serve as a foundation for their personal and professional lives. Technical issues aside, studies reveal the importance of overcoming the considerable influence of the hidden training curriculum (Souza & Vaswani, 2020) which cannot be controlled and significantly undermines the consistency of bioethics teaching (Mahajan et al., 2016) which requires further investments into the teaching of bioethics concepts (AlMahmoud et al., 2017; Vergano et al., 2019). Moreover, several studies recommend facilitation of discussion on ethical issues experienced in clinical practice, resorting to moral deliberation, the exchange of experiences, and the sharing of concerns and doubts within a good learning environment (Abma et al., 2009; Asghari et al., 2009; Heidari & Ebrahimi, 2016; Roberts et al., 2007; Schillinger, 2006; Serodio et al., 2016; Zoboli, 2013).

Recent studies advocate for tailoring bioethics curricula to each culture (Tavares, 2022). Moreover, the diversity of present-day student body in a medical school must also be weighed in when teaching bioethics concepts. Disregarding the learner diversity causes bioethics educators to neglect important differences in the moral understanding of different religious and ethnic groups (Turner, 2001). Unresolved ethics issues can negatively affect the quality of patient care and the culture of healthcare organizations (Nelson et al., 2010). Thus, bioethics education must be mindful of the values it imposes upon the learner (Greenberg et al., 2016). Bioethics education should facilitate identification and understanding of cultural contexts for the educators to determine the best methods to obtain the intended learning outcomes. Medical educators have emphasized the need for a greater curricular allocation to enable the future physicians to address 'the wide range of cultural, environmental and ethical issues that will increasingly impinge on the problems of health' (GMC, 2009).

Conclusion

The current review reveals that heterogeneity still exists in the planning of the curricula, teaching, and assessment methods. There is an evident need for longitudinal and integrated programs making bioethics part of students' life as opposed to sporadic events at one phase of their education. The assessment of bioethics education is still a challenge, which depends mostly on reflections and development of portfolios. Collaborative teaching between ethicists and clinicians with more prominent teaching parallel to clerkships enables learners to discuss and reflect on everyday ethical issues. Contextually relevant bioethics curricula may advance the moral competence and the decision-making power of future clinicians.

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DIFFERENT ENTOMOLOGICAL TECHNIQUES USED FOR SURVEILLANCE OF LEISHMANIASIS VECTOR SAND FLIES (DIPTERA; PSYCHODIDAE); A REVIEW ON THE APPLICABLITY FOR SURVEILLANCE PROGRAMME

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Abstract

Sand flies (Diptera; Psychodidae) are vectors of *Leishmania*, a protozoan parasite that causes the disease leishmaniasis. Since the disease leishmaniasis is prevalent among people in some parts of the world, it is necessary to apply possible control measures to prevent further transmission of the disease. For that, effective vector surveillance plays a vital role. Depending on sand fly species, their resting and breeding habitats, and environmental characteristics, the suitability of an effective trapping method could vary. Therefore, this comparative review was conducted to examine the effectiveness of various entomological techniques for sampling sand fly immature and adults, focusing on their suitability in vector surveillance programs in different environmental habitats. Different field traps including hand operated aspirators, light traps, baited traps, and sticky traps, have been employed in different studies from various geographical areas. This review provides the pros and cons of different techniques, their applicability in different ecological settings, and their productivity in trapping sand flies, highlighting emerging advances of each technique, challenges, and possibilities for improvement of trapping strategies in respect to designing and implementing more productive sand fly surveillance which will ultimately affect the control and possible elimination of leishmaniasis.

***Key-words*:** Entomological techniques, Leishmaniasis, Sand flies, Vector control

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Introduction

Leishmaniasis is caused by a protozoan parasite from over 20 species that belongs to the genus *Leishmania* and is one of the vector-borne diseases that is transmitted through female Phlebotomine (Diptera: Psychodidae) sand flies. Leishmaniasis remains a significant public health concern in various parts of the world. Currently, leishmaniasis is endemic in 98 countries throughout the world, including countries in Africa, Europe, Asia, and America, which is considered a global burden. Nearly one million new cases are reported annually, while around 20,000–30,000 deaths occur per year (WHO, 2019).

Leishmaniasis vector sand flies have a wide distribution in temperate and warm climates and are classified under the family Psychodidae, genera *Phlebotomus* (Old World) and *Lutzomyia* (New World) (Akhoundi et al., 2016). They are small insects that feed on blood from a range of mammalian and avian hosts. Adult flies have a compact body size, typically measuring around 2-3 mm in length (Young & Duran, 1994). Only female sand flies become vectors when they are infected with *Leishmania* parasites, and they can infect mammals other than humans, like dogs and cats, which serve as reservoirs for the parasites (Pimenta et al., 1994; Almeida et al., 2003).

Tropical, temperate, and desert climatic regions are home to around 927–1000 species of sand flies that belong to three new-world genera, namely *Brumptomyia*, *Lutzomyia*, and *Warileya*, and three old-world genera, namely *Phlebotomus*, *Chinius*, and *Sergentomyia* (Picado et al., 2012; Lewis, 1978; Shimabukuro et al., 2017). Only a fraction of the around 800 species of sand flies are of medical significance, and specific sand fly species are capable of transmitting specific types of *Leishmania* parasites (Killick-Kendrick, 1999; Sacks, 2001).

Twenty two species of sand flies have been recorded from Sri Lanka in recent investigations, including sixteen species under the genus *Sergentomyia* that belong to four subgenera: *Grassomyia*, *Neophlebotomus*, *Parrotomyia*, and *Sergentomyia*, and four species of the genus *Phlebotomus* under three subgenera; *Anaphlebotomus*, *Euphlebotomus*, and *Phlebotomus* (Galgamuwa et al., 2018). There are various factors that affect the distribution of phlebotomine sand flies, including geographical differences, habitat availability, availability of vertebrate hosts, environmental factors, etc. (Chamaillé et al., 2010; Nieto et al., 2006).

Morphological identification through taxonomic characterization is still the gold stadrad for vecror identification. Before proceeding into morphological identification, it is necessary to pre-process. To get rid of excess hairs present on sand fly body and to remove excess castor oil (if sticky trap collection method is utilized), specimens should dehydrated by placing them in each of the 70% ethanol, 90% ethanol, absolute ethanol, and xylene for 5 min and to get clear observations through the microscope it is better to use 10% lactophenol for 1-2 hours before making slide mounts (Wijerathna & Gunathilaka, 2020b). Slide mounts can be prepared by dissecting the terminal part of the abdomen, wings, and entire head with a fine needle and mounting in Berlese's medium for later identification. Male and female sand flies can be distinguished by their external genitalia morphology. Morphological identification of sand flies involves a thorough examination of key morphological features under a microscope, such as head morphology (cibarial and pharyngeal structure arrangement), wing morphology, and abdominal appendage arrangements. In instances where morphological identification proves unfeasible, the sand fly identification is confirmed through DNA barcording.

Entomological techniques play a pivotal role in understanding the distribution, behaviour, and infection rates of sand fly vectors. These techniques provide valuable insights into the ecology of these insects

and guide for targeted control measures. To establish a comprehensive background for effective entomological surveillance of leishmaniasis vectors, it is crucial to understand the effective entomological techniques for leishmaniasis vector surveys.

In vector-borne disease programs, different surveillance tools are being used to capture the vectors. These techniques are allied with the behaviour and bionomic characteristics of the vectors, such as biting preference, biting time, resting habit, and attraction to specific chemical-based cures or the life cycle stage/s interested in the survey. Some techniques use animals as bait to attract adult insects, while others may use light sources or capture them through mechanical contact (e.g., Sticky traps). However, the effectiveness of all these methods would not be feasible in all geographic locations since there may be differences in the bionomics/behavioral aspects of vectors, and some techniques may not be feasible in some countries may be minimal due to unaffordability. Therefore, possible and cost-effective techniques should be evaluated at the local setup to identify the most appropriate techniques for surveillance purposes. This needs pilot studies and a thorough review of the literature relevant to field evaluations. Although there is information on the productivity of some techniques in capturing sand flies in sand fly surveys, a comparative review of the applicability of all possible techniques has not been documented. Therefore, this study provides a review of the use of different surveillance tools/methods used in the collection of leishmaniasis vector sand flies and a comparison of all these techniques in terms of productivity, pros/cons of the techniques, and efficiency in using them for disease surveillance and control programs.

Methodology

The review was conducted by online literature search in databases including Google Scholar, PubMed, National Library of Medicine (NIH), and Web of Science. The major research terms used in the search were “Leishmaniasis vector surveys”, “Entomological techniques for sand flies”,” sand fly collection” and some other linked search terms.

Results

Adult collection techniques

Aspirator collection

Sand flies found on various resting surfaces, whether indoors or outdoors, are gathered using an aspirator tube or a test tube. Due to the diminutive size of these sand flies, it is advisable to use a fine muslin gauge as a barrier filter between the glass and rubber tubing, rather than mosquito netting. This method proves effective in assessing the density of sand flies, and the outcomes are quantified in terms of man-hour density (MHD). Sampling the resting sand fly population across a range of habitats, including tree trunks, tree cavities, caves, rodent burrows, soil crevices, stables, chicken coops, and bedrooms, is a practical approach. It is always better to conduct using a battery-operated mechanical aspirator for sand fly collections since these insects carry hairy scales and rest in dusty places, which could lead to allergic reactions to the collectors, which these dust and sales get into the mouth and respiratory tract.

Research conducted in West Bengal, India, a region known for its cases of visceral leishmaniasis, reported that the hand collection technique proved to be the most efficient approach for assessing sand fly density due to its simplicity, time-saving nature, and consistency of results, even in adverse weather conditions (Hati et al., 1987). A survey conducted in the Republic of Moldova showed that, overall, 534 (66.9%) sand fly specimens were collected by manual aspirators out of a total of 793 specimens that were captured by both Centers for Disease Control and Prevention miniature light traps (CDC light traps) and manual aspirators (Șulești et al., 2021). Based on the investigation conducted in Sri Lanka,

it was found that the manual aspirator technique resulted in a substantial sand fly collection (Senanayake et al., 2015). Specifically, 5,073 sand flies were gathered using cattle-baited net traps, 368 from light traps, and 3,627 via the manual method. The manual collection revealed the presence of both *Phlebotomus argentipes* and *Sergentomyia zeylanica* species, with a slightly larger proportion of *P. argentipes*.

While effective, this method can be rather labour-intensive and, if not executed meticulously, may result in damage to the specimens drawn into the aspirator tubes. To mitigate allergen exposure, one can opt for battery-powered aspirators featuring gentle suction pressure. Sand flies gathered using this method can be safely transferred into paper cups lined with fine mesh netting for subsequent examination. The optimal collection periods typically span from dusk to dawn, yet they can be strategically scheduled to ascertain the resting locations and times of sand flies (Khoobdel, 2008; WHO, 2022).

Sticky trap

This is an inexpensive, quantitative method. Sticky traps have been widely employed in ecological studies to assess sand fly species densities across different habitats and seasons (Lane, 1993). Given the intermittent and brief flight patterns of sand flies, they frequently alight on randomly placed sticky traps becoming effectively entrapped. Typically, standard-sized sheets of sticky paper measuring 20×30 cm are utilized as sand fly traps, suspended with the convex side facing the ground at a height of 4-5 cm (Killick-Kendrick, 1999). In a colony, deploying ten such traps have been demonstrated to yield statistically valid results. The effectiveness of these traps can be further enhanced by coating the sticky papers with various vegetable oils (Díaz-Sáez et al., 2022). Oiled papers are strategically positioned wherever population sampling is required, including over and within soil cracks, rodent burrows, and both upright and flat surfaces in diverse environments such as forests, grasslands, trees, bushes, and even on walls within human dwellings and stables in rural areas. Once collected on oiled paper, sand flies can be gently removed using a soft-bristle brushes or camel hair brush (commonly used in entomological work for their gentle handling of small insects), which can later be dipped for conservation purposes or washed in a dilute detergent solution for immediate dissection or preservation for later identification. Flies captured on these sticky traps remain sufficiently fresh for dissection and the isolation of *Leishmania* parasites, as well as for age grading and blood meal identification (Killick-Kendrick, 1999). This enables researchers to make quantitative comparisons of sand fly densities caught within a standardized time frame.

Based on the findings of a study conducted in 2022, a total of 7,495 sand flies have been collected, with a higher quantity of flies, accounting for 60.3% of the total collection, obtained outdoors using sticky traps, in Spain. In this study, *Sergentomyia minuta* was identified as the predominant species overall, with sticky traps proving 2 to 4 times more efficient than CDC light traps in capturing this species across all studied environments (Díaz-Sáez et al., 2022). A research conducted in Northern Ethiopia, the statistical findings indicate that a significant difference existed in the mean density of *P. orientalis* captured between horizontally and vertically placed sticky traps. Notably, the horizontal sticky traps exhibited a relatively greater average density of *P. orientalis* (Gebresilassie, Kirstein, et al., 2015). This factor was further supported by an East African study (Elnaiem et al., 2020), which demonstrated a significant increase in the number of *P. orientalis* caught in horizontally placed sticky traps on the ground. This resulted in an eight-fold higher collection of *P. orientalis* on horizontal traps compared to vertical traps. Additionally, the study compared the quantities of *P. orientalis* captured on differently colored sticky traps, revealing that the vector showed a stronger attraction to white, yellow, transparent, and green traps as opposed to blue and red traps. In addition, a modified version of the sticky trap with a light source as an illuminated stick trap can be used in collecting flying insects such

as sand flies. These traps are designed to attract and capture insects using a combination of light and adhesive surfaces. More sand flies are caught on illuminated sticky traps. In this method, the box-shaped batteries are hung on the wall facing oiled paper and strung to the wall (Kalra & Bang, 1988).

While the sticky trap method offers certain advantages, including the avoidance of trap bias associated with CDC traps due to their light attraction, it has notable disadvantages. One limitation is the inability to collect live specimens using sticky traps (WHO, 2022). Additionally, high relative humidity conditions can impede the effective collection of sand flies over time (WHO, 2022). Furthermore, it's worth noting that the sticky trap method exhibits low sensitivity, necessitating the deployment of numerous traps to effectively capture sand flies (Asilian et al., 2003; Khoobdel, 2008).

Centers for Disease Control and Prevention miniature light traps (CDC light traps)

Battery-powered light traps are commonly employed for the nocturnal capture of sand flies in their quest for hosts, including gravid females and males. This collection method spans from dusk to dawn (Asilian et al., 2003; Khoobdel, 2008). It can be effectively utilized both indoors and outdoors to gather sand flies, with the added benefit of categorizing them based on the time of collection (Asilian et al., 2003; Khoobdel, 2008). The allure of the light source in the trap, positioned approximately 1 meter above the ground (Alexander et al., 1995), draws the sand flies towards it. Meanwhile, the bottom of the collection device hovers about 15 centimeters above the ground level (Alten et al., 2003). These traps are strategically placed in sleeping quarters, the primary area of habitation for most individuals. This strategic placement maximizes the capture of sand flies, including those that are either in a resting state or actively seeking a host.

In a research carried out in Sri Lanka, of the three other techniques (CDC light traps, sticky paper traps, and cattle-baited net traps) used the light trap was identified as more productive (Özbel et al., 2011). Similarly, in other countries, almost 75% of all field collection had been done using CDC light traps for *Phlebotomu*s spp (Amira et al., 2022; Cazan et al., 2021). Further, some research studies have indicated that the effectiveness of light traps varied with the colours of LED light and wavelengths of the light source. The light traps with 395 nm UV LEDs exhibited greater attractiveness when compared to light traps with LEDs of other colours, such as white, red, green, and blue (Gaglio et al., 2018). In addition, some modifications to the light traps, such as adhesive tapes (Amira et al., 2022), and CO_2 as an attractant, would enhance the trapping efficacy (Signorini et al., 2013; Kasap et al., 2009).

Typically, light trap collections predominantly capture females in search of blood meals. Consequently, this can lead to potential over estimations in population densities, as both live and damaged specimens are collected (Asilian et al., 2003; Khoobdel, 2008). Nevertheless, this approach offers a means to obtain quantitative estimates and facilitates the longitudinal evaluation of the effectiveness of vector control measures.

Funnel traps and digging of burrows

Funnel traps are designed to capture emerging sand flies from their breeding sites. These traps are made up of paper/ transparent sheets or glass funnels, and they are placed in possible breeding habitats like sandy areas, animal burrows, and the mouths of holes in the ground substrates. To get maximum productivity from these types of traps, it is necessary to search for suspected breeding grounds for sand flies (Kalra & Bang, 1988). In a research conducted in Colombia, conical-shaped sand fly emergence traps, equipped with nylon coverings and featuring a single opening for adult recovery, were employed and these emergence traps in the field accounted for 2.8% of the entire collection (Vivero et al., 2015). A research carried out in the southeastern region of Brazil to explore potential microenvironments

serving as breeding sites for the sand fly species *Lutzomyia longipalpis*, utilization of the emergence trap method yielded highly productive results (Casanova et al., 2013). A total of 160 sand flies were recorded in the surveyed locations (Casanova et al., 2013). Similarly, another study conducted in southern Brazil used adult emergence traps at the breeding sites of Phlebotomine sand flies and encountered a total of 67 sand flies from 5 different species, with *L. intermedia* being the most numerous species(Vieira et al., 2012). A study in the Judean Desert investigated the setting up of traps targeting both resting and breeding sites of sand flies. The results indicated that approximately two-thirds of the total collection was found in resting sites, while the remaining one-third emerged from breeding sites (Müller, Kravchenko, et al., 2011).

Alencar emergence traps were employed at ground level for capturing newly emerged adult sand flies in research conducted in southern Brazil and the mean of two sand flies captured per trap by Alancar emergence traps closely resembled the findings reported by (Alencar, 2007), where an average of 2.08 sand flies per trap was documented (Castro et al., 2015). Placing emergence traps in the right locations often relies on chance. For instance, a study from Colombia, managed to retrieve just 58 young sand flies from three different species during nearly a year of sampling (Ferro et al., 1997). In contrast, a study carried out in 1986 gathered more than 1500 specimens, predominantly *Phlebotomus perniciosus*, within a single month (Bettini et al., 1986). Therefore, the efficacy and productivity of the technique may depend on various factors such as geographical locations, type of breeding/resting habitat target, seasonality, and environmental factors. Therefore, all these factors are to be considered in selecting emergence traps as a surveillance tool for leishmaniasis vectors in a disease-endemic area.

Animal baited collection

The effectiveness of this approach varies depending on the research objective. Given that sand flies exhibit clustered distributions and that even biting flies have varying degrees of zoophilic behaviour, conducting population sampling across different cattle sheds and stables throughout the entire village can provide valuable insights into species predominance and cluster identification. Subsequent comparative studies can be conducted within these high-prevalence clusters to investigate seasonal activities. Employing bait collections involving cattle, humans, and other domestic animals, using aspirator tubes during nighttime, can reveal the host range of these species. Nonetheless, it's important to note that human bait collection in endemic areas carries certain risks.

In situations where sand flies exhibit a strong preference for animals, this approach proves valuable in gathering sand fly specimens that settle on trap walls after consuming bait animals. This method serves as a valuable tool for acquiring specimens for entomological research, including meticulous investigations into host preferences and assessments of insecticide resistance (Asilian et al., 2003; Khoobdel, 2008). Additionally, there are commercially accessible alternative trap designs.

According to a study in Sri Lanka, the primary contributor to the total sand fly collection in the study sites was cattle-baited net traps (CBNT), accounting for 91.28%, followed by sticky traps at 8.42%, and hand collection, which accounted for a minimal 0.3%. As well as all specimens captured using CBNT were identified as *P. argentipes* (Wijerathna et al., 2021). Another study that was conducted in Sri Lanka revealed that the CBNT technique was also identified as the most productive method for capturing sand flies. In that study, two techniques were employed: CBNT and Indoor Hand Collection (IHC) (Mallawarachchi et al., 2021).

In a study conducted in northern Ethiopia, researchers conducted experiments to assess the preference of *P. orientalis* for different bait types, including humans, domestic animals, and small wild animals.

The findings revealed a notable variation in attraction levels towards various baits. Specifically, traps baited with cows and donkeys exhibited significantly higher levels of attraction compared to other bait types. Concerning small wild animals, it was observed that a higher number of *P. orientalis* females were drawn to squirrels, followed by hares, gerbils, and spiny rats (Gebresilassie, Yared, et al., 2015).

Other traps for adult sand fly collection

In 1939, Shannon devised a mosquito capture method involving the use of white fabric, illumination, and animal bait to lure in mosquitoes (Shannon, 1939). Over time, and through several modifications, researchers have employed this trap in investigations involving mosquitoes and phlebotomines, aiming to confirm their anthropophily (Maroli et al., 1997) . In Brazil, an experiment was conducted to assess the relative attractiveness of the Black Shannon Trap (BST) and the White Shannon Trap (WST) for capturing sand flies. Multiple sets of traps were positioned nearby in front of cave entrances across four sites. The findings of this study demonstrated that BST exhibited significantly higher capture rates compared to WST, particularly in the case of anthropophilic and fly species (Galati et al., 2001). In a study conducted in Brazilian Amazon Basin, both white and black Shannon traps were utilized with lighting. Notably, the species drawn to the black trap differed from those drawn to the white trap, with the black trap capturing more species than the white trap (Brilhante et al., 2017).

Another attempt was evaluated to compare the efficacy of sand fly traps utilizing various baits, including blood, urine, and fruit (Mong'are et al., 2015). The outcomes obtained from the blood-baited traps indicated that the utilization of goat blood attracted the greatest number of sand flies, followed by sheep blood, cattle blood, and chicken blood. Concerning urine-baited traps, the sheep urine-baited trap captured the highest number of sand flies, followed by the goat blood-baited trap, while the cattle urine-baited trap attracted the fewest sand flies. Additionally, the results obtained from fruit-baited traps showed that the trap baited with bananas captured the highest number of sand flies, followed by mango, apple, and grapes.

A study evaluated the efficient sand fly trapping for 56 distinct flowering plant species, along with five plant species contaminated with diverse honeydew types. According to the attraction index employed, the top three plants found to be most appealing in this study were *Ochradenus baccatus*, *Prosopis farcta*, and *Tamirix nilotica*, among the flowering plants (Müller, Revay, et al., 2011).

Collection of adult female sand flies for xenomonitoring and blood meal analysis

Xenomonitoring and blood meal analysis are essential techniques for enhancing vector surveillance programs. Xenomonitoring involves detecting the presence of *Leishmania* parasites in vectors, which helps in assessing the transmission risk in a particular area (Cameron & Ramesh, 2020). Blood meal analysis, on the other hand, identifies the source of blood that the vector has fed on, providing insights into host preferences and the potential zoonotic transmission cycle of leishmaniasis. When applying collection methods for sand flies, it is important to consider the purpose of collection, especially in cases where the objective is to detect parasites/ blood meal in vectors. Therefore, should focus on several factors including the most appropriate technique that collects blood-fed females since those will only target for screening of infection and these techniques must ensure that the pathogen's DNA/RNA is preserved during collection (McIntyre-Nolan et al., 2023). Depending on the technique may affect the preservation of genetic materials in sand flies due to varying conditions exhibited in various collection methods. For example, the hand collection technique involves immediate capture of sand flies and processing may have a varying degree of preservation of genetic materials than those trapped in CDC light traps where sand flies are trapped over 12 hours before proceeding collection into preservation (McIntyre-Nolan et al., 2023). According to a study by McIntyre-Nolan et al. (2023),

while CDC light traps collected a lower proportion of P*hlebotomus argentipes* females containing human DNA compared to mouth aspiration, there was no significant difference in the absolute number of such females captured. This outcome aligns with expectations, as CDC-LTs typically capture more unfed or gravid females rather than blood-fed sand flies (Alten et al., 2015). Similar findings were reported in Bihar (DINESH et al., 2008), where CDC light traps captured proportionally fewer blood-fed *P. argentipes* females than mouth aspirations.

Sampling of immature stages

Direct method

In this approach, soil samples are taken from the potential larval habitats and examined under 40 x magnification using a binocular microscope (Kalra & Bang, 1988). According to a study conducted in Colombia, Phlebotomine sand flies were acquired through direct examination of soil samples, constituting approximately 78.9% of the entire sand fly collection in that study (Vivero et al., 2015). Another study conducted in Brazil has stated that direct examination is the most effective method, with the lowest mortality rate in the immature stages (Alencar et al., 2011). Similarly, a study in Brazil has indicated the sand fly yield was successfully achieved through direct observation (Sangiorgi et al., 2012). However, the use of this technique in surveillance is rather not frequent, since identification of potential breeding habitats for sand flies could be challenging and the examination of soil samples may be time-consuming and tedious.

Floatation approach

The floatation method involves the mixing of soil samples collected from suspected breeding habitats with a saturated solution consisting of three parts sugar and five parts water. This will allow lightweight sand fly larvae and pupae to float in water through sinking soil and other debris to the bottom of the solution (Kalra & Bang, 1988).

In a study conducted by Hanson (Hanson, 1961), a method known as 'floatation-sieving' was employed to collect nearly 2,200 immature sand flies, primarily from the soil surrounding trees characterized by buttress roots in Panama. In a research conducted in Sri Lanka, sand fly immature sampling was carried out using these two methods, and sand fly pupae were retrieved from soil samples collected from rice paddy mudflats (Wijerathna & Gunathilaka, 2020). According to the research conducted in Brazil, it was determined that the floatation sieving method proved to be the most effective in terms of both the total count of immature sand flies extracted and the volume of substrate processed (Alencar et al., 2011). One advantage of this method is that larvae can be collected live and reared under suitable conditions in an insectary to identify species levels if needed because species identification during larval stage is somewhat difficult and tedious.

Discussion

Entomological techniques play a pivotal role in understanding the distribution, behavior, and infection rates of sand fly vectors. These techniques provide valuable insights into the ecology of these insects and guide targeted control measures. The selection of entomological techniques depends on factors such as the study objectives, habitat characteristics, and limitations of the collection technique. Various adult collection techniques, including aspirator collection, sticky traps, light traps, funnel traps, digging of burrows, and animal-baited collection, have been employed for sand fly surveillance.

Sticky traps offer an inexpensive and quantitative method for assessing sand fly densities, although they have limitations in collecting live specimens and exhibit low sensitivity. Sticky traps have been used in various geographical areas, including Sri Lanka (Özbel et al., 2011), Algeria (Amira et al., 2022), and

Ethiopia (Gebresilassie, Kirstein, et al., 2015), to evaluate their effectiveness in capturing insects like sand flies. These studies suggest various degrees of efficiency with sticky traps, resulting in a considerable percentage of sand fly catches in some areas. Furthermore, the colour of the sticky traps and the positioning of these traps show up to affect their performance in capturing sand flies, as observed in East Africa (Elnaiem et al., 2020), suggesting horizontally placed light colours such as white, yellow, and transparent are more positive for sand fly capture. Simplicity, versatility, and the possibility of use for comparative studies in different sand fly breeding and resting habitat types make it advantageous to use sticky traps for various studies while there are some difficulties to use during adverse weather conditions like heavy rains.

Light traps, particularly battery-powered ones, are commonly used for nocturnal sand fly collection and provide quantitative estimates of sand fly populations. The CDC light traps are considered a convenient trapping method because of their easy set-up and field operation. Therefore, many studies have been done to evaluate the efficiency of light traps, and such studies have shown more effective results from various geographical localities with different climatic profiles. The efficiency of LED light traps with various light colours and wavelengths has revealed that light traps with 395 nm UV LEDs are more efficient in capturing phlebotomine sand fly species in the Mediterranean area when compared to the other light colours and wavelengths (Gaglio et al., 2018). This could be due to some colours and specific wavelengths that might be sensitive to their body receptors. Some studies revealed that depending on the sand fly species, the attractiveness varies with the colour of light. A study discovered that red LED attracts *Phlebotomus papatasi* more, whereas *Nyssomyia whitmani* and *Lutzomyia longipalpis* appear to be more drawn to blue and green LED, respectively (Hoel et al., 2007). In some instances, light traps have shown more attractiveness towards females of some groups of sand flies including *Lutzomyia*, and sub-genus *Psychodopygus*, which are phototropic. Since light traps attract other insects rather than sand flies, that might be a reason sand flies get damaged due to the aggressive movements of other larger-sized insects (Alexander, 2000).

Animal-baited traps, in general, reveal the host range of sand fly species. A proper understanding of the feeding and host preferences of sand flies provides important criteria regarding the vector-host relationship and clarifies the epidemiological trends of disease transmission (Elaagip et al., 2020). Therefore, the use of different animal baits to capture sand flies would provide the blood meal preference of the sand flies in an area for different hosts. Most of the time the researchers have used cattle-baited traps for sand fly collections. Few studies have attempted to use different baits including humans, domestic animals, and small wild animals (Gebresilassie, Yared, et al., 2015), use of the blood of different mammals such as goats, sheep, cattle, and chicken (Mong'are et al., 2015), baits including blood, urine, and fruit (Mong'are et al., 2015) for sand fly capturing. Although Human landing collections proved to be productive methods to capture anthrophilic insects like sand flies and mosquitoes, there is a risk of infection transmission.

The cattle-baited traps proved to be one of the most efficient ways to collect various species of sand flies at once since those attract insects toward their vertebrate host. Using these kinds of animal-baited traps helps to get some insights into host vector relationships, which will help to get more ideas about disease transmission dynamics and find out more and less preferable host species. Researchers are focusing on the use of a variety of baits to attract sand flies, and those findings give more positive results employing capturing a higher number of sand flies. A study concluded that goat blood was the most attractive bait for capturing sand flies followed by other baits including sheep, cattle, and chicken blood (Mong'are et al., 2015).

Emergence traps facilitate the identification of various types of breeding habitats, which will help to get an idea of which kinds of ground substrates provide the most suitable environment for sand fly immatures. Therefore, when focusing on the elimination of sand fly breeding habitats, it is suggested to focus on target habitats. Trap efficiency may vary depending on the design of the trap and environmental factors.

Direct examination is a preferable method when contrasting various sand fly larval collection techniques, such as direct observation from soil samples, floatation, and floatation-sieving methods. The results from Brazil (Alencar et al., 2011) show that it has low death rates in larvae and pupae stages, suggesting effective protection and accurate identification of sand fly larvae or pupae. Although the direct examination is proven to be a non-invasive method, it has some limitations, like being time-consuming and labor-intensive, and during the direct observation process, non-developed immatures may be missed. Comparative studies conducted in Brazil have shown that the floatation-sieving method surpass other methods both in terms of yield as well as processing efficiency (Alencar et al., 2011). Its simplicity, reliable time-saving nature, and low cost make it a useful technique to collect both larvae and pupae.

The effectiveness and reliability of different sampling techniques for sand fly larvae and adult flies might vary depending on the geographical region and the characteristics of the sampling localities where these traps are employed. Therefore, doing comparative studies to find the most suitable trapping approach for specific study objectives and environmental conditions would be appropriate to enhance the overall effectiveness of sand fly surveillance and control efforts.

The high effectiveness of animal-baited traps such as CBNT for sand fly collection proved to have considerable implications for field-based vector surveillance and control efforts. By identifying the productivity of each trapping technique, researchers and public health officials will be able to plan surveillance strategies and conduct targeted control measures to reduce vector sand fly populations and prevent leishmaniasis transmission.

It is necessary to consider the purpose of the study when choosing the collection technique. For morphological identification, one should be aware of the choice of a method that will preserve the insect's physical structures and that will be used for species-wise separation. Aspirator collection and baited trap collection would be most suitable since other techniques like CDC light traps and sticky trap collection may damage the sand fly physical structures in trapping and collecting. On the other hand, molecular identification, which involves extracting DNA from the captured specimens, requires the preservation of the genetic material. Techniques like CDC light traps, funnel traps, and animal-baited traps may be useful here, but care must be taken to ensure that the collected samples are preserved under conditions that prevent the degradation of genetic materials. When considering xenomonitoring purposes, the collection method must be optimized to target blood fed or gravid females, as these are more likely to carry infectious agents. Animal-baited traps and aspirators can target blood-fed flies effectively, while CDC light traps may capture more unfed or gravid flies, as noted in previous studies.

Since there are many factors, such as locality, environmental factors, and species composition within that geographical region, that influence the efficiency of different techniques, it's advisable to conduct local studies to determine the most effective baits for specific regions and sand fly species. Climatic factors have a great influence on sand fly population density and distribution around different habitats. Due to high rainfall, breeding grounds get distracted, which reduces the survival of sand fly immature in the ground (Alexander, 2000), and heavy water flow may lead to the displacement of sand fly larval

and pupal stages to places with inappropriate ecological conditions. Continuous rainfall may reduce the availability of resting places for sand flies and affect flight activity, along with other climatic factors including temperature, wind, and humidity. Therefore, it is better to consider specific ecological and environmental conditions of each habitat before selecting a collection method since sand flies exhibit diverse behavioral and ecological traits that are influenced by habitat characteristics such as vegetation cover, humidity, proximity to human or animal hosts, and the presence of breeding grounds and resting places. For example, in places where suitable breeding grounds like mud flats, grounds with decaying organic matter, and floors of animal shelters (Wijerathna & Gunathilaka, 2020) digging of burrows and funnel traps as well as sticky traps may be effective in capturing emerging sand flies. In rural environments where cattle or other animals are abundant, animal-baited traps, including cattle-baited net traps, may prove more effective in capturing host-seeking sand flies that feed on livestock. In the case of areas with populated human settlements in urban areas, CDC light traps and aspirator collection would be great approaches as those methods efficiently target sand flies inside homes.

Conclusion

In conclusion, this comprehensive review highlights the efficacy of diverse techniques used for sand fly vector surveillance, each with its own pros and cons depending on the purpose of sampling. Each method has its applicability depending on the purpose of the surveillance and environmental contexts. CDC light traps are highly favored for indoor collections. In contrast, aspirator collections offer higher precision in capturing blood-fed females, useful for blood meal analysis, while animal-baited traps excel in rural and livestock environments. Sticky traps and funnel traps can be adapted for specific environmental conditions, particularly in outdoor or natural settings. A comprehensive understanding of these techniques and their comparative evaluation is essential for developing targeted control strategies and mitigating the burden of leishmaniasis globally.

Acknowledgement

We acknowledge the University of Kelaniya, Research Council Funded grant RC/SROG/2021/03 for supporting this research work.

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SCIENCE

SUSTAINABLE SOLID WASTE MANAGEMENT IN DEVELOPING COUNTRIES: CONVERTING URBAN WOOD, GARDEN, FOOD, AND CARDBOARD WASTE INTO BIOCHAR USING PYROLYSIS

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Abstract

Effective municipal solid waste (MSW) management presents a critical challenge globally, exacerbated by rapid urbanization, population growth, and shifting consumption patterns. This review paper focuses on the sustainable management of food, wood, garden, and cardboard waste (FW, GWW, and CW) in developing countries, with a particular emphasis on Sri Lanka. The review highlights the urgent need for innovative solutions due to the inefficiencies of current waste management practices, which primarily involve open dumping and limited composting and recycling. The objective of this review is to evaluate the potential of pyrolysis technology in converting these waste streams into biochar, a valuable byproduct with numerous environmental, agricultural, and industrial applications. The methodology involved a comprehensive literature review using resources like Google Scholar and Science Direct, focusing on the application of pyrolysis for transforming waste into biochar. Key findings indicate that pyrolysis offers a viable solution by converting waste into biochar, a substance with beneficial applications in agriculture and environmental management. Pyrolysis techniques are noted for their potential to reduce methane emissions, improve soil fertility, and enhance waste-to-energy conversion. The review recommends enhancing waste segregation and collection infrastructure, promoting sustainable waste management techniques, increasing public awareness, and investing in research and development. Policy support and public-private partnerships are also essential for improving waste management practices. Future research should explore circular economy principles, the long-term impacts of current practices, and advanced waste processing technologies. Implementing these recommendations can significantly advance MSW management, mitigate environmental pollution, and promote public health, fostering more sustainable urban environments.

Keywords: Biochar, Biomass (Food and garden waste), Corrugated Cardboard, Municipal solid waste (MSW), Pyrolysis

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ADVANCES IN FLEXIBLE ORGANIC FIELD-EFFECT TRANSISTORS IN THE APPLICATION OF ARTIFICIAL SKIN

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Abstract

Flexible organic field-effect transistors (FOFETs) represent a breakthrough in the domain of flexible electronics, encompassing roll able displays, bendable smart cards, flexible sensors, and influencing the development of artificial skin. In the realm of artificial skin, flexible electronic systems have achieved remarkable advancements for instance in stretch ability, from 30% up to 300%, through rational structural designs involving rigid inorganic matter. Recent studies highlight the practical applications of these technologies in prosthetics, robotics, and wearable health monitoring devices, particularly in the form of pressure sensors, temperature sensors, and bioelectronic interfaces. OFET can work inside a human body because of their mechanical resilience. The skin-like sensing, skin-biothermal, and self-healing properties endow them with broadband applications. Integration of machine learning and soft robotics has further improved their performance, making them more reliable and efficient in such a way that leading the path to exciting advancements in artificial skin, but it is also important to recognize that many challenges remain including long-term stability and biocompatibility. This review article provides a comprehensive overview of the state-of-the-art advancements in flexible OFETs, underscoring their transformative potential in artificial skin applications. It also addresses the current challenges in the field, including issues related to long-term stability, biocompatibility, and the need for seamless integration with biological tissues. Additionally, the article discusses the potential for future research and development, highlighting the interdisciplinary nature of this domain that bridges material science, electronic engineering, and biomedical technology. The insights provided in this review pave the way for continued innovation, fostering advancements that could revolutionize the fields of prosthetics, robotics, and wearable health technologies.

Keywords: Artificial skin, Flexible electronics, Flexible organic field effect transistors, FOEFT, Flexible skin.

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Introduction

Recent advancements in flexible and stretchable organic field-effect transistors (OFETs) have marked significant milestones in the field of flexible electronics as in Fig. 01 (Zhang et al., 2023; Tsukuru et al., 2014; Brohem et al., 2010; Augestine, 2018; Lucarotti et al., 2013; Xu et al., 2023; Feng et al., 2024). It depicts the development of electronic skin technology over time. The timeline illustrates significant turning points and developments in e-skin, beginning with preliminary ideas and research in the early 2000s. Early prototypes, enhanced biocompatibility, translucent, stretchy, and self-healing e-skins, as well as biodegradable and self-powering e-skins, are some of these achievements and serve as a visual representation of the development in this sector throughout time, from early concepts to more advanced and useful e-skin technology. These advanced devices, characterized by their remarkable adaptability and electronic properties, are paving the way for groundbreaking applications in various domains, including rollable displays, bendable smart cards, and, notably, artificial skin (Zhang et al., 2023). The development of artificial skin, in particular, has profound implications for wearable electronics and health monitoring systems, offering enhanced functionality and improved integration with biological tissues (Sabrina, 2022). These advancements are primarily driven by the use of materials such as polymers (Mokhtar et al., 2020), carbon nanotubes, and graphene (Pyo et al., 2022) combined with stretchable substrates like polydimethylsiloxane (PDMS) and thermoplastic polyurethane (TPU). Such combinations of equipped OFETs with the ability to bend and stretch without compromising their structural integrity and electronic properties, thereby making them ideal for artificial skin applications (Rogers, 2023).

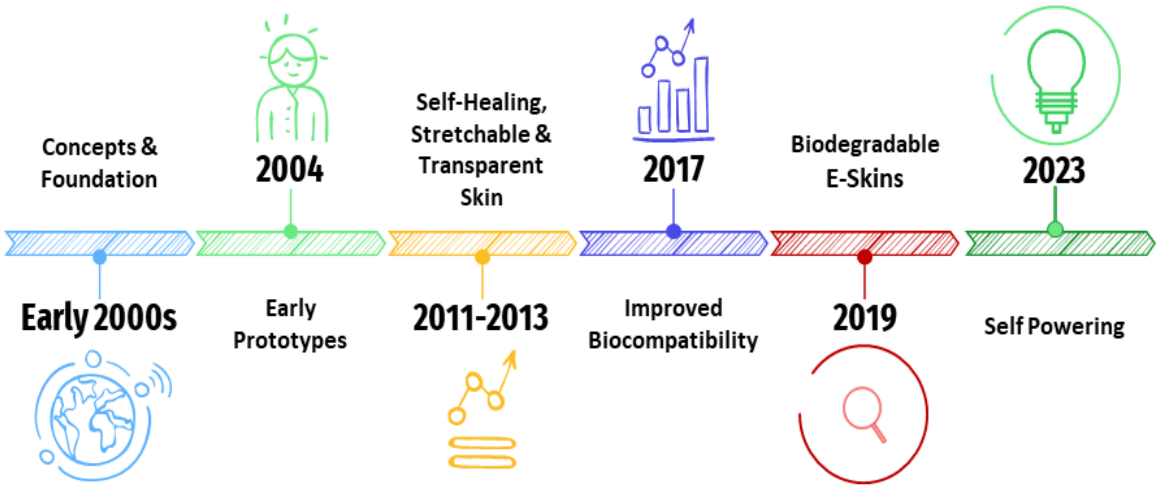

Figure 01: Developments of Artificial Skin.

Innovative designs including wavy or serpentine patterns, allow materials to bend and stretch without damage (Tee et al., 2012) while ultra-thin OFETs just a few nanometers thick, reduce bending stress and improve flexibility (Wang et al., 2017). Strategically placing rigid and flexible parts enhances performance, ensuring these flexible organic field-effect transistors' (FOFETs) work effectively, even after being bent thousands of times (Someya et al., 2016; Hammock et al., 2013) allowing them to be applicable in many sectors as shown in Fig. 02.

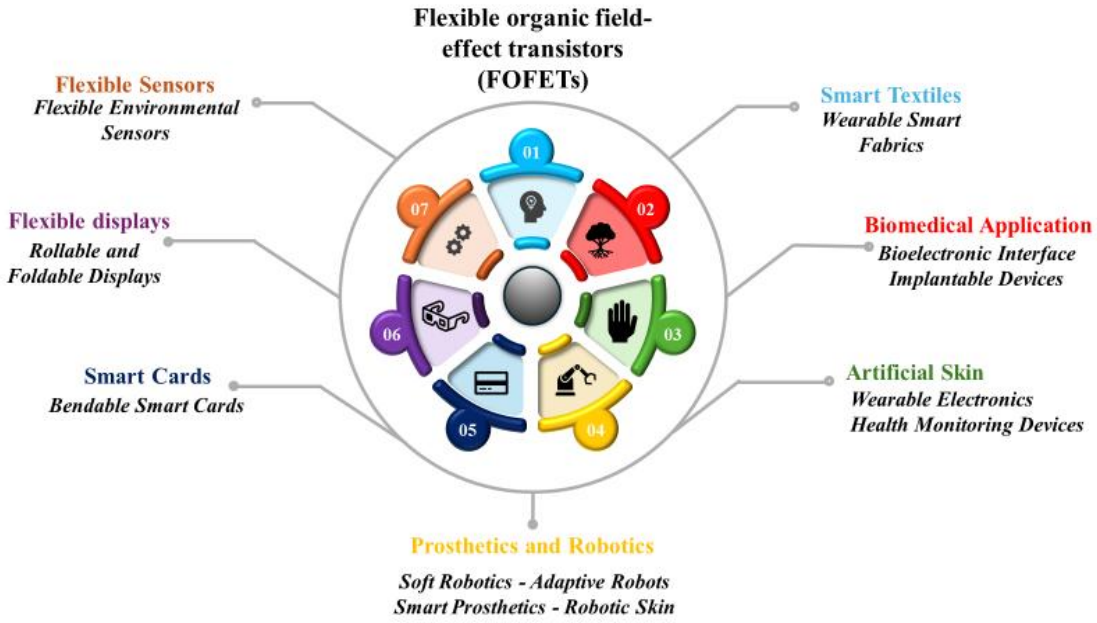

Figure 02: Applications of the FOFETs.

The integration of advanced materials and smart designs has enhanced the sensitivity and durability of FOFETs, making them highly accurate in detecting various inputs such as pressure and temperature (Someya et al., 2016). For example, ultra-thin FOFETs can bend without breaking, making them highly sensitive to minor variations essential for artificial skin applications (Hammock et al., 2013). Researchers have further improved FOFETs by incorporating special materials like polymer semiconductors and nanomaterials, including carbon nanotubes and graphene, which increase their lifespan and ensure reliable performance (Hammock et al., 2013; Tee et al., 2012; Yokota et al., 2016).

Adhesion and conformability are critical for the application and performance of artificial skin. These properties ensure that the artificial skin can adhere seamlessly to irregular, pliable, and dynamic surfaces, maintaining close contact, which is essential for accurate sensing and reliable functionality (Sugano et al., 2018). A notable study demonstrated a flexible, ultra-thin electronic skin that adheres well to human skin, providing good contact for precise monitoring of signals. Developing these materials typically involves incorporating soft stretchable substrate and gold nano mesh electrodes, ensuring the mechanical compliance and durability (Wagner et al., 2004). Easy integration of artificial skin with existing technologies and systems is essential for its widespread application and effectiveness. Recent advancements include the development of multi-functional smart e-skins that can detect temperature, humidity, strain, and pressure simultaneously (Tee et al., 2012). For instance, Gabrial and coworkers developed a prosthetic artificial skin that integrates multiple sensory modules to provide comprehensive feedback, crucial for smart prosthetics and interactive devices (Gabriel et al., 2022).

New developments in FOFETs offer a promising solution for large-scale, cost-effective artificial skin production. However, fabricating large-scale manufacturing products with high performance remains challenging due to the lack of uniformity and reproducibility in the manufacturing process. On top of that, building large-area soft OFETs with reliable performance is too challenging and quite challenging to produce big and soft transistors which ensure that they would perform in the same reliable manner. This review article provides a comprehensive overview of recent progress in flexible OFETs, focusing on their applications in artificial skin. It delves into material innovations, design strategies, and fabrication techniques, as well as the challenges and future directions in this rapidly evolving field.

Materials and Methods

This section's focus revolves around a methodological framework designed to bridge the gap between current research on FOFETs and their practical implementation in artificial skin applications. FOFET technology holds significant promise for revolutionizing fields such as prosthetics and wearable electronics by offering unprecedented flexibility and sensitivity. Accordingly, insights from cutting-edge materials science and bioengineering technologies to address critical challenges in durability, biocompatibility, and signal processing.

Flexibility and Stretch ability

Recent advancements in flexible and stretchable FOFETs have significantly propelled the development of artificial skin. The application of FOFETs is crucial for wearable electronics and health monitoring devices.

The stretchable electrode structures shown in Fig. 03 (Pyo et al., 2022) illustrate how carbon nanotubes and graphene enhance the adaptability of FOFETs, enabling their use as interconnects in high-density transistor arrays. Self-healing materials have also been developed to improve the durability of flexible electronics, incorporating elements such as Diels-Alder chemistry (Tee et al., 2012) for enhanced performance in wearable applications.

Someya and coworkers have discussed the progression of flexible electronics capable of maintaining functionality under mechanical strain, emphasizing their potential in various applications (Someya et al., 2016). Wang et al. 2017 has introduced a highly stretchable, transparent, and conductive polymer confined within an elastomeric matrix that is suitable for artificial skin applications due to its exceptional mechanical and electrical properties (Wang et al., 2017). They developed a highly stretchable, transparent and conductive polymer which has very high mechanical and electrical conductivity applicable in artificial skin area.

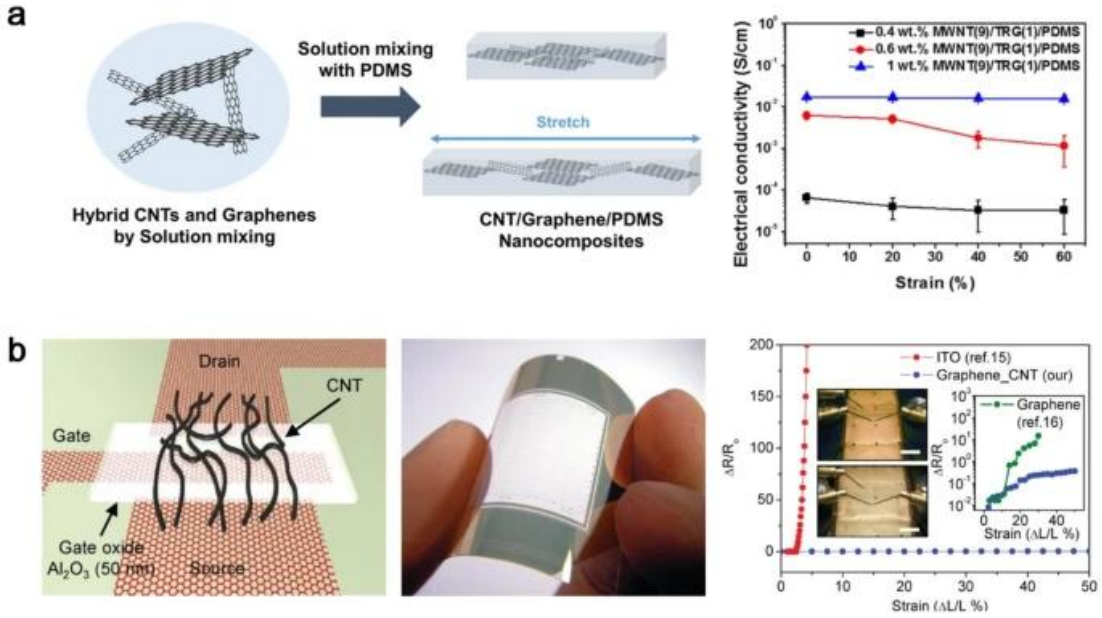

Figure 03: (a) Stretchable electrode based on carbon nanotube (CNT); (b) Flexible transistor utilizing carbon nanotube channel, graphene electrodes, and Aluminum Oxide (Al_2O_3). Re-printed with permission from [Pyo et al., 2022].

These characteristics make it possible to use it as interconnects for field-effect transistor arrays with a density five times as compared with tortuously wave-like interconnects produced by lithography. These advancements hold significant steps towards the creation of durable and high-performance artificial skin for future wearable electronics and medical devices (Roy et al., 2022).

Sensory Specificity, Sensitivity and Self-Powering

The sensitivity of OFETs in detecting subtle pressure, temperature, and humidity changes was assessed using precise techniques like signal-to-noise ratio analysis and calibration curve generation. Someya and coworkers showcased the high sensitivity of OFETs such as a high-performance tactile sensor based on a piezoelectric polymer polyvinylidene fluoride (PVDF) coupled to an OFETS with ultra-low voltage operation in perceiving tactile and environmental stimuli compared to traditional sensors (Someya et al., 2005).

Recently Lipomi and coworkers showed a correlation between the electrical performance of the OFET devices and their sensory responses (Lipomi et al., 2011). Consequently, Tsukuru and coworkers employed an extended-gate-type OFET called immunosensor and rely on anti human IgG detection to be done in water **(**Tsukuru et al., 2014**)**. In this study, IgG concentration has been correlated with connective tissue diseases. Organic transistors of the sensor are isolated in the device thereby avoiding degradation of organic transistors by water. Moreover, a gold (Au) layer has been implemented on plastic film as an extended-gate electrode to modify the surface of the immunosensing for the detection of Nitrogen Dioxide (NO_2) gas using Dinitro phenylenediamine (DNT) at room temperature.

A schematic of this extended-gate OFET design is presented in Fig. 04. Fig. 04(a) represents a schematic of the extended-gate type organic transistor, (b) depicts the photograph of the sensing part, and (c) depicts the reaction scheme for the immobilization of streptavidin on the surface of the extended-gate electrode.

Hammock et al. reported the advancements in materials and design strategies that have enhanced the sensing capabilities of OFETs. This study emphasized the integration of nanomaterials into polymer matrices, which has improved the mechanical strength, reported by Sugano and flexibility, reported by Tee, of OFETs. These enhancements not only prolong the operational lifespan of the device but also ensures their performances under condition for bending and stretching. Such improvements are vital for creating wearable sensors and medical devices that demand more sensitive (Hammock et al., 2013; Tee et al., 2012).

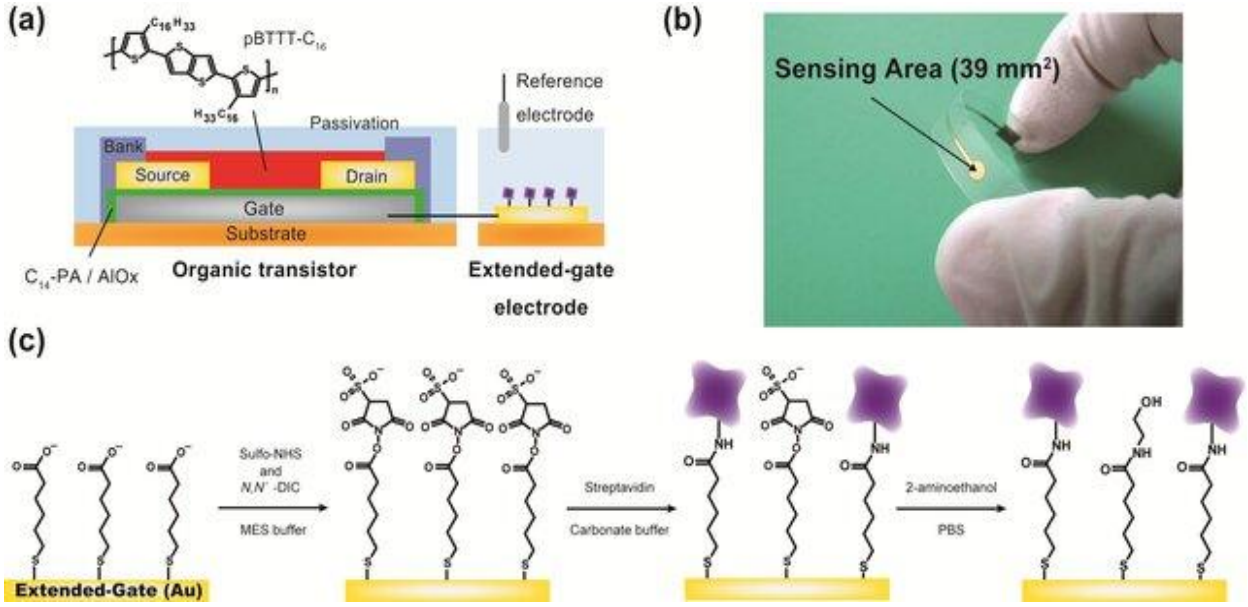

Figure 04: (a) Schematic structure of the extended-gate type organic transistor; (b) Photograph of the sensing part; and (c) The reaction scheme for the immobilization of streptavidin on the surface of the extended-gate electrode. Re-printed with permission from [Tsukuru et al., 2014].

Consequently, improving flexibility through the incorporation of wavy or serpentine patterns, allowing the devices to bend and stretch without sustaining damage (Someya et al., 2016). According to the design strategy which used by Someya and coworkers ensures that the transistors maintain high performance and sensitivity under mechanical stress (value), with the strategic placement of rigid and flexible components further enhancing their ability to accurately detect and respond to various physical signals. The results stress upon the topics like muscles and joints of the human body and there is no word regarding the links with electronic devices or transistors.

A single work proposed a dual signal amplification system that utilizes the presence of an aptamer biosensor to identify the presence of very small amounts of the bacteria Salmonella typhimurium. Using HCR and G-quadruplex DNAzyme bioassay, the biosensor got the detection limit of 10 CFU/mL that is 10-100 times more sensitive than previously used aptamer based approaches. In the case of self powering, low power consuming OFET's and integration of Nano Generators(NGs) are focused area in the research field(Ren et al., 2018). Meanwhile, Chen and team used triboelectric nanogenerator (TENG) for an advanced energy-harvesting device that efficiently converts mechanical energy into electrical energy through the triboelectric effect (Chen et al., 2019). Reason advancements in TENG have led to self-healing, stretchable, and shape adaptive areas (Cheng et al., 2022). Building high performing nanogenerators and low power consumption is a concerned area in research in self-powering OFET's when it comes with artificial skins.

Adhesion and Conformability

Adhesion and conformability are critical for the application and performance of artificial skin, as those properties ensure that the artificial skin can adhere seamlessly to irregular, pliable, and dynamic surfaces, maintaining close contact, which is essential for accurate sensing and reliable functionality.

One notable study by Someya et al. demonstrated a flexible, ultra-thin electronic skin that adheres well to human skin, providing a good contact that allows for precise monitoring of pressure variation signals (Someya et al., 2005). This electronic skin is constructed using a polyimide substrate and gold nano mesh electrodes, providing both flexibility and durability. Another example by Kim's group (Kim et al., 2011) involves an epidermal electronic system that integrates closely with the skin, adhering without adhesives due to its ultra-thin, flexible nature. This system can monitor vital signs such as temperature and heart rate with high fidelity.
The development of elastomers like polydimethylsiloxane (PDMS), polyurethane (PU), natural rubber (NR), styrene butadiene rubber (SBR) and ethylene-propylene-diene monomer (EPDM) typically involves incorporating soft, stretchable substrates and ensuring the mechanical compliance of all components.

Techniques such as the use of elastomeric substrates, like PDMS, and the incorporation of serpentine or kirigami patterns in the material design, enhance both adhesion and conformability. These approaches allow the artificial skin to maintain intimate contact with curved and moving surfaces, critical for applications in wearable health monitors, prosthetics, and soft robotics (Kim et al., 2011; Someya et al., 2005; Kaltenbrunner et al., 2010).

Easy Integration

Easy integration of artificial skin with existing technologies and systems is essential for its widespread application and effectiveness. For an artificial skin designed with flexible OFETs to emulate the complex sensory capabilities of natural skin, it must seamlessly interface with bio-signals and various physical stimuli.

Recent advancements include the development of multi-functional smart e-skins that can detect temperature, humidity, strain, and pressure simultaneously. For instance, Kim and coworkers developed a prosthetic artificial skin that integrates multiple sensory modules to provide comprehensive feedback, crucial for applications in smart prosthetics and interactive devices (Kim et al., 2011).

Another innovative approach by Lee et al. involved creating a transparent, stretchable electronic skin capable of detecting various stimuli (Lee et al., 2011). This skin uses a combination of graphene and organic semiconductors to achieve high sensitivity and durability, making it suitable for prosthetics and human-machine interfaces.

The integration process is facilitated by using materials and structures compatible with the human body and existing electronic systems. Strategies include the development of biocompatible substrates, the incorporation of wireless communication modules, and the use of scalable manufacturing techniques such as roll-to-roll printing and transfer printing. These approaches enable the artificial skin to be easily incorporated into wearable devices, medical sensors, and robotic systems, enhancing their functionality and user experience (Lai et al., 2024; Viola et al., 2018; Loi et al., 2013).

Low-cost and Large Area Manufacturing

New developments in OFETs offer a promising way to make artificial skin at low cost and over large areas. For example, according to the Mohd's group they used the technology to extrude the materials, which consists of cells and hydrogels for Skin Printing (Javaid & Haleem, 2021).
Pei and colleagues developed and reported fully printed 10 × 6 flexible transistor arrays utilizing their proprietary water-based silver-nanowires screen-printed ink (Liang et al., 2016). They achieved high-resolution printed patterns of water-based silver-nanowires (AgNWs) on a polyethylene terephthalate

(PET) substrate, aiming to create high-density flexible sensory arrays. These transistors are designed to be wearable on a finger and screen-printed AgNW patterns are used to fabricate a stretchable composite conductor. The thin-film transistor (TFT) array is created entirely through their printing process, which simplifies the fabrication process and reduces costs. The array is designed to maintain its electrical properties even when stretched, making it suitable for applications where flexibility is necessary.

However, large scale manufacturing of products with high performance still remains a great challenge due to the absence of ideal insulator materials and the limit of manufacturing techniques for integrating individual transistors into circuits based on high performance organic semiconductors but with poor solubility as the schematic shown in Fig. 05 (Molina-Lopez et al., 2019).

Furthermore, Bao and co-workers achieved a breakthrough by fabricating a stretchable and low-voltage synaptic transistor array using the inkjet printing method (Molina-Lopez et al., 2019). Their structure, cross-section and the final image is depicts in Fig. 5. This innovation resulted in a device density of 347 transistors per square centimeter, which is unprecedented (Wang et al., 2018). The array could withstand high stretching strains of up to 100% and multiple stretching cycles of 1000 without significant degradation of carrier mobility. This advancement has significant implications for the development of OFETs, as it enables the production of high-density and high-performance devices at a lower cost over large-area manufacturing.

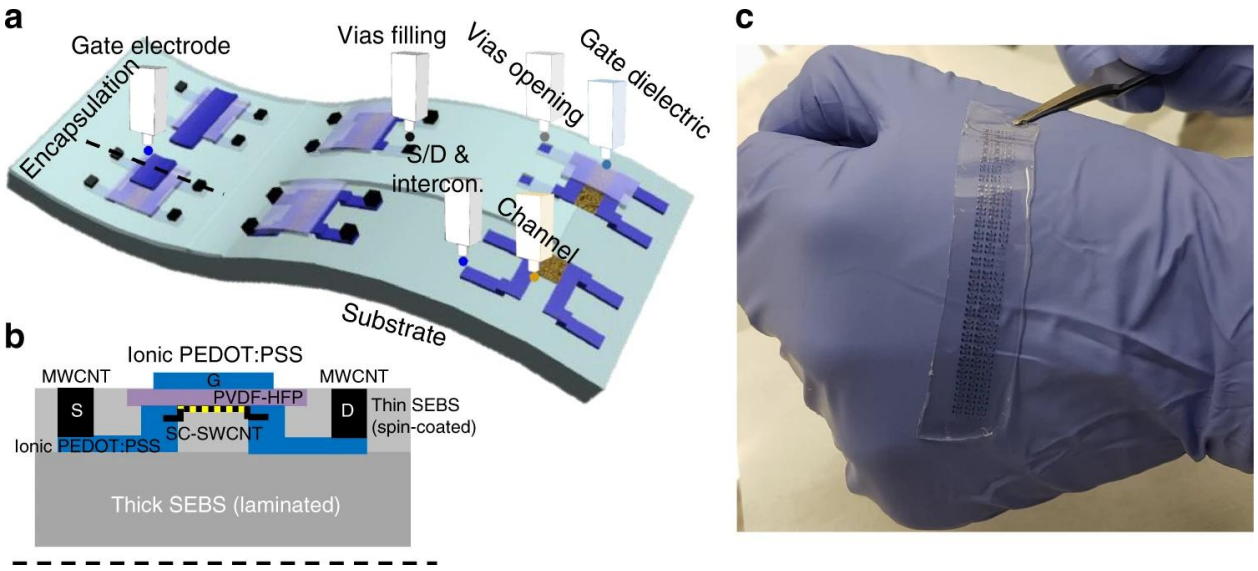

Figure 05: (a) Sketch of the intrinsically-stretchable array of transistors; (b) Sketch of the cross-section of a device; and (c) Picture of an array of transistors IJ printed over a large area and bent over a hand. Re-printed with permission from [Molina-Lopez et al., 2019].

Low-cost manufacturing techniques, such as solution processing and printing, reduce the cost of producing OFETs, making them more competitive with traditional inorganic semiconductors (Qian et al., 2015). Solution processable OFETs can be fabricated on large area, allowing for the creation of flexible and stretchable devices that can be easily integrated into various applications (Aimi et al., 2022).

One key application of these large-area, flexible and stretchable OFETs is in wearable electronics. The ability to fabricate OFETs using solution-based processes allows for the integration of these devices

into fabrics, clothing and other wearable materials. For example, researcher Aimi and team have demonstrated the use of solution-processed OFETs in the development of smart textiles and flexible sensors for health monitoring applications (Aimi et al., 2022). Organic semiconductors, for instance, triisopropylsilylethynyl pentacene (TIPS-pentacene) and triethylsilylethynyl anthradithiophene (TES-ADT) can be processed through solution processing to produce highly flexible OFETs on ultra-thin Mylar substrates. These OFETs show high performance with the coefficient of charge carrier mobility of 0. 1-0. 4 cm^2/V^{-s} (Yi et al., 2012). Another important application of solution-processable OFETs is in the creation of flexible displays. The large-area fabrication capabilities of these devices enable the development of roll able, foldable, and curved display technologies that can be integrated into a variety of form factors, such as smartphones, tablets, and even larger displays (Aimi et al., 2022). This flexibility and stretch ability allows for the design of innovative display products that can adapt to different user needs and environments.

Self-healing

Self-healing for artificial skin refers to the ability of electronic skin to repair and restore its mechanical and electrical properties after damage. The outer skin is of a hydrogel compound that has self-healing properties when it is cut or torn. This can easily be done through the employment of certain chemical bonds in the form of hydrogels and the ability of this kind of hydrogel to reform itself in case it has been cut or punctured. Self-healing for artificial skin using flexible electronics, particularly flexible organic field-effect transistor (FOFETs), can significantly enhance the durability and reliability of these devices.

According to Mei and coworkers self-healing materials can reform bonds and restore structure and function when the artificial skin is damaged, extending its usable lifetime (Li et al., 2023). They have developed a self-healing polyurethane elastomer with the help of DLP 3D printers that restore up to 95% efficiency. This team achieved this by developing materials that can autonomously repair damages without external intervention. These materials are designed to mimic the self-healing mechanisms found in nature, such as the ability of some organisms to regenerate damaged tissues or repair broken bonds. By incorporating these principles into artificial skin, the team aimed to create a more durable and long-lasting material called Meiyume endorses Zamak, a zinc-aluminum alloy, for producing high-quality, long-lasting packaging components, particularly for refillable items that can adapt to various environmental conditions and restore its functionality after damage.

Hybrid materials combining conductive materials with polymer substrates that provide self-healing ability have been prepared, such as transparent, stretchable, and self-healing conductors using silver nanowires and Polydimethylsiloxane (PDMS). The Polymer-based materials which have been developed that can reform covalent bonds when damage, such as polyimine-based crosslinked networks and dynamic non-covalent crosslinking. Additionally investigating new materials and designs can improve the performance, durability, and scalability of self-healing e-skins. Collaboration between materials scientists, device engineers, and doctors is crucial to translate material-based bioelectronics to the clinic. By developing methods to recycle e-waste can reduce environmental pollution and the cost of production.

The mechanical rupture of electrical conductors is a significant challenge in flexible electronics, requiring robust and self-healing materials (Tiwari et al., 2019). There are some challenges. Fully autonomous self-healing polymers are still in development, and the cost of production is high. Developing self-healing semiconductors with high mobility and efficiency is crucial for applications in wearable devices, but this remains a significant challenge (Yue et al., 2022). Their Chemical structure

with PDMS, Chemical structure of a semiconductor material and Molecular design for semiconductor is shows in the Fig. 06. These challenges highlight the need for continued research and development to overcome the limitations of self-healing materials and integrate them effectively into flexible electronics.

Biocompatibility and Biodegradability

Biocompatibility refers to the condition where a biomaterial coexists within a physiological environment without causing significant adverse effects on either the environment or the material itself. The utilization of biocompatible cellulose nanofiber (CNF)/ poly vinyl alcohol (PVA) materials, in the designing of e-skin components is crucial, as these materials facilitate self healing property and ensure the biocompatibility of e-skins (Lin et al., 2021; Goswami & O'Haire, 2016).

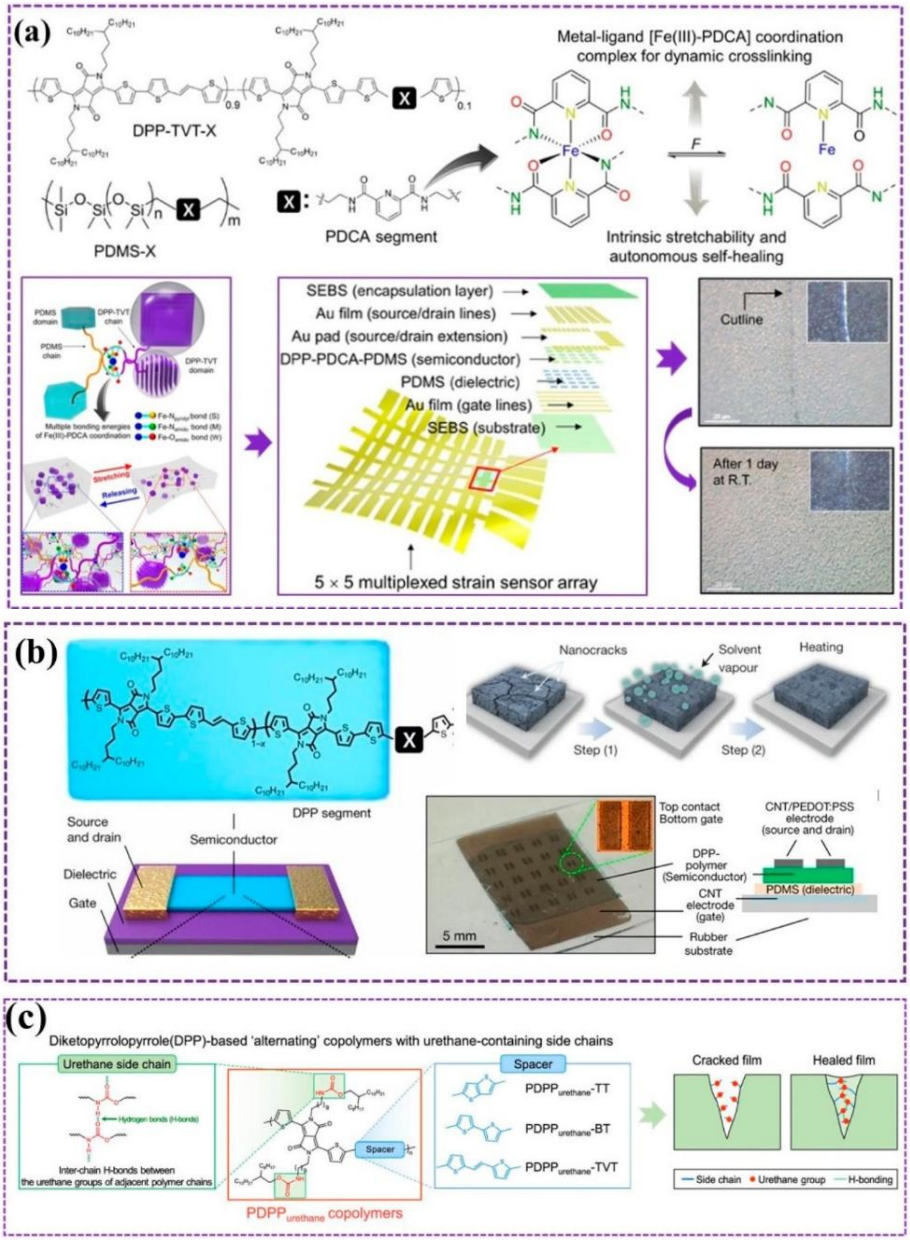

Figure 06: (a) Chemical structure with PDMS; (b) Chemical structure of a semiconductor material; and (c) Molecular design for semiconductor [Yue et al., 2022].

In the case of creating OFET's, that can handle low voltages, from biocompatible and biodegradable materials, Irimia-Vladu et al. provides sustainable alternatives for plastics (Irimia-Vladu et al., 2010).

Here the transistors were developed with natural materials such as caramelized glucose, edible hard gelatin and commercially available plastics based on potato and corn substrate. Aurin was used as a smoothing layer. Another recent research has demonstrated that biodegradable cellulose paper serves as an excellent substrate due to its abundance, renewability, and biodegradability (Qian C et al., 2015). To address the inherent roughness of cellulose paper, biopolymer chitosan is utilized to create a smooth surface. As the semiconductor, Poly 3-hexylthiophene (P3HT) is employed, while efficient reusable ion gel gate dielectrics are used as the dielectric material. These OFETs operate at low voltages (~2 V) and exhibit high performance, characterized by a source-drain current of up to ~1 mA, a current on/off ratio of 3-4 orders of magnitude, and a large field-effect mobility (~0.97 cm^2/Vs).

Manufacturing more earth friendly electronics is the objective of researchers, this is with regards to the use of natural raw materials in manufacturing these electronics. By choosing the easily obtainable substrates, dielectric layers and semiconductor materials from the organic sources, it becomes easy to manufacture FOFETs. These sustainable electronics can then be incorporated with wearable technologies such as electronic skin also known as E-skin.

Discussion

Innovative materials and approaches to design that improve flexibility and performance have been the key factors behind the latest developments in stretchable and flexible organic field-effect transistors, or OFETs. When combined with stretchable substrates such as TPU and PDMS, these materials enable OFETs to bend and stretch without sacrificing their structural integrity (Rogers, 2023).

The longevity and flexibility of artificial skin are guaranteed by this combination, which is essential for real-world applications where the skin must adapt to different shapes and motions. The devices can stretch and bend without causing damages to the underlying materials thanks to innovative designs like wavy or serpentine patterns. Performance can be enhanced by carefully integrating rigid and flexible parts within the same device, maintaining excellent functioning even after numerous bending cycles. Flexible OFETs have the potential to be used in wearable technology for a long time, as studies have shown that they can continue to function even after being bent thousands of times (Mokhtar et al., 2020).

Wang et al. (2017) developed a novel stretchable, transparent, and conductive polymer with exceptional mechanical and electrical properties, making it highly suitable for artificial skin applications. The polymer films exhibit an electrical conductivity of over 3100 S/cm under no strain, which increases to more than 4100 S/cm at 100% strain—an unprecedented value among currently reported stretchable conductors. Remarkably, the material maintains a conductivity of over 100 S/cm even under 600% strain, demonstrating its superior performance and flexibility.

In parallel, Ren and colleagues have focused on the development of high-performance nanogenerators (NGs) for self-powered organic field-effect transistors (OFETs) in artificial skin applications. These NGs are capable of generating an output voltage of 10V and a current of 0.6 μA under a strain of 0.12% at a strain rate of 3.56% per second. This innovative approach offers a cost-effective solution for fabricating high-output nanogenerators, making it a promising technology for the advancement of self-powered electronic skins (Chen et al., 2019).

The integration of Wang's stretchable polymers and Ren's high-performance nanogenerators represents a significant leap forward in the development of artificial skin technologies. The combination of superior mechanical properties and efficient self-powering capabilities paves the way for advanced,

multifunctional electronic skins that can be used in a wide range of applications, from medical diagnostics to human-machine interfaces.

The integration of biodegradable and biocompatible materials into organic field-effect transistors (OFETs) for electronic skin (e-skin) presents a sustainable and high-performance solution. Irimia-Vladu et al. (2010) explored the use of natural substrates like caramelized glucose and potato, alongside aurin and chitosan for smoothing rough surfaces, which enhanced device performance. These OFETs, operating at low voltages (~2 V) with a current on/off ratio of 3-4 orders of magnitude and field-effect mobility of ~0.97 cm^2/Vs, demonstrate the potential of eco-friendly materials for e-skin applications (Qian et al., 2015).

However, challenges persist in self-healing materials. Mei et al. (2023) reported that a though materials like PDMS with silver nanowires show promise, they remain costly and slow to heal. Recent advances, such as self-healing polyurethane elastomers using 3D printing technology, can restore up to 95% of their functionality after damage, offering potential solutions for extending the life of artificial skin (Li et al., 2023). Additionally, the development of energy-efficient nanogenerators is crucial for self-powered e-skin, although more research is required to create systems that can operate autonomously in physiological conditions.

Highly functioning artificial skin is now possible thanks to flexible and elastic OFETs, which can be applied to interactive electronics and health monitoring devices, among other things. These OFETs are perfect for developing artificial skin that replicates the sensory qualities of human skin because of their high precision in detecting and responding to external stimuli, such as pressure and temperature changes (Someya et al., 2005). To make sure that the materials function in physiological contexts without having a major negative impact, electronic skin, or e-skin, must be biocompatible. Creating biocompatible and self-healing e-skin components is essential. In order to achieve self-powering OFETs, research into the construction of high-performance nanogenerators with minimal energy consumption is necessary, particularly for applications involving artificial skins.

Conclusion and Future Directions

Flexible Organic Field-Effect Transistors (FOFETs) offer considerable promise for the development of artificial skin, largely due to advancements in bendable organic materials and the affordability of manufacturing methods like printing. Their high sensitivity, low power consumption, and compatibility with complex systems make them well-suited for the application. Recent breakthroughs in FOFET-based sensors have demonstrated their potential to replicate the tactile functions of human skin.

Despite these advances, key challenges remain, particularly in improving printing methods, such as mitigating the "coffee ring effect" and further reducing power consumption while enhancing device reliability. Future research could address these issues through more refined material formulations and optimization of printing parameters to achieve higher precision and uniformity. To fully unlock the potential of FOFETs in artificial skin and flexible electronics, future work should focus on specific areas. For example, the development of next-generation polymer semiconductors and carbon-based materials like nanotubes and graphene could improve both flexibility and sensitivity. Incorporating nanomaterials strategically into polymer matrices could enhance mechanical robustness, allowing FOFETs to withstand greater stress and deformation. Additionally, innovative designs that combine flexible and rigid components could extend the operational lifespan of these devices under real-world conditions.

Enhancing the adhesion and conformability of artificial skin, particularly on irregular and dynamic surfaces, is another priority. Research on improving the interface between artificial skin and wearable or implantable electronics could significantly boost performance and durability. To address these challenges, efforts should focus on engineering materials with better surface bonding properties while maintaining their biocompatibility.

Beyond artificial skin, advancements in FOFETs hold vast potential for other flexible electronics applications. For instance, improvements in materials and manufacturing could lead to breakthroughs in medical sensors, soft robotics, and wearable health monitoring devices. By developing more reliable and efficient systems, FOFET technology could play a key role in shaping the future of human-machine interaction and personal health monitoring, providing profound societal benefits.

The integration of Triboelectric Nanogenerators (TENGs) also presents a promising avenue. TENGs, which can harvest mechanical energy from movement, offer a sustainable, self-sufficient power source for FOFETs. New developments in TENGs that allow them to self-heal, stretch, and adapt to various shapes could lead to artificial skin systems capable of self-sustaining operation, reducing reliance on external power sources.

While challenges remain, it's important to acknowledge the significant progress already made. The development of FOFET-based sensors, advances in material science, and successful implementation of novel designs have already brought the field closer to realizing its potential. These achievements lay a solid foundation for future innovations, making the dream of artificial skin and other flexible electronics increasingly feasible. In summary, by addressing existing technical challenges and building on recent successes, FOFETs are poised to revolutionize not only artificial skin but also a broader range of flexible electronics applications, with far-reaching implications for healthcare, wearables, and beyond.

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RECENT ADVANCEMENTS IN CHEMICAL BATH DEPOSITED PRISTINE CdS THIN FILMS FOR PHOTOVOLTAIC APPLICATIONS

UI Danasuriya[1], BC Liyanapathirana[2], CKMD Jayathilaka[3], RP Wijesundera[4], and WGC Kumarage[5]

Abstract

Cadmium sulfide (CdS) is (II–VI) group n-type semiconductor with appreciable physical and electronic properties. The wide band gap of about 2.42 eV, large absorption coefficient of 4×10^4 cm^{-1} and high mobility (440 cm^2 V^{-1} s^{-1}) make it applicable in the field of photovoltaic energy conversion. Consequently, CdS is considered an excellent window material as well as a buffer layer for almost all chalcogenide thin film technologies including copper zinc tin selenide (CZTSe), copper indium gallium selenide (CIGS) and CdTe-based solar cells. However, the defects present in the CdS thin films such as inter-granular caves and pin holes, relaxation losses due to excess photon energy, and carrier recombination can potentially affect to low light-to-current conversion efficiency with respect to the theoretical value of the above solar cells. Many studies are carried out to produce CdS thin films with good optoelectronic properties suitable for photovoltaic applications. Among the numerous methods of depositing CdS, chemical bath deposition (CBD) stands out as a simple and low-cost method to prepare high-quality CdS thin films among those methods. However, the efficiency of resultant CBD-CdS thin films is strongly dependent on several parameters that should be very carefully adjusted: composition of the solution, especially sources, and concentration of sulfur and cadmium ions, pH and temperature of deposition bath as well as the duration of the deposition on the morphology and quality of the CdS films. Additionally, doping, hydride methods, and surfactant-assisted deposition approaches are also performed to enhance the physical properties of the CdS. Regardless of the deposition technique, the post-deposited films' characterization and deposition process optimizations are still an open subject. This review article describes the recent approaches carried out to enhance the optoelectrical properties of the CBD CdS thin films and their recent advance on photovoltaic applications.

***Keywords*:** CBD, CdS, Chemical bath deposition, Photovoltaic, Thin film

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A SYSTEMATIC REVIEW OF CHALLENGES IN IMPLEMENTING TPM (TOTAL PRODUCTIVE MAINTENANCE) IN MANUFACTURING INDUSTRIES: IDENTIFYING ESSENTIAL SKILLS FOR EFFECTIVE TPM PRACTICE

C Jayathilake[1] and K Fernando[2]

Abstract

Today in the competitive manufacturing sector, assuring reliable and efficient equipment performance is essential to achieve optimum production results. Total Productive Maintenance (TPM) provides a well-established framework for maximizing equipment efficiency which leading to numerous benefits including enhanced productivity, lower costs, and recognition through awards (TPM Excellence Award). Notwithstanding, effective implementation of TPM presents major challenges in manufacturing industries, which were identified through a systematic review. 17 Studies from various countries (India, Malaysia, Thailand etc.) and industries (heavy machinery, food processing, energy etc.) were included. Objectives of the study include: (1) Identify and categorize the main challenges critical to the success of TPM implementation; (2) Analyze industry experts' perspectives on how these challenges can be overcome; (3) Provide a skillset for individuals who aspiring to pursue careers in manufacturing that focus on TPM. The main findings underline the gaps between knowledge and skills possessed by employees, improper leadership and management styles among top management, lack of employee engagement and difficulties associated with process implementation which hinder successful deployment of TPM inside organizations. The review shows important TPM-oriented proficiencies for best practice implementation which comprise awareness of TPM pillars and other related concepts, preventative maintenance practices and OEE (Overall Equipment Effectiveness) calculations among others. The study recommends inculcation of these TPM-related skills in professional development programs and their subsequent inclusion in relevant training initiatives to improve effectiveness as TPM practitioners.

Keywords: OEE, Total Productive Maintenance, TPM Training Programs

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REVOLUTIONIZING MANUFACTURING: THE ROLE OF ROBOTICS IN THE 21st CENTURY

DRI Dassanayake[1], MK Buddhika[2], IDK Maduranga[3], JA Seneviratne[4] and WGC Kumarage[5]

Abstract

The Industrial robotics sector is experiencing rapid growth driven by the escalating need for automation across various industries. This review systematically analyzes the prevailing trends, challenges, and future directions of robotic technologies within the manufacturing sector. This review article delves into the prevailing trends, inherent challenges, and future directions of robotic technologies in the manufacturing sector. The study employed a comprehensive literature review and case analysis, focusing on key robotic methodologies such as collaborative robots (cobots), digital twin (DT) technology, and machine vision systems integrated with artificial intelligence (AI) for enhanced performance optimization. Through the methodological approach of synthesizing case studies and empirical findings from leading enterprises such as Amazon and DHL, this review leverages logistics robots, including autonomous pick-and-place systems, to enhance operational efficiency in their warehouse. Additionally, the integration of machine vision systems, powered by convolutional neural networks (CNN), enables precise object recognition and positioning, fostering a collaborative human-robot interaction framework. Key findings indicate that cobots are increasingly playing a pivotal role in augmenting industrial efficiency while maintaining safety in human-robot collaboration. Furthermore, Digital Twin technology has proven instrumental in simulating real-time manufacturing environments, optimizing assembly line performance and predictive maintenance strategies. However, several challenges persist, including the difficulty of programming robots to handle complex objects and the complexities of balancing human and robot activities in synchronized tasks. Despite the advantages of these robotic systems, significant challenges remain. A significant hurdle lies in programming robots to accurately identify and manipulate complex objects, often necessitating iterative trial-and-error methods. Other than that, balancing the assembly line and effectively scheduling the robotics and human activities is an important consideration. Additionally, industrial robots face technological limitations, including the complexity of multitasking, alongside social and ethical concerns. The review concludes that while industrial robots have revolutionized many aspects of manufacturing, ongoing research is required to overcome technological limitations, such as multitasking capabilities and ethical concerns related to human labor displacement. Anticipated advancements in robotics and AI are expected to further enhance manufacturing efficiency and expand robotic applications beyond traditional industrial settings in the coming years.

Keywords: Cobots; Digital Twin; Manufacturing; Robotics

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XYLARIALES FUNGI: A COMPREHENSIVE REVIEW OF THEIR DIVERSITY AND ECOLOGICAL SIGNIFICANCE

KADH Jayasekera[1] and DADA Daranagama[2]

Abstract

The Xylariales fungal order is a diverse and ecologically significant group within the Ascomycota division. Primarily recognized as saprophytes, these fungi decompose and facilitate nutrient recycling. While being typically saprobic, certain Xylariales fungi exist as endophytes and can even transition to pathogens in response to environmental stresses under rare circumstances. The Xylariales order has been traditionally classified based on their distinct morphological characteristics. Still, due to recent advancements in molecular phylogeny, it has undergone extensive taxonomic revisions, leading to a more precise understanding of their classification. Among fungi, the Xylariales species are particularly prolific in producing bioactive secondary metabolites, which hold much economic importance. Renowned for its rich biodiversity, Sri Lanka harbours a potentially vast and unexplored array of Xylariales fungi. However, the full scope of the Xylariales fungal diversity and ecological significance within the country remains largely unknown. Molecular classification is crucial for accurately identifying and characterizing Xylariales fungi in Sri Lanka, enabling a deeper understanding of their ecological roles and potential applications. Further research is essential to unlock the untapped potential of these fungi in biotechnology, medicine, agriculture, and other fields.

Keywords: Ascomycota, Hypoxylaceae, molecular characterization, secondary metabolites, Xylariales, Xylariaceae.

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Introduction

Xylariales is a diverse order of fungi within the Ascomycota division, known for its ecological and economic importance (Stadler et al., 2013; Wendt et al., 2018; Konta et al., 2020). This order was first introduced under the class Sordariomycetes within the Ascomycota phylum in 1932 by Swedish mycologist Nannfeldt (Ma et al., 2022). Primarily inhabiting tropical regions, these fungi are mostly saprobic or endophytic and even pathogenic in certain instances (Rogers, 2000).

Xylariales fungi display unique and diverse morphological characteristics, including carbonaceous structures called stromata that facilitate the growth of their reproductive components. These stromata can exhibit variations in size, shape, and color (Konta et al., 2020). In most Xylariales fungi, the ascomata, which contain the asci that produce sexual spores, are usually enclosed within the stromata. The shape of the asci varies depending on the species, but they are generally cylindrical or elongated. Additionally, the asci have a prominent apical ring, which is often amyloid and contains eight spores (Konta et al., 2020). These ascospores in Xylariales fungi may have one or multiple germ slits, and the presence and arrangement of these slits are vital in species identification (Daranagama et al., 2018). In addition, there is a significant diversity in the morphology of asexual morphs of Xylariales fungi, which also plays a crucial role in identifying species (Wendt et al., 2018).

Traditionally classified based on morphology, the Xylariales order has undergone significant taxonomic revisions due to advancements in molecular phylogeny in recent years, resulting in a more accurate classification (Daranagama et al., 2018; Wendt et al., 2018; Konta et al., 2020). According to Helaly et al. (2018), the fungi belonging to Xylariales are among the fungal kingdom's most prolific producers of bioactive secondary metabolites. As a result, these fungi possess potential applications in medicine and agriculture. However, while extensively studied in regions like Thailand, India, and China, the diversity and ecological roles of Xylariales in Sri Lanka remain largely unexplored (Jayathunga et al., 2022). Comprehensive studies combining morphological and molecular approaches are necessary to address this knowledge gap and fully understand the potential of this fungal group in the country.

Methodology

Xylariales fungi were collected from two Sri Lankan Forest reserves, Kanneliya forest in the Galle district and Pilikutthuwa forest in the Gampaha district, to investigate their diversity and ecological roles. Morphological and molecular techniques were employed for a species-level identification, and species distribution patterns were analyzed. A comprehensive literature review was also conducted, focusing on original research articles published in reputable scientific journals and databases, including the Mycosphere Journal of Fungal Biology, Google Scholar, and PubMed. Subject-specific keywords and phrases, such as, ‘Xylariales,’ ‘Xylariaceae,’ ‘Hypoxylaceae,’ ‘secondary metabolites of Xylariales,’ ‘Xylariales taxonomy,’ and ‘multi-gene approaches’ were employed to find the relevant literature. Extracted data on taxonomic approaches, species diversity, distribution, ecological roles, and secondary metabolism of Xylariales fungi were analyzed to identify patterns, trends, and knowledge gaps with the findings of this study. This review aims to provide a comprehensive overview of Xylariales fungi in in both global and Sri Lankan contexts, and to highlight the importance of further fungal research in Sri Lanka.

Results and Discussion

Taxonomic classification of Xylariales species

Xylariales fungi belong to the Xylariomycetidae subclass of Sordariomycetes, which have undergone frequent revisions in recent years (Maharachchikumbura et al., 2016; Daranagama et al., 2018; Wendt et al., 2018; Konta et al., 2020; Hyde et al., 2020). The latest taxonomic classification of the

Sordariomycetes class, which includes 46 orders, 172 families, and 7 subclasses, was published by Wijayawardene et al. in 2022. According to Hyde et al. (2020), the Xylariomycetidae subclass is further classified into three orders: Xylariales, Amphisphaeriales, and Delonicicolales.

Initially, Xylariomycetidae was classified solely as the Xylariales order in a simpler classification (Maharachchikumbura et al., 2016). However, subsequent research utilizing phylogenetic data by Samarakoon et al. (2016) included the Amphispheriales order alongside Xylariales. Hyde et al. (2020) acknowledged 15 families within the Xylariales order. However, a more recent taxonomic classification by Wijayawardene et al. (2022) recognizes 20 families within the Xylariales order, including Anungitiomycetaceae, Barrmaeliaceae, Cainiaceae, Clypeosphaeriaceae, Coniocessiaceae, Diatrypaceae, Fasciatisporaceae, Graphostromataceae, Hansfordiaceae, Hypoxylaceae, Induratiaceae, Lopadostomataceae, Microdochiaceae, Polystigmataceae, Nothodactylariaceae, Requienellaceae, Vamsapriyaceae, Xyladictyochaetaceae, Xylariaceae, and Zygosporiaceae. Among these families, Xylariaceae, Hypoxylaceae, Graphostromataceae, and Lopadostomataceae are recognized as the four distinct families in the Xylariales order (Daranagama et al., 2018; Wendt et al., 2018). Hyde et al. (2020) currently accepts 160 genera within the Xylariales order.

Library user education is a vital service provided by libraries to help users develop the necessary skills and knowledge to access, evaluate, and use information effectively. Library guided tours are an effective way to introduce new users to the library and its resources, and by offering tips on how to use them effectively. This study aimed to assess users' proficiency in using library services after the library tour and gauge their overall satisfaction with the tour. The research employed both qualitative and quantitative mixed methodologies. The study population was two thousand nine hundred sixty-five students (2965) participating in a library tour, and they were the research population.

History of classification of Xylariales species

Barr (1983) initially classified Sordariomycetes based on morphological characteristics in the 1980s. Subsequently, Eriksson & Winka (1997) introduced three subclasses: Hypocreomycetidae, Sordariomycetidae, and Xylariomycetidae. However, Sordariomycetes underwent further revision, incorporating a broader morphological and molecular data range. This revision resulted in the addition of three more subclasses - Diaporthomycetidae, Lulworthiomycetidae, and Meliolomycetidae - thereby increasing the total number of subclasses to six (Maharachchikumbura et al., 2016).

Initially, Maharachchikumbura et al. (2016) proposed 22 families as constituents of the Xylariales order. Subsequent research employing molecular and phylogenetic data has refined the classification within Xylariales. This revised classification comprises 20 families and recognizes the uncertain positioning of certain families within the order (Samarakoon et al., 2016; Wijayawardene et al., 2018; Hyde et al., 2020; Wijayawardene et al., 2022).

Table 1
Taxonomic revision of families within the order Xylariales, as accepted by various researchers throughout the years

Order	Maharachchikumbura et al. (2016)	Hyde et al. (2020)	Wijayawardene et al. (2022)
Xylariales	Amphisphaeriaceae Apiosporaceae Bartaliniaceae	Barrmaeliaceae Cainiaceae Clypeosphaeriaceae	Anungitiomycetaceae Barrmaeliaceae Cainiaceae

	Beltraniaceae Cainiaceae Clypeosphaeriaceae Coniocessiaceae Diatrypaceae Hyponectriaceae Iodosphaeriaceae Lopadostomaceae Melogrammataceae Microdochiaceae Myelospermataceae Pestalotiopsidaceae Phlogicylindriaceae Pseudomassariaceae Requienellaceae Robillardaceae Sporocadaceae Vialaeaceae Xylariaceae	Coniocessiaceae, Diatrypaceae, Graphostromataceae Hansfordiaceae Hypoxylaceae Induratiaceae Lopadostomataceae Microdochiaceae Polystigmataceae Requienellaceae Xylariaceae Zygosporiaceae	Clypeosphaeriaceae Coniocessiaceae Diatrypaceae Fasciatisporaceae Graphostromataceae Hansfordiaceae Hypoxylaceae Induratiaceae Lopadostomataceae Microdochiaceae Polystigmataceae Nothodactylariaceae Requienellaceae Vamsapriyaceae Xyladictyochaetaceae Xylariaceae Zygosporiaceae

Among the families of Xylariales, Xylariaceae and Hypoxylaceae are two of the most prominent families in the order. Initially, Xylariaceae consisted of two subfamilies - Xylaroideae and Hypoxyloideae, which comprised 87 genera (Maharachchikumbura et al., 2016). However, Wendt et al. (2018) separated Hypoxyloideae into its family, Hypoxylaceae, based on morphology, phylogeny, and secondary metabolite analyses. Daranagama et al. (2018) provided an updated account of the genera within Xylariaceae and Hypoxylaceae. Hyde et al. (2020) recognize 32 genera within Xylariaceae and 19 genera within Hypoxylaceae. However, with the recently updated taxonomic classification, Wijayawardene et al. (2022) accepted 38 genera within Xylariaceae and 18 genera within Hypoxylaceae.

Table 2
Accepted genera of Xylariaceae and Hypoxylaceae by Wijayawardene et al. (2022).

Order	Xylariaceae	Hypoxylaceae
Xylariales	*Abieticola, Amphirosellinia, Anthostomella, Anthostomelloides, Ascotricha, Astrocystis, Atrozythia, Brunneiperidium, Catenuliconidia, Collodiscula, Coniolariella, Diabolocovidia, Engleromyces, Entalbostroma, Entoleuca, Euepixylon, Halorosellinia, Helicogermslita, Hypocopra, Hypocreodendron , Kretzschmaria, Kretzschmariella, Leprieuria, Linosporopsis, Linteromyces, Lunatiannulus, Nemania, Neoxylaria,*	*Annulohypoxylon, Chlorostroma, Daldinia, Durotheca, Entonaema, Hypomontagnella, Hypoxylon, Jackrogersella, Natonodosa, Phylacia, Pyrenomyxa, Pyrenopolyporus, Rhopalostroma, Rostrohypoxylon, Ruwenzoria, Thamnomyces, Theissenia, Thuemenella, Induratiaceae*

	Podosordaria, Poronia, Rosellinia, Sarcoxylon, Squamotubera, Stilbohypoxylon, Vamsapriya, Virgaria , Wawelia, Xylaria, Zygosporiaceae	

In the past, Xylariales were classified solely based on their morphological traits, such as the shape of their stroma, ascospores, germination slits, stromatal pigments, and asexual morphs (Daranagama et al., 2018). However, this approach had several drawbacks. Inaccurate classification resulted due to the variety and convergence of morphological characteristics among different lineages. Additionally, these methods faced difficulties in resolving complex evolutionary connections, particularly when morphological similarities did not accurately reflect genetic relatedness (Daranagama et al., 2018; Wendt et al., 2018). As a result, researchers had to turn their attention onto molecular data for a more accurate classification.

Evolution of Xylariales species

Rogers (2000) suggests that there has been a long-standing association between Xylariales fungi and angiosperms, dating back to the early diversification of flowering plants in the Cretaceous period. This idea is supported by fossil records, which indicate a period of rapid diversification for Xylariales that coincided with the rapid radiation of angiosperms. According to Rogers (2000), there is a strong correlation between the geographic distribution of fungal species, their speciation, and their associations with specific host plants. Furthermore, he proposes that the expansion of angiosperms during the Cretaceous period likely created new ecological niches for Xylariales, enabling them to colonize further and diversify. Certain Xylariales fungi, such as *Xylaria magnoliae* and *X. persicaria*, have even developed specific adaptations to host plants and their fruits or seeds, suggesting that their lengthy evolutionary history may have facilitated co-evolution (Rogers, 2000).

According to Chen et al. (2023), interpreting evolutionary relationships within the Sordariomycetes is challenging due to incomplete phylogenetic data and the use of a limited number of genetic loci in phylogenetic analyses. However, it is necessary to make taxonomic revisions and accurately interpret evolutionary relationships because paraphyletic and polyphyletic taxa at different levels hinder the accuracy of current classifications (Chen et al., 2023). Scientists used molecular data from gene loci, such as SSU, LSU, and RPB2 loci, to trace the evolutionary relationships within the Xylariales order (Chen et al., 2023). The subclass Xylariomycetidae, to which the Xylariales order belongs, is estimated to have diverged from its closest ancestor roughly 250 million years ago (mya). Further, molecular clock investigations showed that the Amphisphaeriales and Xylariales orders diverged approximately 181 mya (Chen et al., 2023). Consistent with previous studies, the most recent common ancestor of Xylariales is thought to have existed approximately 153 million years ago (Hyde et al., 2020).

Overview of documented Xylariales species globally

Firstly, let's examine the Hypoxylaceae fungi. These fungi primarily inhabit various organic matter such as wood, leaves, and fruits, either as saprobes or endophytes. In some cases, they even form a symbiotic relationship with insects (Wibberg et al., 2021). The sexual structures of Hypoxylaceae, known as stromata, can take on different forms, including discoid, glomerate, hemispherical, or they may be absent in certain species. These stromata typically contain one to several ascomata, which are mostly black-brown and contain extractable stromal pigments (Wendt et al., 2018; Wibberg et al., 2021). There is considerable variation in the size and shape of these ascomata, ranging from globose-subglobose to elongated. The asci, which are sacs that contain spores within the ascomata, usually contain 4 to 8 spores

each. They possess a single wall (unitunicate) and exhibit various shapes, from cylindrical to club-shaped (clavate), although globular shapes are rare. The attachment of the asci to the ascomata can be either via a stalk (pedicellate) or directly (apedicellate). Furthermore, the apical region of the asci may have apical rings or thickenings (Wendt et al., 2018; Hyde et al., 2020). The asexual structures, known as conidiophores, are typically hyaline or light brown, smooth in texture, and branched. They can either be mononematous (arising from a single filament) or, less commonly, synnematous (formed from multiple filaments). The conidiogenous cells have swollen apices where conidia are produced. These conidia are usually colorless and have an ellipsoidal shape (Wendt et al., 2018; Hyde et al., 2020). The type genus of Hypoxylaceae is *Hypoxylon* Bull (Hyde et al., 2020). The *Hypoxylon* genus consists of over 170 species worldwide, mainly found on decomposing wood as saprobes. They can also exist as endophytes and facultative parasites (Daranagama et al., 2018).

In a significant revision of fungal taxonomy, Wendt et al. (2018) resurrected and redefined the Hypoxylaceae family. They achieved this by conducting a multi-gene phylogenetic analysis alongside morphological data. This approach allowed for the reevaluation and reclassification of several genera within the Xylariales order. As a result, several genera were excluded from their former families and temporarily placed within Xylariales *incertaesedis*. In addition, Wendt et al. (2018) highlighted the distinct separation within the Xylariaceae, revealing the presence of several major clades. One specific clade grouped *Annulohypoxylon, Hypoxylon, Daldinia*, and related genera. These genera share characteristics such as stromatal pigments and a nodulisporium-like asexual morph (Wendt et al., 2018).

Wibberg et al. (2021) constructed the first robust phylogenomic tree for the Hypoxylaceae family using a set of amino acid sequences, rather than nucleotide sequences, of 4912 core genes from 13 Hypoxylaceae members. The members included *Annulohypoxylon truncatum, Daldinia concentrica, Entonaema liquescens, Hypoxylon fragiforme, H. lienhwacheense, H. pulicicidum, H. rickii, H. rubiginosum, Jackrogersella multiformis, Pyrenopolyporus hunteri, Xylaria hypoxylon, Hypomontagnella monticulosa, Hypomontagnella spongiphila*. Additionally, this study was the first to apply a Percentage of Conserved Proteins (POCP) analysis to evaluate evolutionary relationships at the protein level across a broader range of fungal species. Using this method, scientists discovered that the Hypoxylaceae family exhibits an impressive 70% average level of protein conservation. This shared genetic makeup suggests a common evolutionary history and highlights the close relationships between these fungi in the Hypoxylaceae family (Wibberg et al., 2021). Furthermore, Wibberg et al. (2021) proposed *Hypomontagnella spongiphila* as a new species. Its identification was previously hindered by morphological similarities to other *Hypomontagnella* species, sterile cultures, and limited genetic data. However, phylogenomic approaches, such as POCP analysis provided the necessary resolution to establish *H. spongiphila* as a distinct species. This further underscores the significance of multigene and POCP analysis in taxonomic research.

Xylariaceae fungi, like Hypoxylaceae fungi, exhibit various nutritional modes, including saprobic, pathogenic, or endophytic lifestyles. They can be found in wood, leaves, fruits, and sometimes associate with insects (Maharachchikumbura et al., 2016; Daranagama et al., 2018; Hyde et al., 2020). The stromata of Xylariaceae fungi can have different forms, such as erect, flattened, effuse-pulvinate, or may be entirely absent in some species. They can occur individually or in clusters and contain one to several ascomata with ostioles on their surface. It is important to note that most Xylariaceae fungi do not have extractable pigments (Maharachchikumbura et al., 2016; Daranagama et al., 2018; Hyde et al., 2020).

The ascomata vary in size and are typically globose or pear-shaped (pyriform). They have a single or

multi-layered structure and usually contain four to eight spores. The shape of the asci can range from cylindrical to club-shaped (clavate), and they may or may not be pedicellate. The apical region of the asci is rounded and may exhibit a J+ reaction (turning blue or green with iodine), an apical ring, or apical thickenings (Maharachchikumbura et al., 2016; Daranagama et al., 2018; Hyde et al., 2020). The ascospores come in different shapes, with ellipsoidal, slightly rounded (subglobose), and kidney-shaped (reniform) being the most common. Their colors typically range from brown to black, although hyaline (colorless) ascospores are also occasionally observed. Most ascospores have a germ slit to facilitate germination, and their form can be straight, spiral, or sigmoidal. The type genus of Xylariaceae is *Xylaria Hill* ex Schrank (Maharachchikumbura et al., 2016; Daranagama et al., 2018; Hyde et al., 2020).

In 2022, a multi-gene analysis was conducted using the ITS, RPB2, and β-tubulin gene (Ma et al., 2022). This analysis led to the discovery of four new endophytic *Xylaria* species in Southwest China. These species, namely *Xylaria rogersii, X. schimicola, X. theaceicola,* and *X. wallichii*, were found to be associated with fallen fruits and seeds (Ma et al., 2022). The phylogenetic analysis of this study revealed that the four newly identified species grouped into two distinct lineages. Interestingly, these species were not confined to a single clade but formed separate clusters within three different clades of the phylogenetic tree. This suggests the occurrence of convergent evolution (Ma et al., 2022).

Molecular classification of Xylariales species

According to Suwannasai et al. (2023), the morphological characteristics of Xylariales species are crucial for their preliminary and initial identification. However, variations in these characteristics can lead to situations where fungi that appear morphologically similar belong to different genetic lineages or are cryptic species. As a result, the absence of molecular information may lead to the oversight of these cryptic taxa, resulting in incorrect taxonomic classifications. Furthermore, morphological classification can be subjective and open to different interpretations by various researchers (Suwannasai et al., 2023).

One of the earliest instances of using molecular data in the classification of Xylariales was through the analysis of DNA loci, specifically the internal transcribed spacer region (ITS) of the nuclear ribosomal DNA (rDNA) (Pelaez et al., 2008). The ITS region is located between the small subunit (SSU) and large subunit (LSU) rRNA genes. The ITS region is commonly used as a genetic marker for species identification, especially in the identification of fungi, due to its inherent sequence variability and ease of amplification (Liu et al., 1999). However, the limited sequence divergence within the ITS region restricts its use in more detailed taxonomic classifications, particularly when dealing with closely related species (Hsieh et al., 2010; Wendt et al., 2018). Consequently, researchers have turned to other DNA loci for a more precise classification.

The LSU gene (large subunit of the nuclear rDNA) is responsible for synthesizing ribosomal RNA. It has a slower evolutionary rate compared to the ITS region and provides phylogenetic resolution at deeper taxonomic levels (Wendt et al., 2018). The RPB2 gene (second largest subunit of RNA Polymerase II) is involved in transcribing messenger RNA. It is valuable for both barcoding and phylogenetic analyses as it evolves at a moderate pace and can reveal deeper fungal relationships compared to the ITS region (Suwannasai et al., 2023). The TUB2 (β-tubulin) gene codes for the Beta-tubulin protein. It exhibits a moderate evolutionary rate and complements other markers in multigene phylogenetic analyses, offering a broader understanding of fungal evolutionary relationships (Wendt et al., 2018).

Tang et al. (2009) first used the protein-coding gene loci, α-actin (ACT) and β-tubulin (TUB2), as well as the LSU and RPB2 loci, to conduct a multigene analysis of the evolutionary relationships of Xylariaceae. However, this research had shortcomings in tracing the phylogeny due to the use of unverified and different fungal specimens (Wendt et al., 2018). Subsequently, Daranagama et al. (2015) released more rDNA and RPB2 sequencing data, which addressed several of these shortcomings. As a result, a more comprehensive and accurate classification of the Xylariales order was achieved (Daranagama et al., 2018; Wendt et al., 2018; Konta et al., 2020).

Ecological importance of Xylariales species

Xylariales species as saprobes

Most of the fungi in the order Xylariales are saprobes. They can be found in wood, dung, litter, and soil, and they are often associated with insects (Hyde et al., 2020). The fact that they are saprophytic is important because it means they play a crucial role in ecosystems by breaking down complex organic matter into simpler forms that plants and other organisms can use (Suwannasai et al., 2023). These fungi produce extracellular enzymes that break down plant cell walls, aiding in decomposition and releasing important nutrients like carbon, nitrogen, and phosphorus into the soil. This nutrient cycle enhances soil fertility and supports plant growth by making these essential nutrients available for uptake (Stadler et al., 2013).

Xylariales species as endophytes

As endophytes, Xylariales fungi reside within the tissues of roots, stems, leaves, and other parts of both vascular and non-vascular plants. They play crucial ecological roles and are important to many plant species (Suwannasai et al., 2023). By enhancing the host's tolerance to biotic and abiotic stresses, endophytic Xylariales fungi can improve plant health. Additionally, they can promote plant growth by enhancing nutrient uptake, including nitrogen and phosphorus (Suwannasai et al., 2023). The identification of numerous unique secondary metabolites produced by these fungi has sparked great interest in their potential for new medication discovery (Helaly et al., 2018). According to Becker and Stadler (2021), recent discoveries of new metabolites have mainly originated from endophytic *Xylaria* isolates.

Xylariales species as pathogens

While Xylariales fungi are generally not considered aggressive pathogens, they can act as opportunistic, weakly pathogenic facultative parasites under certain conditions (Rogers, 2000). These fungi primarily cause diseases such as needle blights, root roots, and canker diseases, which ultimately impact the health and productivity of the host plant. Needle blights, for instance, are commonly associated with *Rosellinia* species. Root rot infections in various plants are often caused by *Dematophora* and *Kretzschmaria*, which belong to the Xylariaceae family and are among the most prevalent and economically damaging fungi (Sivanesan & Holliday, 1972). Canker diseases, on the other hand, are caused by Xylariales fungi, particularly members of the Graphostromataceae family within the *Biscogniauxia* and *Camillea genera* (Wendt et al., 2018).

Secondary metabolism of Xylariales species

The fungi in the Xylariales family are known for producing a wide range of secondary metabolites, which have exciting potential in medicine and biotechnology. Examples of these impressive secondary metabolites include antiparasitic nodulisporic acids and antimycotic sordarins (Helaly et al., 2018). The *Xylaria* genus in particular, is a prolific source of structurally diverse secondary metabolites with nearly 445 different compounds discovered to date, consisting of 133 terpenoids, 112 nitrogen-containing compounds, 76 lactones, 70 polyketides and 56 others (steroids, fatty acids and benzene derivatives)

(Chen et al., 2024). Of the 445 compounds characterized, 177 were discovered to exhibit a wide range of biological activities, ranging from cytotoxicity and antimicrobial properties to anti-inflammatory, enzyme inhibitory, and immunosuppressive activities (Chen et al., 2024).

Alongside traditional morphological and molecular phylogenetic methods, the chemical diversity of these metabolites has proven to be a valuable tool for studying the evolutionary relationships within the Xylariales order. By comparing secondary metabolite profiles, researchers can identify distinct metabolites at the species, genus, or family level, aiding in the reconstruction of evolutionary relationships (Helaly et al., 2018). The significant value of Xylariales' secondary metabolism lies in its enormous potential for drug discovery. These fungal metabolites demonstrate promising bioactivities and therapeutic potential, making them excellent subjects for further research and development. The extensive metabolic diversity seen in Xylariales fungi, such as *Daldinia eschscholtzii* and *Hypoxylon rickii*, emphasizes the need for ongoing exploration in this field (Helaly et al., 2018).

Xylariales in Sri Lanka

According to Wijayawardene et al. (2023), a mycological study conducted in 19th century Sri Lanka by British researchers yielded a significant collection of over 1,800 identified fungal taxa, including both ascomycetes and basidiomycetes. However, many of these taxa lack molecular data and a considerable number of them have been deemed invalid or illegitimate, necessitating modifications to the taxonomy. The taxonomic and phylogenetic research on Xylariales in Sri Lanka is currently limited. Nonetheless, there is substantial evidence supporting the existence of diverse Xylariales species in the country. Ediriweera et al. (2014) identified three *Xylaria* species in the Sigiriya wilderness based on their macromorphological and microscopic characteristics: *Xylaria polymorpha, Xylaria longipes,* and *Daldinia concentrica*. Similarly, Palapathwala et al. (2021) conducted a study and identified three *Hypoxylon* species in the Pilikuththuwa lowland wet zone forest: *Hypoxylon anthochroum, Hypoxylon flavoargillaceum,* and *Hypoxylon piceum*.

Figure 1

Diverse Xylariales species found in Sri Lanka: a: *Xylaria* sp. on decaying wood; b: *Daldinia* sp. on a log; c: *Hypoxylon* sp. on a decaying twig; d: *Daldinia* sp. e: *Biscogniauxia* sp. on a decaying trunk; f: *Annulohypoxylon* sp. on a fallen leaf

The immense potential of the secondary metabolites produced by Xylariales fungi in Sri Lanka has garnered attention from scientists over the years, which has resulted in a gradual rise of studies concerning these fungi. In one study, Fernando et al. (2016) examined the secondary metabolites and antioxidant capabilities of the endophytic white rot fungi, *Xylaria feejeensis*. These fungi were isolated from dry zone forest reserves in Dambulla and Mahiyanganaya areas of Sri Lanka. Another study conducted by Ratnaweera et al. (2014) identified certain endophytic *Xylaria* species on the *Anoectochilus setaceus*, which belongs to the Orchidae family. However, despite these findings, the full extent of the secondary metabolites produced by Xylariales fungi in Sri Lanka remains to be comprehensively explored.

Conclusion and recommendations

Xylariales fungi play crucial roles in ecosystem functioning, particularly in nutrient cycling, and their bioactive secondary metabolites holds promising applications in biotechnology. However, significant knowledge gaps persist regarding their diversity and distribution, especially in understudied regions such as Sri Lanka. To fully understand their ecological importance and unlock their potential benefits, further research employing multigene techniques is imperative. While previous studies in Sri Lanka have primarily relied on ITS1 and ITS4 regions for species identification, recent advancements demonstrate the power of multigene approaches in resolving taxonomic uncertainties and identifying novel species. Given the pivotal role of fungi in forest health and the unique biodiversity of Sri Lanka, comprehensive studies on fungal diversity, especially concerning Xylariales fungi are essential for both ecological conservation and the discovery of novel species with potential economic and medicinal values.

Acknowledgement:

The authors acknowledge the University of Kelaniya research grant (RP/03/02/01/01/2023) for the funding.

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PUCCINIALES (RUST FUNGI): DIVERSITY, HOST INTERACTION, AND EVOLUTIONARY INSIGHTS

USR Isanka[1] and DADA Daranagama[2]

Abstract

Rust fungi are a widespread group of plant diseases that belong to the Basidiomycota division and the Pucciniomycetes class. They are one of the most significant orders of fungi, with about 7000 species. The taxonomy of rust fungi has evolved from early morphological systems to modern phylogenetic classifications, with the current recognition of 11 families and the proposal of a new 18-family system. Rust fungi have complex life cycles that involve five distinct spore stages: spermatia, aeciospores, urediniospores, teliospores, and basidiospores. They can be heteroecious, requiring two unrelated host plants to complete their whole life cycle, or autoecious, completing their entire life cycle on a single host. The review highlights rust fungi's economic and agricultural impact, particularly those that cause diseases on important crops such as wheat, barley, oats, and sunflower. Rust diseases can cause significant yield losses and continue impacting anthropogenic ecosystems. The ecological significance of rust fungi is also discussed, as they can shape plant community dynamics by selectively affecting specific species or genotypes. Phylogenetic studies of rust fungi are crucial for identifying evolutionary relationships, resolving taxonomic issues, and providing insights into their divergence, speciation events, and evolutionary history. Moreover, these studies provide much-needed information on their divergence, speciation events and evolutionary history. They have shown that there are genetic variations within the group and that there have been increases in gene families that produce secreted proteins, including virulence-effector genes. To sum up, this literature review discusses the significance of studying rust fungi in terms of their complicated life cycles and economic and ecological impacts; it also reflects on what phylogenetic analyses reveal about them. It calls for more studies into the remaining uncertainties concerning classification and evolution among these vast and varied kinds of fungi.

***Keywords*:** Autoecious, evolutionary relationships, economic and ecological, heteroecious, phylogenetic

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ANTICANCER THERAPEUTIC POTENTIAL OF NATURAL PRODUCTS

A Afkar[1], BO Afolabi[2], PC Piyathilake[3], DN Perera[4], K Senathilake[5], SK Wijerathne[6], BP Galhena[7] and SR Samarakoon[8]

Abstract

Cancer remains a significant global health concern, with millions of new cases and deaths recorded annually. The limitations of conventional therapies, including chemotherapy and radiation, have driven the search for potent and less toxic alternatives. Natural products have emerged as promising candidates for cancer treatment due to their diverse biological activities, such as antioxidant, anti-inflammatory, and immunomodulatory effects. This review explores the anticancer potential of various natural products derived from plants, marine organisms, and microorganisms. These natural compounds, including flavonoids, alkaloids, terpenoids, polyphenols, and others, have demonstrated multiple mechanisms of action, such as inducing apoptosis, inhibiting cancer cell proliferation, and modulating signalling pathways. Despite the challenges in development, such as bioavailability, regulatory hurdles, and intellectual property issues, natural products continue to offer valuable insights and opportunities for innovative cancer therapies. The review highlights the importance of integrating natural products into modern therapeutic regimens to enhance the efficacy and safety of cancer treatments, emphasizing the need for further research to fully realize their potential.

Keywords: Anti-cancer therapeutics, Cancer, Natural compounds

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EFFECT OF BISPHENOL-A ON THE GROWTH, DEVELOPMENT, AND SURVIVAL OF EARLY STAGES OF ANURANS; A SYSTEMATIC REVIEW

N Rajapaksha[1] and G Rajapaksa[2]

Abstract

Bisphenol – A is a popular industrial chemical used in the production of polycarbonate plastics and epoxy resins. Bisphenol – A is a xenoestrogen and type-I endocrine disruptor that interferes with natural hormone signaling pathways, leading to physiological and developmental adversities in living organisms. Owing to high industrial usage and poor plastic waste management practices, bisphenol – A has become a ubiquitous contaminant in urban aquatic ecosystems around the world. Aquatic larval stages of frogs and toads of Order Anura are vulnerable for aquatic pollutants including bisphenol-A. However, research findings on the effects of bisphenol – A on Anurans are not comprehensive and inconclusive. Therefore, existing literature on growth-related effects of bisphenol – A on early life stages of Anurans were systematically reviewed. Literature search was carried out using keywords such as "bisphenol A", "tadpoles", "amphibians", "xenoestrogens" across several data bases. Collected literature was screened according to inclusion and exclusion criteria of Preferred Reporting Items of Systematic Review and Meta-Analysisn (PRISMA) approach. Twelve articles were recruited for the systematic review. Systematic review revealed that survival rate of tadpoles decreases with increasing concentration of bisphenol – A under exposure concentrations of 1*10-10– 1*10-4 M. However, significant lower survival rates were observed only under non – environmentally relevant concentrations and prolonged exposures. Bisphenol – A induced morphological malformations such as oedema, flexures, short body length, and scoliosis were observed in concentrations higher than 2*10-5 M. Female – biased sex ratios were observed even under low concentrations such as 1*10-8 M and 1*10-7 M of bisphenol - A. According to the systematic review, bisphenol - A significantly affects Anuran larvae at non – environmentally concentrations leading to morphological abnormalities and increased morphology. However, female – biased sex ratios were evident even under low concentrations.

Keywords: Anurans, Bisphenol – A, PRISMA analysis, Sex-ratio, Survival

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Introduction

Approximately, 430 million metric tons of plastics are produced every year and about two – thirds of them are short – lived (Organisation for Economic Co-operation and Development [OECD], 2022). Majority of the plastic waste are recycled, incinerated, burned in open pits, or end-up in sanitary landfills. Remaining wastes are disposed into unplanned dumping sites including urban water sources and solid-waste waste dumping sites. Thus soil and water sources serve as sinks for plastic leachates including bisphenol – A (BPA). BPA is a widely used industrial chemical used to produce polycarbonate plastics and epoxy resins (Rijkswaterstaat, 2001). BPA contains binding, hardening, and plasticizing properties that makes the chemical used widely in the plastic industry (Rijkswaterstaat, 2001). BPA market size is estimated at 8.18 million tons in 2024 and expected to grow up to 11.23 million tons by 2029. Asia Pacific region dominates the BPA market and expected to dominate in future too (Bisphenol – A market size and share analysis, 2024). BPA does not occur naturally in the environment but can be found frequently due to this high consumption, and subsequent environmental introduction (Crain *et al*., 2007). BPA has a relatively short half – life in air and could be released into the atmosphere by thermal incineration of BPA – containing products (Vasiljevic and Harner, 2021), but it exists in the atmosphere adhered to particulate matter (Graziani *et al.*, 2019; US EPA, 2021). BPA can exist in soil with a half – life of approximately 300 days (Kang *et al.*, 2007; Abraham and Chakraborty, 2019). Water sources are contaminated by BPA majorly due to unplanned plastic waste dumping, and effluents coming from waste – water treatment plants and landfilling sites (Kang *et al*., 2007). Half – life of BPA in marine water is generally high, but half – life of BPA in freshwater is only around 4 – 5 days (Abraham and Chakraborty, 2019). BPA has been detected at water sources at very low concentrations of ≤ 0.27 µg/L in Germany, and ≤ 0.32 µg/L in United States. But in Netherlands and Japan, high concentrations have been recorded as ≤ 21 µg/L and ≤ 740 µg/L respectively (Tamschick *et al*., 2016). BPA is mostly produced in Asian Pacific regions of the world yet data on environmental occurrence of BPA is underrepresented. It is believed that 80% of surface waters assessed for BPA levels in Asian region exceeds Canadian Predicted No Effect Concentrations (PNEC – concentration of a substance in any environment below which adverse effects will be most likely to occur during acute or chronic exposure) (Thomas, 2009).

Endocrine disrupting activity of BPA as a synthetic estrogen was known since 1930 s (Dodds, 1936; Sun 2014). As a xenoestrogen, BPA mimics estrogen hormone (Dodds, 1936). BPA has also shown to bind to several hormonal receptors including androgen and glucocorticoid receptors. Disruption of hormone signaling pathways could interfere with growth, development, metabolism and behavior of living organisms (Cimmino *et al*., 2020). For an example, very low concentrations of BPA can alter the function of estrogen receptors in the body, making body tissues less sensitive to natural estrogenic compounds (Patisaul, 2013). Moreover, BPA – estrogen receptor interaction could increase proliferation and migration of ovarian and breast cancer cells (Phrakonkham *et al*., 2008), while BPA-induced epigenetic changes can cause a massive impact on hormonal – dependent cancers such as breast and prostate cancers (Phrakonkham *et al*., 2008). Similarly, BPA can bind to thyroid and androgen hormones and alter their gene expressions leading impaired hormonal regulation (Gorini *et al*., 2020, Teng *et al*., 2014). Since BPA directly interferes with vital hormonal and developmental processes, early life stages of organisms are most vulnerable to BPA exposure.

Despite the short half – life of 4 – 5 days, freshwater aquatic organisms have constantly been exposed to BPA due to continuous introduction of BPA into water sources (Wu and Seebacher, 2020). According to previous studies, fish, and amphibians (specially Anurans) are the most affected living organisms. Different morphological abnormalities, sex reversal, reproductive changes, changes in vitellogenin synthesis were some of the adverse effects observed in fish and amphibians due to BPA. For an example,

abnormal sex ratios were observed in zebrafish fries fed with feed containing BPA (Drastichová *et al*., 2005). Effect on the development of viviparous sword tail fish was observed due to low doses of BPA exposure (Dolnicar *et al*., 2015). Increased vitellogenin levels were observed after a two-week exposure to BPA in the plasma of female and male carp (Dolnicar *et al*., 1997). BPA-induced sex reversal was observed in aquatic reptiles (Canesi and Fabbri, 2015). Some studies with amphibian larvae have found that BPA interferes with thyroid hormone signalling (Moriyama *et al*., 2002, Iwamuro *et al*., 2006) leading to dramatic effects on amphibian metamorphosis in the form of delayed development, reduced body weights, and lengths in *Rhinella arenarum* (Wolkowicz *et al*, 2014).

Anurans (frogs and toads) are used as model organisms for ecotoxicological studies of several environmental stressors (Pereira *et al*, 2020). The presence of an aquatic larval stage continuously exposes the developing embryo to toxicants as Anuran eggs lack a protective eggshell. Also, after hatching, larval skin is highly permeable, allowing an easy penetration of chemical substances leading to bioaccumulation of hazardous substances. Thus, the larval stages of Anurans are most sensitive to aquatic pollutants. Therefore, Anurans are used as model organisms to study the effects of environmental pollutants such as BPA on freshwater ecosystem health. Also, Anurans were the model of choice for many physiological experiments due to their small body size, local availability, and tolerance of surgical procedure (Bennett, 1999).

When considering the past scientific literature, not many experiments were carried out to investigate the impact of BPA on Anurans. Even among this existing literature, there are contradictions to be noted. For an example, Kloas and Lutz., 2006, Pickford *et al*., 2003, and Levy *et al*., 2004 have pointed out that there are anatomical malformations due to BPA exposure in model amphibians. But Tamschick *et al*., 2016 have claimed that there are no BPA – induced anatomical malformations. According to them, malformations were caused due to reasons other than BPA. Pickford *et al*., 2003, Sone *et al*., 2004, and Iwamuro *et al*., 2003 have suggested that BPA has no impact on morphometric parameters of amphibians. But Tamschick *et al*., 2016 have suggested that there is a species–wide effect on snout – vent length and body weight of amphibians. Iwamuro *et al*., 2003 have also suggested that BPA could exert anti – metamorphic effects on Anurans only when treated with high concentrations of BPA. Oehelmann *et al*., 2006 have claimed that exposure to very low concentrations of BPA (around 10^{-7}M) can promote feminization in Anurans. Tamschick *et al*., 2016 have also agreed on BPA induced-sexual alteration under very low BPA concentrations, but they have claimed that it could not be defined as female – biased, male – biased, or a mixed ratio. But Pickford *et al*., 2003 have suggested that there is no sexual differentiation in very low concentration of BPA.

In this context where the experimental data are not conclusive, a systematic review can be considered as a plausible approach to scientifically analyze and scrutinize the existing data. A systematic review collects and analyses all possible studies related to a particular research design and concept (Uman, 2011). In the present study, previous studies regarding Anuran exposure to BPA were reviewed systematically.

Methodology

A systematic review on the published literature on the growth - related effects of BPA on amphibians was carried out in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta – Analyses) guidelines (Hwang *et al*., 2018). A comprehensive search on literature was conducted in several databases including Google Scholar, PubMed, and Microsoft Academics. Keywords used were “Amphibians”, “Bisphenol A”, “Tadpoles”, “Freshwater amphibians”, “Xenoestrogen” and

"Endocrine disruptors" during the period of June 2021 – November 2021. Search results were limited to English.

Articles obtained after searching the databases were pooled together and duplicate articles were removed. Initially, remaining articles were screened by reading the title and abstracts. Studies meeting the exclusion criteria were removed. Remaining articles were screened by reading the full – text and articles meeting the exclusion criteria were removed. Additional articles were recruited by screening the reference lists of included articles. Some excluded articles were retrieved after reading reviews and meta-analyses as some parameters which were failed to notice before were noticed in these reviews and meta-analyses.

Systematic review was restricted to order Anura from amphibians because most of the studies are based on Anurans. Only very few studies were found about other two orders in class Amphibia (Order Urodela and Order Apoda) overall, and no study upon Urodele or Apoda on exposure of BPA. Also, the chemical discussed here is associated with urban and domestic environment where Anurans are thriving than Urodeles and Apoda.

Exclusion Criteria was based on, effects of chemicals other than BPA on Anurans, effects of BPA on species other than Anurans, non – full text articles, meta – analyses and reviews, studies not following a proper methodology (e.g.: without control experiments, no statistical analyses, no replicates etc.), studies carried out using adults/ non – Anurans, and studies with genetic experiments.

Inclusion Criteria was based on, effect of BPA on growth, survival, and development parameters on early life stages of amphibians (e.g.: mortality rate, metamorphosis, sex ratio)

Results and discussion

The literature search identified 458 research articles from database search of Google Scholar (n = 421), PubMed (n = 18), and Microsoft Academic (n = 19). Four additional articles were recognized after reading meta-analyses and reviews. 20 duplicate articles, 4 non – English studies, 20 meta-analyses and reviews, 375 articles on other endocrine disrupting chemicals were excluded initially. Secondly, articles regarding amphibians other than Anurans, studies on adult stages of Anurans, molecular genetic studies, and studies with non – relevant exposures and outcomes were excluded. After removing duplicate articles and articles meeting the exclusion criteria, 12 articles met the eligibility criteria of present study (Figure 1). Among them, 7 articles have focused on the effect of BPA on the survival of Anurans. 8 articles have focused on the effect of BPA on Anuran morphological abnormalities, while 4 articles were focused on the effect of BPA on sex ratio of Anurans. Some articles have investigated into one or more response variables. Only one article has investigated into all the three parameters.

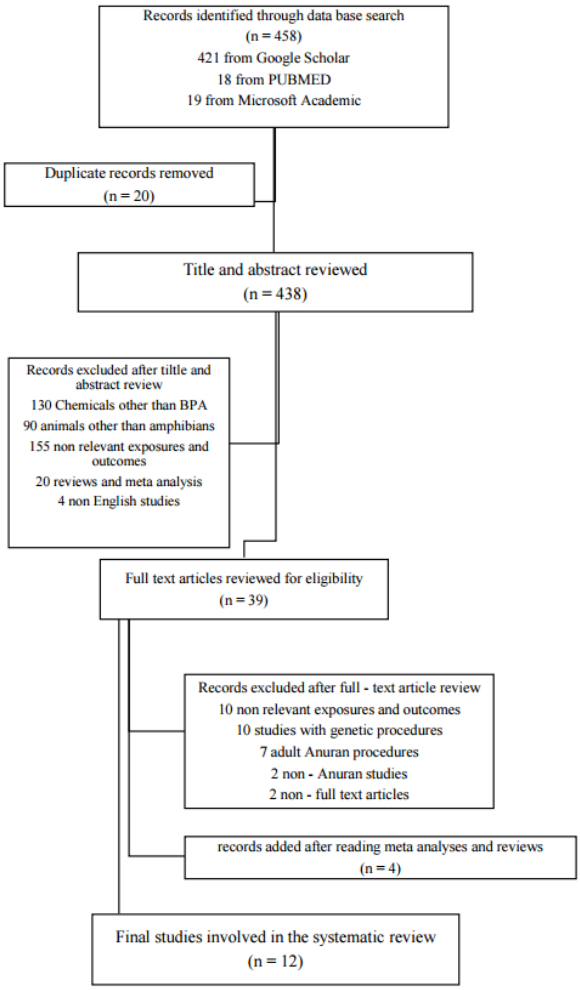

Figure 4: Recruitment strategy of published literature for PRISMA analysis

57% of the 7 studies have used *Xenopus laevis* as the model organism. Other 43% of 7 studies have used different model organisms such as *Rana temporaria*, *Hyala arborea*, *Bufo viridis*, and *Rhinella arenarum*. All 7 studies were conducted out of Southeast Asia. Three studies were conducted in Eastern Asia (Japan). Two studies were conducted in Europe, while remaining two studies were conducted in USA and Argentina. 57% of the 7 studies have used ethanol as the treatment control. BPA stock solution in these products were prepared by dissolving BPA in ethanol. Other studies have used de chlorinated water, acetone, and dimethyl sulfoxide (DMSO) as solvent control and for dissolving BPA. Studies were conducted between the period of 2002 – 2015.

In all the studies, survival rate of tadpoles has decreased with increasing BPA concentration in the concentration range between $1*10^{-10}$ M – $1*10^{-4}$ M. Survival rate has shown to be higher with prolonged exposures (more than 14 days) than with acute exposures (less than 14 days) to BPA. Iwamuro *et al*., 2003 and Sone *et al*., 2004, and Wolkowicz *et al*., 2016 have used acute exposures. Iwamuro *et al*., 2003 has used concentration between $1*10^{-5}$M – $1*10^{-4}$M and experienced lowest survival rates of 0% in $5*10^{-5}$M and $1*10^{-4}$M concentrations. Sone *et al*., 2004 has used concentrations between $1*10^{-6}$M – $1*10^{-5}$M and has reported on lowest survival rates of 0% in $4*10^{-5}$M and $5*10^{-5}$M. Wolkowicz *et al*., 2016 has used concentrations between $4*10^{-6}$M – $7*10^{-5}$ M and experienced lowest survival rates of 0% in concentrations between $2*10^{-5}$ M – $7*10^{-5}$M. In chronic exposures, Koponen and kukkonen., 2002 has used concentrations $4*10^{-6}$M, $4*10^{-7}$M, and $4*10^{-8}$M. Higher survival rates have been observed in 10^{-7}M (10 µg/L) and 10^{-8}M (100 µg/L) concentrations, which are environmental relevant

concentrations. But only a 30% survival rate has been reported under $4*10^{-6}$M concentration which is a supra environmental concentration (1000 µg/L). Pickford *et al*., 2003 has used concentrations between $4*10^{-9}$M – $2*10^{-6}$M. Lowest survival rate of 40% has observed in $2*10^{-6}$M concentration. Tamschick *et al*., 2016 has used very low environmentally relevant concentrations $1*10^{-10}$M, $1*10^{-9}$M, and a higher $1*10^{-6}$M concentrations and observed a similar average survival rate of 60%. Baba *et al*., 2009 has used concentrations between $2*10^{-8}$M – $2*10^{-5}$M and observed very high survival rates ranging between 88% - 99%.

Table 5 Summary of Literature used in systematic review.

Literature and species	**Concentration**	**Percentage Survival Rate**	**Treatment Duration**
Koponen and Kukkonen., 2002	4.38*10-8 M	95%	20 days
Rana temporaria	4.38*10-7 M	97%	
	4.38*10-6 M	30%	
	Control	96%	
Iwamuro *et al.*, 2003	1*10-5 M	98%	5 days
Xenopus laevis	2*10-5 M	90%	
	2.5*10-5 M	22%	
	3.0*10-5 M	11%	
	5*10-5 M	0%	
	1*10-4 M	0%	
	Control	88%	
Wolkowicz *et al.*, 2016	4.38*10-6 M	97%	14 days
Rhinella arenarum	1.01*10-5 M	90%	
	2.20*10-5 M	0%	
	3.28*10-5 M	0%	
	4.38*10-5 M	0%	
	5.34*10-5 M	0%	
	6.57*10-5 M	0%	
	Control	100%	
Pickford *et al*., 2003	4.38*10-9 M	95%	90 days
Xenopus laevis	1.00*10-8 M	90%	
	4.38*10-8 M	65%	
	1.00*10-7 M	60%	
	4.38*10-7 M	50%	
	2.19*10-6 M	40%	
	Control	89%	
Tamshick *et al*., 2016 *Hyla arborea*	1.00*10-10 M	85%	30 days

	1.00*10-9 M	80%	
	1.00*10-6 M	93%	
	Control	90.00%	
Bufo viridis	1.00*10-10 M	90%	
	1.00*10-9 M	85%	
	1.00*10-6 M	90%	
	Control	95%	
Xenopus laevis	1.00*10-10 M	100%	
	1.00*10-9 M	98%	
	1.00*10-6 M	100.00%	
	Control	97.50%	
Sone *et al*., 2004	1*10-6 M	96%	4 days
Xenopus laevis	2.5*10-6 M	99%	
	5*10-6 M	96%	
	1*10-5 M	94%	
	2*10-5 M	97%	
	3*10-5 M	59%	
	4*10-5 M	23%	
	5*10-5 M	0%	
	Control	94%	
Baba *et al*., 2009	2*10-8 M	99%	21 days
Xenopus laevis	4*10-8 M	95%	
	6*10-8 M	97%	
	8*10-8 M	91%	
	1*10-7 M	98%	
	1*10-6 M	98%	
	1*10-5 M	88%	
	2*10-5 M	91%	
	Control	97%	

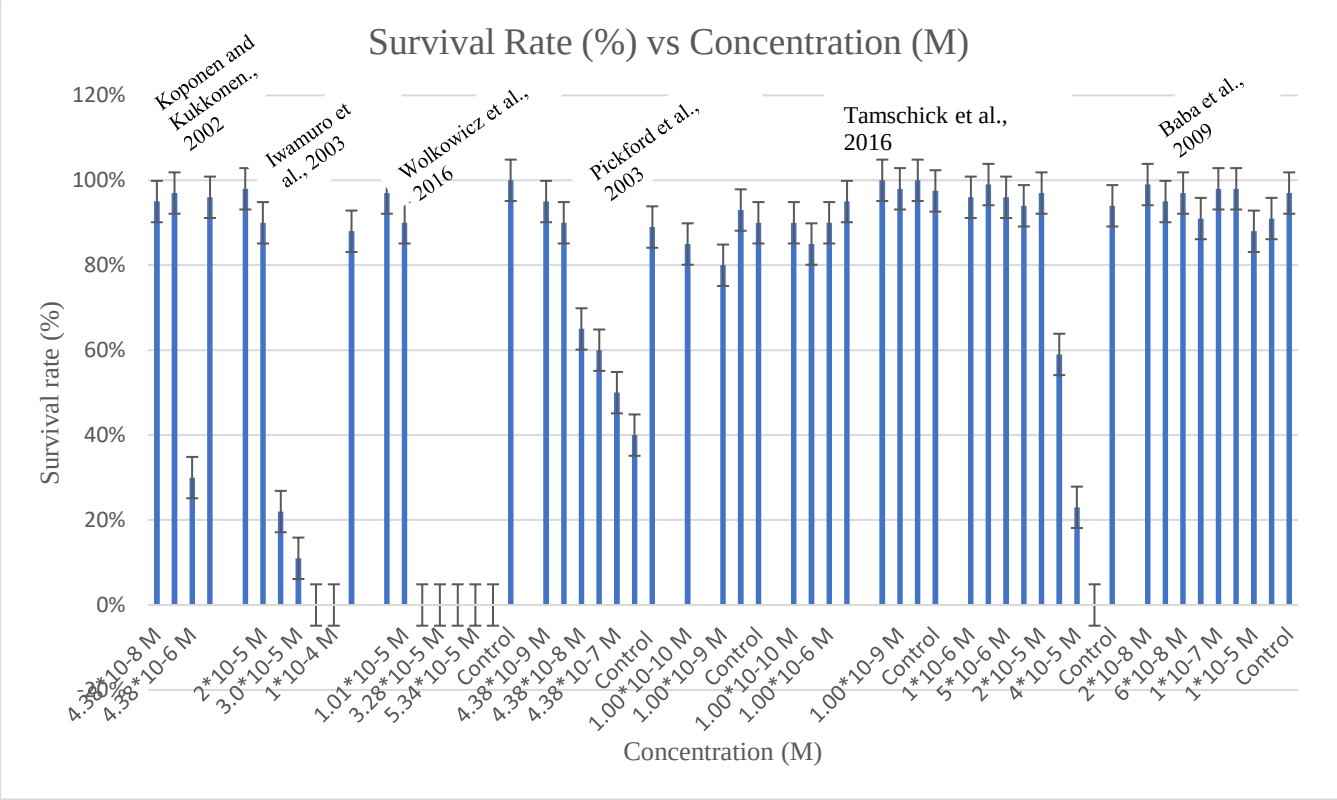

Figure 5: Graph of Percentage Survival vs Concentration (M)

There was no difference in survival rates based on model organism used. Highest survival rate of 99% has been observed for a concentration of $1*10^{-8}$M and lowest survival rate of 0% has been observed for concentrations between $6*10^{-5}$M – $1*10^{-5}$M. Extremely high mortality and high survival rates have been recorded only with very high (> $4*10^{-5}$ M) and very low (<$1*10^{-5}$) doses of BPA respectively. However, in environmentally relevant concentrations, survival rate has not been changed significantly (Tamschick *et al*., 2016).

Eight articles have discussed on the effects of BPA on Anuran morphological abnormalities. 4 studies have carried out in Japan. 3 studies have carried out in Argentina. Only one study has been carried out in USA. 2 studies have used ethanol as the control, while other 2 studies have used de – chlorinated tap water as the control. Another two studies have used acetone and AMPHITOX solutions along with water as controls. One study has used NaOH and ethanol along with tap water as controls, while the remaining study has used ethanol and DMSO as controls along with a tap water control. Studies were conducted during the period of 2003 – 2015.

50% of the 8 studies have *used Xenopus laevis* as the model organism. Morphological abnormalities observed were not associated with model organism used or the type of control used. Most common abnormalities discussed were microcephaly (smaller head), short body length, flexure (bent/curved body), abnormal gut coiling, oedema (abnormal swelling in body tissues), scoliosis (curved spine), delayed development (delaying metamorphosis compared to control), abnormal skin pigmentation, and shortened distance between eyes.

Accordingly, most common types of morphological abnormalities discussed are oedema, short body length, flexure, and scoliosis. These abnormalities are observed in concentrations over $2.5*10^{-5}$M of

BPA, while fewer abnormalities were reported under low exposures. $2.5*10^{-5}$M exceeds environmentally relevant concentrations (Tamschick *et al*., 2016).

Goto *et al*, 2006 has observed no specific morphological abnormalities in the concentration range of $1*10^{-6}$M to $1*10^{-8}$M. Iwamuro *et al*., 2003 has observed a shortened distance between eyes and a crooked vertebrae in tadpoles exposed to concentrations higher than $2.5*10^{-5}$M. Wolkowicz *et al*., 2016 has observed hydropsy, and flexures in concentrations higher than $2*10^{-5}$M of BPA. Pickford *et al*., 2003 and Iwamuro *et al*., 2006 have observed no significant morphological abnormalities throughout the exposure period. Wolkowicz *et al*., 2014 has observed morphological abnormalities such as delayed development, reduced body size, hydropsy, and flexures in all concentrations used. Baba *et al*., 2009 has observed severe scoliosis conditions in tadpoles exposed to $2*10^{-5}$M concentrations.

Table 6 Summary of Morphological abnormalities observed in published literature.

Literature and species	**Concentration Range**	**Morphological abnormalities observed**
Goto *et al,* 2006 *Rana rugosa* *Silurana tropicalis*	$1*10^{-6}$ – $1*10^{-8}$ M	No abnormalities
Iwamuro et al, 2003 *Xenopus laevis*	>$2.5*10^{-5}$ M	Shortened distance between eyes. Crooked vertebrae
Wolkowicz et al, 2016 *Rhinella arenarum*	>$2*10^{-5}$ M	Hydropsy Flexures
Wolkowicz et al, 2014 *Rhinella arenarum*	$1*10^{-5}$ M – $7*10^{-5}$ M	Delayed development Reduced body size Hydropsy Flexures
Baba et al, 2009 *Xenopus laevis*	$2*10^{-8}$ M – $2*10^{-5}$ M	Severe scoliosis
Iwamuro et al, 2006 *Xenopus laevis*	$1*10^{-7}$ M	No abnormalities
Pickford et al, 2003 *Xenopus laevis*	$4*10^{-9}$ M – $2*10^{-6}$ M	No abnormalities

Only 4 studies have discussed the effect of BPA on the sex ratio of Anurans. These studies have been conducted in Asia. 3 out of 4 studies were conducted in Germany. Different types of solvent controls were used, such as water, ethanol, and DMSO. But there was no impact from the solvent control on results. Studies were conducted during the period of 1999 – 2016.

Results have indicated that in very low concentrations, including environmentally relevant concentrations ($1*10^{-10}$ M – $1*10^{-9}$ M), sex ratio of Anurans could be altered. Tamschick *et al*., 2016 have reported on on a possibility of altering gonadal morphology along with sex ratio. But at the same time, Tamschick *et al*., 2016 have claimed that there is no possibility of mixed – sex phenotypes, or female – biased sex ratios occurring in Anurans due to BPA exposure in the concentration range of $1*10^{-10}$M to $1*10^{-6}$M for 30 days. But Levy *et al*., 2004 have reported on a female – biased sex ratio among Anurans due to BPA exposure in the concentrations between $1*10^{-7}$ M - $1*10^{-8}$ M for 120 days. Pickford

et al., 2003 have also suggested that there is no female-biased sex ratio generated by BPA under concentrations between $4*10^{-8}$M – $2*10^{-6}$M for 90 days with *Xenopus laevis* as the model organism.

Overall, systematic review pointed out that there was an effect of BPA on Anurans. But whether this effect is from environmentally relevant concentrations, or laboratory-induced high concentrations, was not very clear. As of the analysis, lower survival rates were observed under acute exposures. Morphological malformations were observed in both acute and prolonged exposures. However, it could be seen that lower survival rates and high morphological abnormalities were observed in concentrations above $2*10^{-5}$ M. Also, Pickford *et al*., 2003, Tamschick *et al*., 2016, directly denied that BPA do not have an impact on survival, development, metamorphosis, or sex ratio of Anurans.

Twelve studies were recruited in the present systematic review. These studies were recruited from 458 articles using PRISMA analysis guidelines (Hwang *et al*., 2018). From the selected articles, majority of the studies have claimed on BPA-induced altered growth, development, survival, sex ratio and metamorphosis in Anurans. But some articles have opposed the claim and have denied the effect of BPA on Anurans (Pickford *et al*., 2003; Tamschick *et al*., 2016). There were many differences among these studies including geographic area, concentration range, model organisms, duration of the study and experimental setup. Therefore, results may be different from one study to the other. For examples, Koponen and kukkonen, 2002 has used environmentally unrealistic concentrations such as 1000 µg/L BPA for the exposure, which will surely induce considerable higher mortality rates. In contrast, Pickford *et al*, 2003 has used very low concentrations starting from 0.83 µg/L. These concentrations mostly correspond to BPA concentrations in the environment (Tamschick *et al*., 2016). Lowest survival rates were observed in acute treatment durations (less than 14 days) in concentrations between $1*10^{-6}$ M – $1*10^{-4}$ M. Treatment durations of studies that have supported the claim of BPA affecting Anuran growth had been around 5 days to 20 days, but treatment durations of studies that have opposed the claim had been longer, around 90 – 120 days. There has been no indication to point out this difference would have occurred due to model organism. For an example, Pickford et al., 2013 has used *Xenopus laevis* as the model organism. Eventhough Iwamuro *et al*, 2003, Levy *et al,* 2004, Baba *et al,* 2009, and Sone *et al*, 2004 have noticed different results, they also have used *Xenopus laevis* as the model organism.

Presence of morphological deformities were widely discussed in systematic review. Most common deformities were oedema, short body length, flexures, and scoliosis. These deformities were mostly prevalent during very early stages of Anurans. Deformities were mostly reported in high concentrations, which are environmentally non relevant, and deformities were increasing with concentration. In most of the studies, deformities were recorded in concentrations higher than $2*10^{-5}$ M.

A female-biased sex ratio was discussed in systematic review. In studies where sex ratio change has observed, significant changes have occurred in very low concentrations such as $1*10^{-7}$ M and $1*10^{-8}$ M. Change of sex ratio could affect the population dynamics affecting the ecosystem health.

After systematic review, it could be concluded that significant effects from BPA exposure on survival and morphological malformations were due to environmentally non-relevant and high concentrations. However even under low concentrations, a female – biased sex ratio could occur.

Conclusion and recommendations

From the analyzed results of systematic review, it could be concluded that, at environmentally relevant concentrations, there was no significant effect of BPA on survival rate and morphology of tadpoles. However there was a significant predisposition towards on female – biased sex ratio indicating the

requirement of comprehensive scientific studies for further clarification. Most studies were carried out outside of South – East Asia. Hence, it is difficult to conclude the impacts of BPA on local amphibian population. Also, there were no consistent records about environmentally relevant concentrations of BPA in local aquatic environments. Taking these factors into consideration, further studies on environmentally relevant BPA exposure on aquatic wildlife are recommended. Plastic waste is one of the major pathways of environmental introduction of BPA. Therefore it recommended to implement laws and regulations to promote responsible plastic usage and waste management, to minimize the potential threats to ecosystem health.

Acknowledgement: Department of Zoology, Faculty of Science, University of Kelaniya is acknowledged.

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A SYSTEMATIC REVIEW ON THE EFFECTS OF SHORT-TERM EXPOSURE TO BISPHENOL-A AND BISPHENOL-S DURING EMBRYONIC STAGES OF ZEBRAFISH *(Danio rerio)*

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Abstract

Bisphenol-A is a highly used industrial chemical and a pervasive environmental oestrogen. Therefore, bisphenol-S was introduced as a safe alternative, yet endocrine disruption properties have been reported. Therefore, the safety of bisphenol-S as a safe substitute of bisphenol-A has become questionable. Yet, the existing published literature on comparative assessment of bisphenol effects are not conclusive. Therefore, a systematic review was carried out to comprehend the relative effects of bisphenols, by comparing the growth-related effects of early-life exposure to bisphenol-A and bisphenol-S in the model organism, *Danio rerio* (Zebrafish). The review analysed the published research through Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) strategy. The search was conducted in Research Gate, Pub Med, Google Scholar, and Science Direct databases for articles published from the start of database coverage until August 2021, searching for articles on survival and growth-related effects of bisphenols in embryonic stages of zebrafish. Out of 181 articles, only 7 articles became eligible for inclusion criteria of early life (embryo) short-term bisphenol exposure. In recruited articles, hatching rate, body length, locomotion, malformations and survival of zebrafish were analysed under bisphenol concentrations of 0.0001 mg/L to 100mg/L. Studies on hatching rate have reported that exposure to both types of bisphenols in the concentration range of 1-100 µg/L significantly increase the hatching rate in a comparable manner. One study has reported that bisphenol-S significantly decreases embryo survival in lower concentrations than bisphenol-A. Decreased body length under the concentration range of 0.1-100 µg/L were evident for both bisphenols in a comparable manner. Based on the systematic review, it can be concluded that acute exposure to bisphenol-A and bisphenol-S exert similar effects to zebrafish embryos. Therefore the claim on the bisphenol-S as a safe bisphenol-A substitute warrants further investigations.

Keywords: Bisphenol-A, Bisphenol-S, PRISMA analysis, Short-term exposure, Zebrafish

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ISBN - 978-624-5507-87-0
ISBN - 978-624-5507-88-7