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Nanomaterials in point-of-care diagnostics: Bridging the gap between laboratory and clinical practice

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ABSTRACT

The integration of nanomaterials into biosensing technologies represents a paradigm shift in medical diagnostics and environmental monitoring, marking a significant advancement in the field. This comprehensive review examines the role of nanomaterials, such as gold nanoparticles, carbon nanotubes, graphene, and quantum dots, in enhancing the performance of biosensors. These nanomaterials contribute unique physical and chemical properties, including exceptional electrical, optical, and thermal conductivities, which significantly improve the sensitivity, specificity, and versatility of biosensors. The review provides an in-depth analysis of the mechanisms by which these nanomaterials enhance biosensor functionality, including increased surface-to-volume ratio, improved electron transfer rates, and enhanced signal transduction. The practical applications of these advanced biosensors are explored across various domains, including oncology, infectious diseases, diabetes management, cardiovascular health, and neurodegenerative conditions, emphasizing their role in early disease detection, real-time health monitoring, and personalized medicine. Furthermore, the review addresses the critical challenges and limitations facing the field, such as biocompatibility, biofouling, stability, and integration into existing healthcare systems. Strategies to overcome these challenges, including advanced material engineering and novel fabrication techniques, are discussed. The future of nanomaterial-based biosensors is envisioned through the lens of emerging trends and technological innovations. The integration with microfluidics, artificial intelligence, and wearable technology is highlighted as a path toward more personalized, efficient, and accessible healthcare solutions. This review underscores the transformative impact of nanomaterials in biosensing, projecting a future where these advanced technologies play a pivotal role in reshaping diagnostics, patient care, and environmental monitoring, thereby significantly enhancing healthcare and public health outcomes.

1. Introduction

The advent of nanomaterials in biosensing and diagnostic technologies heralds a paradigm shift in medical science, significantly elevating the capabilities of disease detection and management [1,2]. These nanomaterials, defined by their minuscule dimensions, are not merely incremental improvements but a quantum leap in the domain of biosensors. They bring to the table a suite of extraordinary physical, chemical, and biological properties, attributable to their nanoscale size and exceptional surface-to-volume ratio. These characteristics endow them with unparalleled electrical and thermal conductivities, optimizing them for the nuanced demands of biosensing applications. Key

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materials such as gold nanoparticles, quantum dots, carbon nanotubes, and graphene stand out in this arena [3,4]. Their prowess in enhancing electron transfer rates and augmenting signal transduction is not just notable; it's a game-changer. These nanomaterials are instrumental in forging paths toward early disease intervention and the dawn of personalized medicine [1,5–7].

In the healthcare landscape, the role of nanomaterials is not just significant; it's transformative. Graphene, carbon nanotubes, and magnetic nanoparticles, in particular, have been at the forefront of developing biosensors that are not only exquisitely sensitive but also remarkably specific. This leap forward in technology is reshaping the way we detect a plethora of analytes, offering precision and speed that were once unthinkable. This advancement paves the way for breakthroughs in early disease detection, ongoing health condition monitoring, and personalized medicine [8,9]. The evolution of nanotechnology-based biosensors reflects the maturation of biosensing from a niche science into a cornerstone technology in clinical settings and personal health monitoring [10–14].

The integration of biosensors into healthcare has revolutionized patient care and disease management. These devices facilitate rapid, sensitive, and non-invasive detection of a wide range of biomarkers, playing an instrumental role in the early detection, monitoring, and treatment of diseases [15–17]. This technological revolution has ushered in a new era of cost-effective, portable, and rapid-response devices for clinical applications, overcoming many challenges inherent in personalized medicine [6]. The enhanced electrical, optical, and mechanical characteristics of nanomaterials make them ideally suited for refining the sensitivity and specificity of biosensors, crucial for detecting clinically important molecules [5,7].

This review examines the progress of nanotechnology in biosensing and diagnostics, focusing on nanomaterial-based biosensors. It explores their design, operational principles, and applications while addressing challenges such as scalability and regulatory hurdles. The integration of nanomaterials with emerging technologies like AI and microfluidics offers promising advancements in personalized medicine and point-of-care diagnostics. By analyzing successful case studies and ongoing trials, the review highlights the transition of these biosensors from laboratory research to clinical use, emphasizing their role in improving healthcare accessibility and effectiveness.

2. Methodology

This review was conducted to cover recent advancements in nanomaterial-based biosensors and their clinical applications. A literature search was performed across multiple scientific databases, including PubMed, Web of Science, Scopus, and Google Scholar. The following keywords and their combinations were used: nanomaterial(s), biosensor(s), nanotechnology, point-of-care diagnostics, clinical applications, translational research and medicine. Eligible studies were original research articles and reviews published in between January 2018 and April 2023, focusing on nanomaterial-based biosensors with potential clinical applications, particularly those demonstrating progress in translating laboratory findings to clinical settings. Articles in English were included. Excluded were studies focused solely on the fundamental properties of nanomaterials without biosensing applications, as well as articles lacking clinical relevance, conference abstracts, letters to the editor, and opinion pieces. Studies published before 2018 were omitted unless they were seminal papers that provided essential background information.

3. Nanomaterials in biosensing

The integration of nanomaterials into biosensing technologies marks a significant leap in the field of medical diagnostics, offering unprecedented enhancements in biosensor capabilities. This innovation pivots on the unique physical and chemical attributes of these materials, which are fundamentally transforming the landscape of healthcare diagnostics.

Metallic nanoparticles, particularly gold (AuNPs) and silver are at the forefront due to their exceptional optical properties and functionalization ease. Their role is accentuated in surface plasmon resonance, a phenomenon that critically amplifies the sensitivity of biosensors. This characteristic of AuNPs facilitates not only the attachment of biomolecules for targeted detection but also enables their use in sensitive detection methodologies, such as changes in absorbance, fluorescence, or Raman scattering, because of their superb electron transfer properties [5,6,18].

Parallelly, carbon-based nanomaterials like carbon nanotubes (CNTs) and graphene are making remarkable contributions to biosensor development [19–21]. CNTs, known for their high surface area and exceptional electrical conductivity, are enhancing the electrochemical performance of biosensors. Graphene, while not as conductive as monolayer graphene, stands out due to its high surface area, biocompatibility, and flexibility, rendering it ideal for a wide array of biomolecular detections [6,7,18,22].

The realm of one-dimensional structures, such as silicon nanowires, is also pivotal. Utilized extensively in field-effect transistor (FET) biosensors, these nanowires, due to their high surface-to-volume ratios, contribute significantly to the sensitivity and specificity in detecting biomolecules at low concentrations [23,24]. Furthermore, semiconductor nanowires and nanorods, along with zinc oxide, are notable for their excellent electrical properties and high surface-to-volume ratios, enhancing the detection capabilities of biosensors [9,25].

Quantum dots (QDs) also hold a special place in the spectrum of nanomaterials utilized in biosensing. Known for their unique optical behaviors and size-tunable optical properties, QDs are instrumental in optical biosensing applications. Their high photostability makes them valuable in scenarios where enduring optical characteristics are essential [25].

The high surface area of materials like nanoparticles and nanotubes plays a crucial role in immobilizing a higher density of biorecognition elements, thereby increasing biosensor sensitivity. The electrical conductivity of graphene and CNTs is a key factor in facilitating rapid electron transfer in electrochemical biosensors [26,27]. Similarly, the optical properties of gold nanoparticles and quantum dots are exploited for sensitive detection of analytes. Additionally, the magnetic properties of magnetic nanoparticles (MNPs) are utilized in biosensors for concentrating analytes and for signal transduction in magnetic biosensors [18,22].

Chemical reactivity and functionalization are other aspects that cannot be overstated. The ability to bind biomolecules specifically to nanomaterials for selective detection of target analytes is a game-changer. The biocompatibility of materials like graphene ensures minimal toxicity and better stability in biological environments. Materials like fullerenes also contribute significantly with their unique spherical structure and electrical properties, acting as both electrophilic and nucleophilic agents, thus enhancing the versatility of biosensing applications [22].

In essence, the diverse types of nanomaterials each contribute distinct properties to biosensors, enhancing their sensitivity, specificity, and versatility. This integration into biosensor design has led to significant advancements in applications ranging from healthcare to environmental monitoring. The burgeoning field of biosensing, revolutionized by the integration of nanomaterials, offers enhanced capabilities in detecting and quantifying biological analytes, which is pivotal for effective disease diagnosis and management [10,12–14]. The integration of these nanomaterials into biosensors has resulted in devices with improved analytical performance, including lower detection limits, faster response times, and higher specificity. This has been crucial in advancing the field of biosensing, opening new avenues for the early diagnosis and monitoring of various diseases and environmental monitoring [10,12–14]. Fig. 1 and Table 1 summarise the types of nanomaterials used in biosensing.

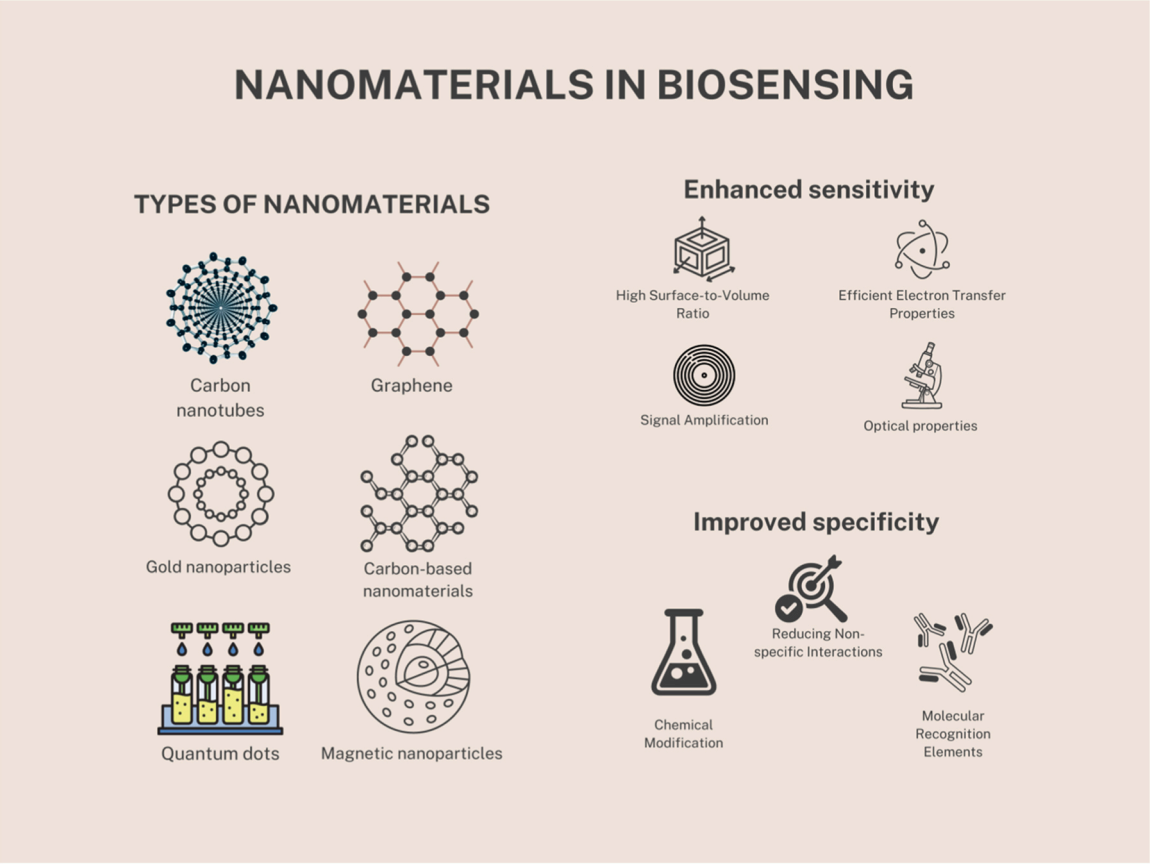

Fig. 1. Types of nanomaterials used in biosensing and their properties. Created with biorender.com.

Table 1
Types of Nanomaterials Used in Biosensing.

Nanomaterial	Properties	Applications in Biosensing
Gold Nanoparticles (AuNPs) [28,29]	High electrical conductivity, optical properties	Immunoassays, optical biosensors
Carbon Nanotubes (CNTs) [30,31]	High surface area, electrical conductivity	Electrochemical biosensors
Graphene [32,33]	High surface area, biocompatibility	Biomolecular detections
Quantum Dots [34,35]	Optical behaviors, size-tunable properties	Optical biosensing
Silicon Nanowires [36,37]	High surface-to-volume ratio	FET biosensors
Magnetic Nanoparticles [38,39]	Magnetic properties	Magnetic biosensors

4. Advances in nanomaterial-based biosensors

The integration of nanomaterials into biosensing technologies has marked a significant advancement in the field, enhancing both the sensitivity and specificity of biosensors [20,40]. This progress stems from the unique properties of nanomaterials and their interactions with biological entities. Nanomaterials such as nanoparticles, carbon nanotubes, and graphene, known for their high surface-to-volume ratio, increase the binding capacity for analytes and amplify detection signals. This enhanced sensitivity is crucial for detecting low-abundance biomarkers, which is vital in early disease diagnosis and monitoring [13,22,41,42].

Gold nanoparticles are renowned for their large surface area, which enables them to bind to a considerable number of antibody molecules, thereby enhancing the sensitivity of immunoassays. Similarly, carbon-based nanomaterials, due to their efficient electron transfer properties, play a significant role in electrochemical biosensors, leading to a more pronounced signal per interaction event. This results in lowering the limit of detection (LOD) and improving sensitivity [8,9,12]. Additionally, the unique optical properties of nanomaterials like quantum dots are exploited in optical biosensors. Their size-dependent fluorescence enables sensitive detection of target molecules, even at very low concentrations [6].

Nanomaterials can also be chemically modified to introduce specific binding sites for target analytes, thus enhancing the specificity of biosensors. Selective functionalization ensures that the biosensor responds only to the target molecule, reducing non-specific interactions and false positives. This is exemplified by tailoring the surface chemistry of nanomaterials with molecular recognition elements such as antibodies, aptamers, or enzymes, which bind specifically to target molecules. This ensures that the biosensor detects only the intended analytes [10,14].

The successful application of nanomaterials in biosensors is evident in various examples. Gold nanoparticles have been used in colorimetric biosensors for the detection of various biomarkers, where their aggregation in the presence of a specific analyte results in a visible color change [43]. Graphene-based Field-Effect Transistor (FET) biosensors and carbon nanotube-based electrochemical biosensors have shown high sensitivity and specificity in detecting viruses like SARS-CoV-2, glucose, proteins, and DNA. Their high electrical conductivity and surface area contribute significantly to the performance of these biosensors [44,45]. Quantum dots have been utilized in optical biosensors due to their luminescent properties, effective in multiplexed detection of biomarkers [42]. Additionally, magnetic nanoparticles have been employed in biosensors for the separation and concentration of RNA from a sample, enhancing the sensitivity of the detection process [46].

The advent of nanomaterials in biosensing has not only improved the

detection capabilities but also broadened the application range of biosensors. These improvements are evident in a wide range of applications, from healthcare diagnostics to environmental monitoring, underscoring the transformative impact of nanotechnology in the field of biosensing. The diverse examples of nanomaterial-based biosensors, ranging from gold nanoparticle-based colorimetric sensors to graphene-based electrochemical sensors, illustrate the broad applicability and potential of these devices in various fields. This progress not only enhances current biosensing capabilities but also paves the way for future innovations in medical diagnostics and environmental monitoring [10,12].

5. Applications in Diagnosis and Monitoring

Nanomaterial-based biosensors, with their advanced properties, have significantly revolutionized the field of medical diagnostics and monitoring. These sensors, incorporating materials like gold nanoparticles, magnetic nanoparticles, graphene, and carbon nanotubes, demonstrate exceptional sensitivity and specificity [39,43,45]. The application of nanotechnology in various aspects are described in brief below.

6. Infectious diseases

The burgeoning field of point-of-care diagnostics (POCT) for infectious diseases has been revolutionized by the integration of nanomaterials, culminating in innovative and efficient devices [47–49]. Central to this advancement are graphene-based FET biosensors and quantum dot-enhanced optical biosensors, which provide rapid and precise detection of viruses, including pathogens like SARS-CoV-2. This is indispensable for managing pandemics and diagnosing co-infections, especially crucial in early outbreak stages. Role of nanotechnology in enhancing POCT is multi-faceted. It contributes to the development of compact, portable, and integrated devices such as lab-on-chip (LOC), lab-on-disc (LOAD), microfluidic paper-based analytical devices (μPADs), lateral flow devices, miniaturized PCR devices, and isothermal nucleic acid amplification (INAA) devices. These advancements not only streamline infectious disease diagnostics but also make these tools accessible in low-resource settings [50,51]. The exceptional electrical, chemical, and optical properties of nanoparticles enhance the sensitivity and speed of electrochemical, optical, and instrumental biosensors. This review delves into various nanomaterials employed in biosensors, exploring their synthesis methods and properties, and presenting comparative data to illustrate their role in improving sensor performance [52]. The cutting-edge technologies in microfluidics, MEMS, nanotechnology, and materials science have significantly influenced POC device development. These technological strides have resulted in portable, miniaturized, and highly integrated POC devices that facilitate on-site detection of infectious pathogens, critical for timely therapeutic intervention against diseases like COVID-19 [50,51]. Nanotechnology has also been pivotal in advancing the next generation of sensing tools for selective biomolecule detection in infectious diseases. The potential integration of nanoparticles with biological markers targeting specific microorganisms is expected to enhance diagnostic sensitivity and specificity, enabling timely therapeutic intervention against life-threatening infectious diseases [53]. Integration of nanotechnology in POCT has enabled the development of advanced platforms for the fast and accurate detection of infectious diseases. These innovations are particularly vital in low-resource settings, where they can identify individuals at risk and in need of treatment, thereby playing a crucial role in the control of infectious diseases [54]. Recent clinical trials have demonstrated the efficacy of graphene-based FET biosensors in detecting SARS-CoV-2 in patient samples, showcasing the successful transition of this technology from laboratory to clinical settings [55–59]. For instance, a study published in Nature Biomedical Engineering in 2020 reported the use of a graphene-based biosensor for rapid COVID-19 detection in clinical samples, with sensitivity comparable to RT-PCR tests [60].

7. Diabetes mellitus

The integration of nanomaterials into diabetes management represents a significant advancement in medical research, particularly in enhancing diagnosis, treatment, and patient care. Carbon Nanomaterials (CNMs), including Carbon Nanotubes (CNTs), have become pivotal in this realm. They are utilized as implantable nanosensors for blood glucose monitoring, noted for their structural specificity and high drug-loading capacity, which makes them suitable for both diagnostic and therapeutic uses in diabetes. These nanomaterials serve versatile roles, acting as agents for imaging, diagnosis, and treatment [7,12,13,22,61]. Further advancements in nanotechnology have led to the development of theranostic nanomaterials, which combine therapeutic and diagnostic functions. These are instrumental in detecting diabetic biomarkers and treating diabetes, thereby addressing both diabetes management and the prevention of its associated complications [62]. In the field of glucose monitoring and insulin delivery systems, nanoparticles have shown significant promise. Nanoparticles used as carriers for orally administered insulin and in glucose biosensors equipped with Quantum Dots (QDs), Magnetic Nanoparticles (MNPs), and CNTs, have demonstrated increased sensitivity. This has steered research towards continuous glucose monitoring methods, enhancing accuracy and patient compliance [63]. Additionally, wearable sweat glucose biosensors for non-invasive, continuous monitoring of glucose levels in sweat are under development. These devices are crucial for systematic diabetes management. Ongoing research is focused on correlating sweat glucose with blood glucose, which is key to assessing the viability of wearable glucose biosensors in health monitoring [64]. Nanozymes, or nanomaterial-based artificial enzymes, are also gaining attention in biosensing due to their enzyme-mimicking capabilities, stability, and ease of surface modification. These nanozymes are employed in various biosensing strategies, including electrochemical, colorimetric, fluorescent, and immunological sensors. Their integration into point-of-care diagnostics is expected to significantly enhance the accuracy and sensitivity of diagnostic tools, thus improving patient outcomes and reducing healthcare costs [65,66].

8. Cardiovascular diseases

Advancements in biosensor technology, particularly those incorporating nanomaterials, have profoundly impacted the diagnosis and treatment of cardiovascular diseases (CVDs). These nanomaterial-based point-of-care (POC) diagnostics are characterized by their heightened sensitivity, selectivity, and quality, significantly enhancing early-stage diagnosis and personalized treatment strategies for CVDs [5,10,14]. Among these, optical nanobiosensors, employing nanomaterials for detecting cardiac biomarkers, have emerged as a pivotal innovation [67]. These sensors operate by translating the interaction of analytes with bioreceptors into detectable light signals. Their advantages, such as ease of monitoring, affordability, broad detection range, and high sensitivity without external interference, make them particularly effective for POC cardiac biomarker detection, offering a low detection limit. The effectiveness of these nanomaterial-based POC diagnostics hinges on the optical, electrochemical, and physical properties of the nanomaterials, which are influenced by their composition, size, and shape [68]. This ability to tailor nanomaterials enhances the performance of diagnostics in detecting various cardiovascular conditions. Furthermore, the field of nanotheranostics, which integrates diagnostic and therapeutic capabilities for CVDs, is rapidly evolving [69]. Utilizing the unique physicochemical properties of engineered nanoparticles, this approach aims for early diagnosis and treatment of conditions such as atherosclerosis, myocardial infarction, and aneurysms. This represents a shift from traditional diagnostic tools to more integrated nanotechnological platforms. The exploration of emerging nanostructures in

POC biosensing, including 0D structures like nanoparticles and quantum dots, 1D structures such as nanorods and nanowires, 2D structures like nanoplates and nanopores, and 3D structures including nanocomposites and complex hierarchical formations, is ongoing [70]. These structures hold promise in developing the next generation of miniaturized, portable POC biosensors. They could play a critical role in the early diagnosis and prevention of life-threatening diseases, including CVDs, potentially integrating with the internet of medical things (IoMT) and artificial intelligence (AI) for improved diagnosis and disease management. Lastly, the progression in POC testing for CVDs has been remarkable, with enhancements in biorecognition elements, optimization of detection techniques, and the development of tailored fluid handling systems [71]. These advancements have led to the creation of commercial assays that are not only economically viable but also highly sensitive, thereby supporting expedited diagnostic pathways and possibly influencing early interventions for individuals at an increased risk of cardiovascular diseases.

9. Neurodegenerative conditions

In neurodegenerative diseases like Alzheimer's and Parkinson's, the role of biosensors in early diagnosis is crucial. These biosensors are adept at detecting specific proteins and neurotransmitters associated with these conditions, facilitating early intervention and a better understanding of these diseases [1,12]. Nanomaterials, with their unique properties such as stability, biocompatibility, and novel physical and chemical characteristics, are increasingly utilized in diagnosing and treating neurodegenerative diseases (NDDs). In vivo techniques, including magnetic resonance, fluorescence, and surface-enhanced Raman imaging, leverage nanomaterials to study brain tissue structures, cerebral vessels, and biomarker distributions. Conversely, in vitro studies focus on detecting fluid biomarkers in cerebrospinal fluid and peripheral blood using methods like fluorescence, electrochemical, Raman, and surface plasmon resonance [72]. A key application of nanomaterials is in the electrochemical detection of neurotransmitters (NTs), which are essential for brain functions. Nanomaterials enhance the sensitivity and speed of these detections due to their high surface coverage and superior sensitivity. Electrochemical sensors, integrated with nanomaterials, offer a sensitive, simple, and rapid determination of NTs. These sensors are often part of portable devices for point-of-care diagnostic platforms [73]. Nanozymes, nanomaterial-based artificial enzymes, mimic natural enzymes and surpass their limitations. They are cost-effective, stable, and easily tunable. Utilized in various biosensing systems, these nanozymes include metal, metal oxide, and metal-organic framework-based types, and are crucial for point-of-care analysis. The design and function of these diagnostics are influenced by size, shape, composition, surface charge, and chemistry, as well as external factors like pH and temperature [65]. Addressing the challenge of transporting therapeutic agents across the blood-brain barrier, engineered nanomaterials, typically 1–100 nm in size, offer a promising solution. Their physico-chemical features and multi-functionalization capabilities, including the ability to cross this barrier, make them suitable for therapy, diagnostic imaging, neuroprotection, and neuronal tissue regeneration in neurodegenerative disorders [74]. Advances in nanomaterial-based biosensors have led to the use of various shapes, sizes, and compositions of nanomaterials, including gold and silver nanoparticles, quantum dots, and carbon nanomaterials in point-of-care testing. These nanomaterials enhance analytical performance and simplify the detection process, serving as carriers for immobilizing biorecognition elements or as labels for signal generation, transduction, and amplification. Recent innovations like lateral flow tests, printable electrochemical biosensors, and microfluidics-based devices underscore the growing application of nanomaterials in analyzing disease biomarkers [75].

10. Oncology

The evolution of point-of-care diagnostics (POCT) in oncology, particularly through the incorporation of nanomaterials, represents a significant leap in cancer diagnostics. Graphene-based biosensors, notable for their high efficiency in detecting low concentrations of tumor markers, are crucial in the early diagnosis of cancers like breast and prostate cancer [5,7–11,13,14]. A variety of nanomaterials, including gold and silver nanoparticles, quantum dots, mesoporous silica nanoparticles, and carbon nanomaterials, alongside hybrid nanocomposites, have been instrumental in enhancing POCT. Their unique properties are ideal for roles such as immobilizing biorecognition elements and acting as labels in signal generation, transduction, and amplification, thus improving the detection of disease biomarkers, including those for cancer [75]. Further advancements in cancer diagnostics are attributed to functionalized nanobiosensors. These sophisticated nanoscale sensing systems utilize diverse mechanisms like electrochemical, optical, mass, and calorimetric sensing to detect disease-specific biomarkers. Comprising carbon nanostructures, metal nanoparticles, magnetic nanoparticles, silica-based nanomaterials, conducting polymers-based nanoparticles, and quantum dots, these biosensors offer rapid, reliable, and cost-effective diagnostic approaches [76]. The design and efficacy of nanomaterial-based PoC diagnostics are greatly influenced by the composition, size, and shape of the nanomaterials. This enables the creation of devices that are not only sensitive but also compact, facilitating the miniaturization and improvement of diagnostic devices. This innovation leads to enhanced efficiency in detecting cancer biomarkers, surpassing traditional in vitro diagnostics [68,77]. These advancements, encompassing biosensors, smartphone interfaces, and lab-on-a-chip (LOC) devices, are set to revolutionize healthcare. However, challenges such as sampling procedures, sensitivity and specificity in clinical samples, system integration, and signal readout requirements need to be addressed for their widespread adoption in clinical practice [68,77].

11. Environmental monitoring

Nanomaterial-based biosensors are crucial in both disease diagnosis and patient care, as well as in environmental health monitoring. Their widespread use encompasses detecting allergens, environmental pollutants, toxins, and pathogens in water and air, crucial for public health, particularly in managing asthma and allergies. In analytical chemistry, nanomaterials are fundamental for environmental analysis and monitoring. They enhance various technologies, including sensors, and techniques for separation and extraction. In sensors, nanomaterials act as transducer elements in electrochemical types and as nanolabels in optical sensors. They also serve as stationary phases in liquid and gas chromatography, and as pseudostationary phases or buffer additives in capillary electrophoresis. Additionally, they are used as extraction materials for enrichment in chromatographic analysis. These techniques are vital for detecting diverse environmental pollutants, such as organic contaminants, heavy metals, and air pollutants [78]. A significant innovation in this domain is the development of nanozymes, specialized nanomaterials with enzyme-like properties. Nanozymes combine catalytic functions with the distinct physicochemical characteristics of nanomaterials, broadening their use in monitoring and remediation of environmental pollutants. They are effective in quantitatively and qualitatively detecting heavy metal ions, molecules, and organic compounds, and in degrading persistent pollutants like antibiotics, phenols, and textile dyes. Their applications extend to indoor air purification and combating pathogenic bacteria. However, the review of nanozymes highlights their inherent toxicity and the need for thorough evaluation of their interactions with the biosphere to ensure safety. To mitigate these toxicity issues, the green synthesis of nanozymes is suggested as a promising strategy [79].

Moreover, wearable nanomaterial-based biosensors are gaining

prominence in personalized healthcare [80–82]. They monitor various health parameters like heart rate, blood pressure, and glucose levels, essential for preventive medicine. Additionally, these sensors find use in prenatal diagnostics and the identification of hereditary diseases, especially in detecting specific DNA sequences related to genetic disorders [22].

The broad spectrum of applications, ranging from cancer detection, infectious diseases, diabetes, and cardiovascular diseases, to neurodegenerative conditions, and environmental monitoring, underscores the critical role of nanomaterial-based biosensors in early disease detection, personalized medicine, and continuous health monitoring. Their ongoing research and development promise further advancements and innovations, potentially expanding their applications and enhancing their impact on healthcare and public safety [10–14]. Fig. 2, Fig. 3, and Table 2 illustrate the diverse applications of nanomaterials in healthcare, detailing the associated mechanisms and challenges.

12. Challenges and limitations

Nanomaterial-based biosensors, representing a significant advancement in medical diagnostics, face an array of challenges that impede their widespread application. One of the primary concerns is biocompatibility. Nanomaterials, while offering unique properties, may trigger adverse biological responses such as toxicity or inflammatory reactions [83–86]. This is particularly crucial in in vivo applications, where long-term interaction with biological tissues is involved. Materials like graphene and certain nanoparticles are known for their biocompatibility, but the potential long-term effects and toxicity of some nanomaterials, especially in clinical settings, necessitate rigorous testing and validation to ensure safety [7,8,12,13].

Additionally, biosensor functionality is often compromised by biofouling – the unwanted accumulation of biological materials on the sensor surface. This phenomenon is especially problematic in devices intended for implantation or prolonged contact with biological fluids, where the accumulation can significantly impair sensor functionality [18].

The stability and durability of these biosensors are also significant concerns. Over time, the nanomaterials may degrade, or their functionalization may deteriorate due to environmental factors like temperature, pH, and the presence of enzymes. These factors can lead to a reduction in biosensor performance, posing challenges for their practical application, particularly in chronic disease monitoring and wearable biosensors [1,9,10,14].

In terms of production, scaling up while maintaining quality and performance is a daunting task. The complex and costly fabrication processes limit the availability and affordability of these biosensors, especially in resource-limited settings. Achieving uniformity and reproducibility in nanomaterial synthesis is crucial for consistent biosensor performance, yet variations in size, shape, and surface properties can lead to inconsistencies. This highlights the need for standardization of fabrication methods to ensure safety, effectiveness, and interoperability across healthcare systems [5,6,12,13,87].

Integration with existing systems and the regulatory process adds further complexity. Compatibility with current medical devices, data systems, and clinical protocols is essential for seamless integration in healthcare settings. The regulatory approval process, particularly for clinical use, involves stringent compliance with safety, efficacy, and quality standards, which can be time-consuming and resource-intensive. Furthermore, the sensitivity of these biosensors to environmental factors like humidity and light exposure must be addressed to ensure reliable operation under varying conditions [1,10,12].

Moreover, there is a gap between current laboratory-scale research and real-world application. Extensive clinical trials and testing are needed to validate the efficacy and safety of these biosensors. The limited understanding of the long-term effects of nanomaterials on human health and the environment necessitates continuous research to assess these impacts comprehensively. This gap emphasizes the need for multidisciplinary collaboration and alignment with regulatory standards to overcome these limitations and fully harness the potential of these innovative diagnostic tools [10,13,14,18,22,25,87,88]. While nanomaterial-based biosensors offer immense potential for revolutionizing diagnostics and monitoring, addressing these multifaceted challenges is crucial for their successful integration into healthcare. Continuous innovation, rigorous testing, and interdisciplinary collaboration are key to overcoming these hurdles and realizing the full potential of nanotechnology in biosensing applications. Fig. 4 and Table 3 delineate the challenges associated with nanomaterial-based technology in the field of medicine. The translation of nanomaterial-based

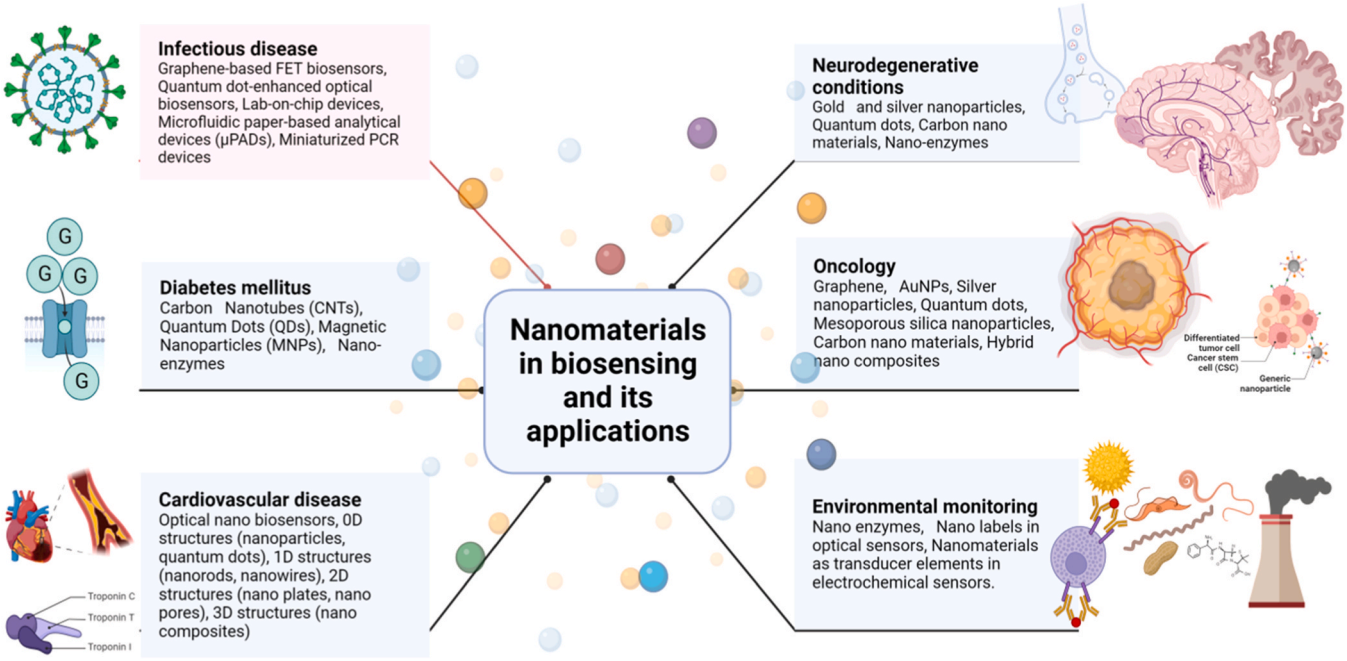

Fig. 2. Mechanisms involved in biosensing applications within the healthcare context. Created with biorender.com.

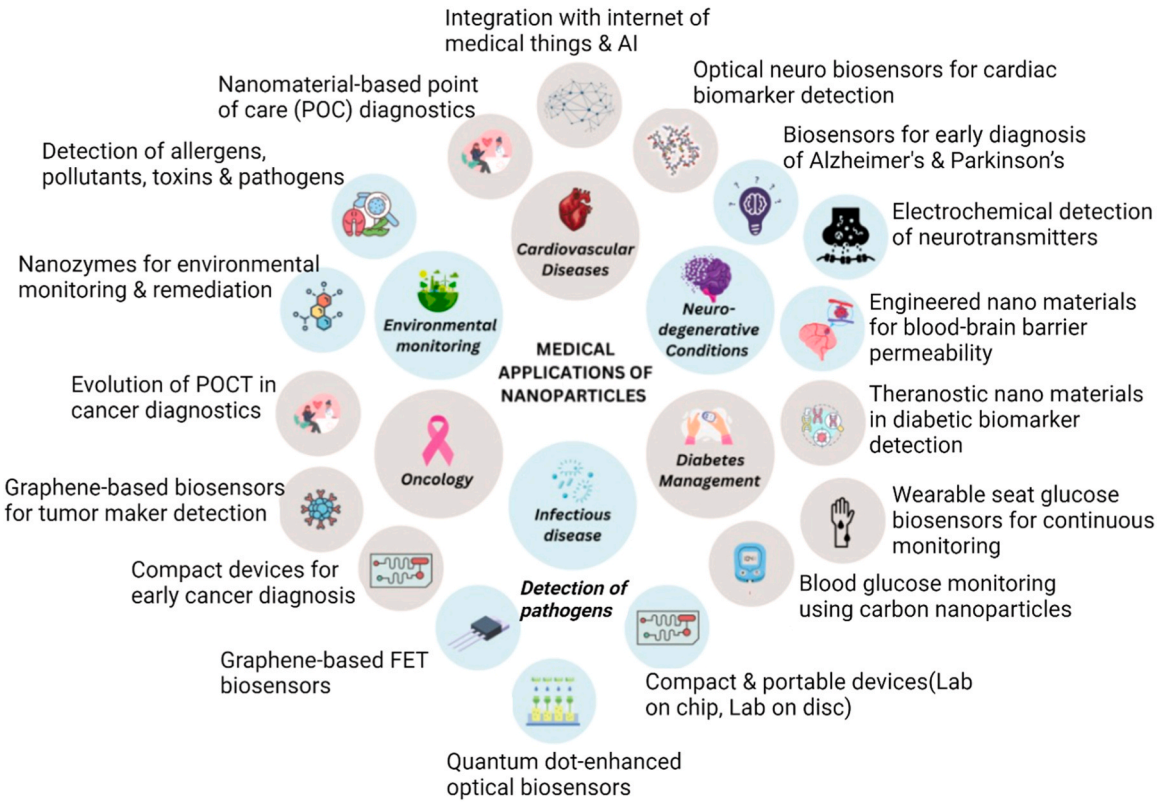

Fig. 3. Applications of nanomaterials in healthcare. Created with biorender.com.

Table 2
Biosensing Applications in Healthcare.

Application Area	Biomarkers/ Detection	Nanomaterial Used	Detection Method	Advantages	Challenges	Future Directions
Infectious Diseases	Pathogens like SARS-CoV−2	Graphene-based FET biosensors, Quantum dot-enhanced optical biosensors, Lab-on-chip devices, Microfluidic paper-based analytical devices (μPADs), Miniaturized PCR devices	FET, Optical	Rapid and precise detection, Portability	Sensitivity in clinical samples, System integration	Integration with smartphone interfaces, Increased accessibility in low-resource settings
Diabetes Management	Glucose	Carbon Nanotubes (CNTs), Quantum Dots (QDs), Magnetic Nanoparticles (MNPs), Nanozymes	Electrochemical, Optical	Continuous monitoring, Non-invasive methods	Correlation of sweat and blood glucose levels, Patient compliance	Wearable glucose biosensors, Enhanced accuracy and patient compliance
Cardiovascular Diseases	Cardiac markers like troponin	Optical nanobiosensors, 0D structures (nanoparticles, quantum dots), 1D structures (nanorods, nanowires), 2D structures (nanoplates, nanopores), 3D structures (nanocomposites)	Optical, Electrochemical	High sensitivity, Broad detection range	Optimization of detection techniques, Fluid handling systems	Integration with IoMT and AI, Personalized treatment strategies
Neurodegenerative Diseases	Specific proteins, neurotransmitters	Gold and silver nanoparticles, Quantum dots, Carbon nanomaterials, Nanozymes	Electrochemical, Fluorescent	High sensitivity, Rapid determination of NTs	Transport across blood-brain barrier, Stability of nanomaterials	Enhanced in vivo imaging, Improved therapeutic delivery
Oncology	Tumor markers	Graphene, AuNPs, Silver nanoparticles, Quantum dots, Mesoporous silica nanoparticles, Carbon nanomaterials, Hybrid nanocomposites	Electrochemical, Optical	High sensitivity and specificity, Early detection	Integration in clinical practice, Sampling procedures	Enhanced PoC diagnostics, Improved biomarker detection
Environmental Monitoring	Allergens, pollutants	Nanozymes, Nanolabels in optical sensors, Nanomaterials as transducer elements in electrochemical sensors	Electrochemical, Optical	High specificity, Environmental pollutant degradation	Toxicity of nanomaterials, Interaction with biosphere	Green synthesis of nanozymes, Indoor air purification applications

biosensors from laboratory prototypes to clinically viable tools faces several hurdles. These include ensuring reproducibility in large-scale manufacturing, addressing variability in clinical sample matrices, and navigating complex regulatory pathways. For example, the FDA's approval process for novel diagnostic devices requires extensive validation studies and often necessitates new regulatory frameworks for these innovative technologies. Addressing these challenges is crucial for bridging the gap between promising laboratory results and widespread

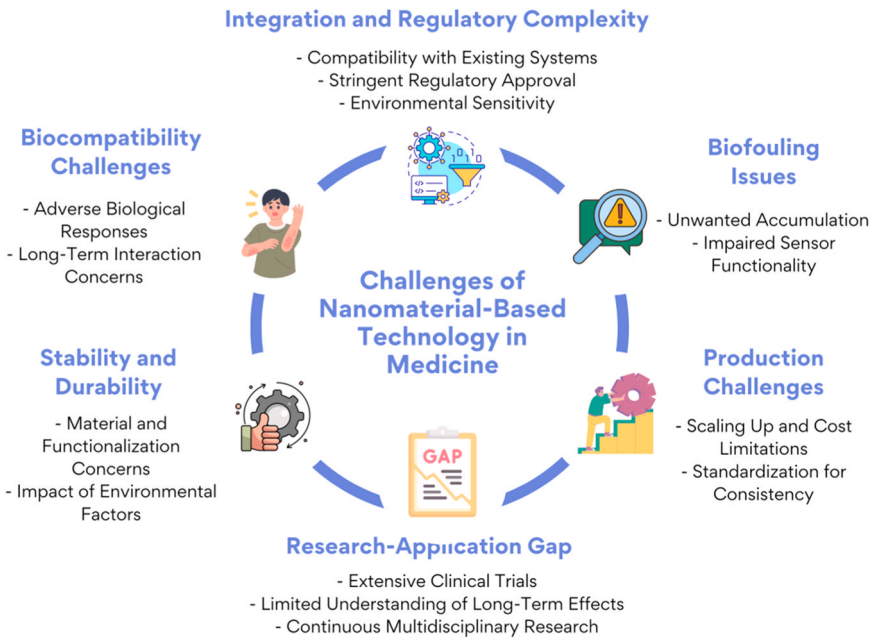

Fig. 4. Challenges associated with nanomaterial-based technology in healthcare. Created with biorender.com.

Table 3
Challenges and Limitations of Nanomaterial-Based Biosensors.

Challenge	Description	Impact on Biosensors
Biocompatibility	Potential toxicity and inflammatory responses	Safety in clinical settings
Biofouling	Accumulation of biological materials	Impairs sensor functionality
Stability and Durability	Degradation over time	Reduces performance, especially in chronic monitoring
Fabrication and Scalability	Complex production processes	Limits availability and affordability
Regulatory and Integration Issues	Compliance with standards	Challenges in clinical integration

clinical adoption.

13. Future perspectives

The future development of nanomaterials in biosensing is shaping up to be a dynamic and transformative field, marked by several groundbreaking advancements and innovative applications. A primary area of focus is the enhancement of biocompatibility and stability of nanomaterials, as ongoing research aims to address concerns regarding biofouling and long-term functionality, a trend echoed in the evolution towards wearable and implantable biosensors that incorporate advanced nanomaterials for real-time health monitoring [18,22]. These developments align with the trends in carbon allotropes for non-destructive detection.

There is also a growing trend in integrating nano biosensors with microfluidic technology and lab-on-a-chip systems, facilitating the creation of compact, multiplexed, and efficient diagnostic platforms [18]. These integrated systems are poised to perform complex analyses rapidly and efficiently, using minimal sample volumes, and have immense potential in point-of-care diagnostics. Additionally, the field is witnessing a convergence with artificial intelligence (AI) and advanced data analytics, which promises to revolutionize diagnostic accuracy and utility [89,90]. This integration aligns with the sophisticated detection capabilities of nanomaterial-based sensors, offering unprecedented sensitivity and specificity [20,91–93].

The potential for single-molecule detection technologies, crucial for early disease detection, is another exciting avenue. This advancement reflects the sensitivity improvements nanomaterials can offer, enabling the detection of biomarkers at the earliest stages of disease, well before clinical symptoms manifest [22,25]. Nanobiosensors are also expected to significantly contribute to personalized medicine, offering detailed biological insights for tailored therapies.

Moreover, the role of nano biosensors in regenerative medicine and theranostics represents a new frontier in medical technology. This aligns with the multifunctional capabilities of nano biosensors and is complemented by their potential impact on global health, especially in resource-limited settings [18]. The practical implications of nano biosensors in democratizing healthcare access are significant, highlighting the importance of cost-effective and user-friendly diagnostic methods [22].

The convergence of several emerging technologies and innovations promises to revolutionize the field of nanomaterial-based biosensing across various applications. The integration of these biosensors with advanced technologies such as AI, machine learning, and the Internet of Things (IoT) is expected to significantly enhance diagnostic capabilities, enabling sophisticated data analysis and real-time monitoring. Research is likely to focus on developing multi-functional biosensors capable of detecting multiple biomarkers simultaneously, improving diagnostic accuracy and efficiency, especially in complex diseases. The emergence of wearable and implantable biosensors using nanomaterials offers continuous health monitoring and early intervention possibilities.

Furthermore, the development of environmentally responsive biosensors that adapt to changing conditions will enhance reliability across various applications [94,95]. Enhancing the biocompatibility and safety of nanomaterials is crucial, especially for clinical applications, ensuring that these biosensors do not trigger adverse biological responses. Novel nanomaterials and nanostructures, like 2D materials beyond graphene and bio-inspired nanomaterials, are expected to open new avenues in biosensor development, potentially enhancing sensitivity and specificity. The shift towards point-of-care and rapid diagnostic tools is particularly beneficial in low-resource settings and urgent diagnostic scenarios. Lastly, the global health impact of these biosensors, especially in addressing infectious diseases, chronic conditions, and environmental monitoring, cannot be overstated, offering significant benefits in regions with limited access to advanced medical facilities.

In terms of specific advancements, controlled synthesis of nanomaterials with tailored properties is a key focus area, aiming to improve biocompatibility, stability, and functionalization. The synthesis of hybrid nanomaterials, combining different nanostructures, promises biosensors with superior performance. The integration with nanoelectronics, microfluidics, and the emergence of wearable biosensors are anticipated to lead to compact, efficient platforms suitable for diverse applications. AI and machine learning are set to revolutionize biosensing, enhancing data analysis and diagnostic decisions. Personalized medicine will benefit from targeted diagnostics and therapies enabled by these biosensors, fostering individualized patient care. Beyond medical diagnostics, the application of these biosensors is expected to expand into environmental monitoring, food safety, and industrial processes. Finally, evolving regulatory frameworks and a focus on ethical aspects, particularly data privacy and security, will ensure the responsible use of these transformative technologies.

The field of nanomaterial-based biosensing stands at the threshold of a transformative era, driven by technological innovations, interdisciplinary research, and a focus on personalized healthcare [96–98]. These advancements are poised to address current limitations and unlock new capabilities, significantly enhancing the impact of biosensors in healthcare, environmental monitoring, and beyond. The future of nanomaterial-based biosensors lies in their seamless integration into clinical workflows. Ongoing research is focusing on developing user-friendly interfaces, standardizing data interpretation, and creating robust quality control measures. These efforts aim to make these advanced diagnostic tools accessible to healthcare professionals without specialized training in nanotechnology, thus truly bridging the gap between cutting-edge laboratory innovations and day-to-day clinical practice. Table 4 outlines the prospective outlook for biosensing applications based on nanomaterials.

Table 4
Future Perspectives in Nanomaterial-Based Biosensing.

Area of Focus	Description	Potential Impact	Emerging Technologies
Biocompatibility and Stability	Improvement in long-term functionality	Enhanced safety in clinical applications	Wearable and implantable sensors
Integration with AI and Microfluidics	Advanced data analysis, compact diagnostics	Revolutionizing diagnostic accuracy	Lab-on-a-chip systems
Personalized Medicine	Tailored diagnostics and therapies	Individualized patient care	Multi-functional biosensors
Environmental Monitoring	Detection of pollutants and pathogens	Public health and safety	Environmentally responsive biosensors

14. Conclusion

In conclusion, the integration of nanomaterials into biosensing technologies heralds a new era in medical diagnostics and environmental monitoring. Nanomaterials such as gold nanoparticles, carbon nanotubes, graphene, and quantum dots have enhanced the sensitivity, specificity, and versatility of biosensors, offering significant advancements in early disease detection, personalized medicine, and continuous health monitoring. Despite facing challenges related to biocompatibility, stability, and integration into existing healthcare systems, ongoing research and development are addressing these issues, promising more effective, accessible, and sophisticated biosensing solutions. Future perspectives include the integration of these technologies with AI and microfluidics, the development of wearable and implantable sensors, and the expansion into global health applications. This evolution of nanomaterial-based biosensors signifies a pivotal shift towards more personalized, rapid, and accurate diagnostic methodologies, poised to profoundly impact healthcare and public health.

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CRediT authorship contribution statement

Ramya Lakshmi Rajendran: Writing – review & editing, Supervision, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Prakash Gangadaran:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Karthikeyan. P. Iyengar:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Vijay Kumar Jain:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Swaminathan Ramasubramanian:** Writing – review & editing, Formal analysis, Data curation. **Sangeetha Balaji:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Madhan Jeyaraman:** Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Naveen Jeyaraman:** Writing – review & editing, Supervision, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

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Data Availability

The data is contained within the manuscript.

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