Emerging Nanobiotechnology Solutions for Diagnosis and Treatment of Infectious Diseases

Saji Mathew Perinjelil

B. Pharm, Department of pharmacy, MLR institute of pharmacy, Hyderabad, Telangana, India

Abstract: Nanotechnology has emerged as a transformative force in combating infectious diseases, especially highlighted by its applications during the COVID - 19 pandemic. This review discusses the multifaceted roles of nanotechnology in enhancing diagnostic accuracy, therapeutic efficacy and vaccine development. It emphasizes the critical importance of rapid, sensitive diagnostics for early infection identification, utilizing fluorescent nanoparticles and nanosensors that enable detection at unprecedentedly low and light concentrations. Additionally, the review explores the development of nanoparticle - based drug delivery systems for targeted therapy and immune response modulation, which promise to improve the outcomes of infectious disease treatment. The potential of point - of - care POC diagnostics leveraging nanotechnology for real - time cost - effective and portable disease monitoring, particularly in resource - limited settings, is thoroughly examined. Through detailed examples including graphene - based biosensors and nanoparticles enhanced immunotherapeutics, the paper illustrates how nanotechnology is reshaping the landscape of infectious disease management, offering novel solutions to the age - old problems of diagnosis, treatment and prevention, challenges such as cost, regulatory approval and the need for global collaboration are acknowledged. Alongside the optimistic outlook for nanotechnology role is advancing public health and global infectious disease.

Keywords: Nanotechnology, Infectious diseases, Drug delivery, Point - of - care testing

1. Introduction

As demonstrated during the current COVID - 19 pandemic, nanotechnology can play a major role in global health. From better screening and diagnostics, to therapeutics and vaccines, as well as health monitoring devices, nanotechnology - enabled approaches have the potential of making a tangible impact in the field of infectious diseases. [1]

Prevention of the spread of infectious pathogens requires rapid and accurate identification of the infectious agents for treatment. Recently developed fluorescent proper nanoparticles are so sensitive that even a single nanoparticle is capable of emitting a strong enough signal to be captured, thus enabling early identification of infections. Proper and effective treatment not only saves the patient, but also prevents the spread of the pathogens. Specific nanoparticle vehicles developed to encapsulate therapeutic agents and deliver them to a target site represent a promising strategy to boost immune responses for vaccination and boost the efficacy of drugs for treatment. Here, we describe a variety of nanotechnologies for use in applications such as immune response modulation, drug delivery, diagnostics, and treatment, which are especially needed in developing countries.

Recently, nanotechnology has been employed to enhance immune responses against antigens for effective vaccination, to deliver pharmaceuticals to a target site and release them at a controlled rate, and to detect and identify diseases accurately and rapidly at low cost.

2. Recent Advancement's

Point of Care

Point of care (POC) diagnosis is a modern approach to medical testing, performed in close proximity to the patient's care. It aims to provide rapid, accurate, and real - time detection of medical conditions at point of need. POC

diagnostics have gained increasing attention in recent years, particularly in clinical medicine where on - site detection is in high demand, especially in areas with limited resources. This has led to the development of various methods, devices, and biosensors that can fulfill the need for POC diagnostic tools.

Nanotechnology has been instrumental in advancing clinical applications, including tissue engineering, drug delivery, bio - imaging, and diagnostics. In particular, nanodiagnostic's have gained significant interest in the field of infectious diseases due to their distinctive features such as rapid detection, enhanced sensitivity, and potential for point - of - care testing. Novel and effective nanodiagnostic's for infectious diseases have been developed, offering the potential to create portable, robust, and affordable POC diagnostic platforms for detecting infectious diseases in developing countries.

To be effective, POC diagnostic technologies should be disposable, cost - effective, easy to use, and portable. They should be capable of analyzing small volumes of bodily fluids, such as blood, saliva, and urine. Cost is an important factor for global health applications [23] and efforts should be made to reduce costs by using minimal expensive reagents, inexpensive manufacturing methods for mass production, and ensuring quality control. Miniaturization is also crucial for developing portable POC diagnostic devices. Moreover, the environmental conditions of resource - limited settings, such as insufficient water, unreliable electricity, high temperatures, and humidity, should be considered for the clinical use of medical diagnostic devices.

Nanosensors:

Infectious diseases have become a severe global public health problem. Timely and accurate diagnosis of infected individuals is the key step to control the spread of infectious diseases. Nanosensors that combine the advantages of nanomaterials and biosensing technology have been utilized for sensitive, selective, and rapid disease diagnosis and gained great attention within the chemistry, biology, and medical communities. This review presents a broad overview of a wide range of nanosensorsfor diagnosis of various infectious diseases using different methodologies.

In order to develop smart health care with nanosensors, a network of nanosensors, often called nanonetwork, need to be established to overcome the size and power limitations of individual nanosensors. Nanonetworks not only mitigates the existing challenges but also provides numerous improvements. Cell - level resolution of nanosensors will enable treatments to eliminate side effects, enable continuous monitoring and reporting of patients' conditions.

Current Diagnostic Techniques and Limitations:

Effective treatment and prevention of infectious diseases requires up - to - date diagnostics. In addition, the efficacy of treatment should be monitored during therapy by detection of pathogens. Conventional techniques available for the diagnosis of infectious disease include microscopy, tissue culture, lateral flow immunoassays (also known as dipsticks or immune chromatographic test, ICTs), enzyme linked immunosorbent assays (ELISAs), and biochemical tests (Table II). More recently, molecular diagnostics techniques such as polymerase chain reaction (PCR) and real - time PCR have been widely used to diagnose and monitor infections such as HIV/AIDS and HCV because they have a higher specificity and sensitivity than ELISA - based diagnostics. However, because these techniques are costly and time - consuming and require prior sample preparation, they are commonly used in developed countries but are often poorly suited for developing countries, where infectious diseases are leading causes of morbidity and mortality, because the availability of trained clinical staff and specific laboratory facilities may be limited. [2] Thus, there is a great demand for new diagnostic technologies. The ideal diagnostic device for developing countries would be a cost effective, portable, and pointof - source detection system that is also highly reliable, sensitive, and accurate. [3] Furthermore, the ideal diagnostic technique would be able to detect multiple pathogens in a single reaction.

Applications of Nanotechnolgy in Infectious Diseases:

• Increased Accuracy and Efficacy of Diagnostic Tests

In addition to serving as treatments, nanotechnology has improved the accuracy of diagnosing bacterial infectious diseases. [4, 5, 6, 7] The rapid development of nanoscience and nanotechnology has been used to design nanomaterial assisted biosensors with better detection performance for bacterial infections, as shown in the examples listed below [8, 9]:

• Graphene - Based Biosensors:

The unique 2D structure and single - atom thickness of graphene sheets enable graphene - based biosensors to be highly flexible to any tiny changes in the surrounding environmental conditions [9]. Graphene - based biosensors have been widely used in infectious disease, especially in coronavirus (COVID - 19) infection. [10]For example, an novel aptameric dual channel graphene - TWEEN 80 field effect transistor (DGTFET) biosensing machine with on - site analyzing of interferon (IFN) - γ , TNF - α , and

interleukin (IL) - 6 works as quickly as 7 min with limits of detection (LODs) and as low as $476-611 \times 10^{-15}$ m in bio - fluids]. [10]

AU NP'S:

Au NPs have been widely used as biosensors for bacteria detection. Thiolation of the chimeric phages directed on various bacterial pathogens caused aggregation of AuNPs, resulting in a visible colorimetric reaction in front of at least about 100 cells of the target bacteria [11]. The photoelectronic Au nanostructure biosensor could detect citrullinated histone H3, an important biomarker during neutrophil cell death in bacterial infection. The Au NP - based biosensor has been used to detect the colistin (an important antimicrobial agent for gram negative bacteria) resistance gene *mcr*.

Nanoseiving Microfluidic System:



An electropolymerized self - assembled layer of Au NPs was fabricated in a portable nanosieving microfluidic system (NS - MFS). Redox - active gold NPs (raGNPs) enhanced the electrical conductivity and provided the detection limit of the device, reaching 10 CFU/mL for *P. aeruginosa* and *S. aureus* spiked in plasma. A microwave - microfluidic biosensor has been developed for quick, contactless and non - invasive detection of the concentration and growth of *E. coli*. [12]

Nanoparticles as Therapeutic Drugs

NPs that have been developed to have novel immunotherapeutic properties can themselves be used as drugs. [13] Under UV light, metallic NPs and their oxides produce reactive oxygen species that possess antimicrobial activityMetallic NPs incorporating Ag, [14, 15, 16]Au, Cu, Ti, 96 Mg, Zn, Fe, or metal oxideshave significant antimicrobial, antifungal, and antiviral activities. Ag - NPs effectively kill many bacterial species including E. coli, S. aureus, B. subtilis, and S. typhai.103 Cu - NPs can also have a profound toxic effect; in one study no colonies were formed when S. cerevisiae was incubated on a CuNP loaded polymer thin film. [17] Nanomaterials with inherent antimicrobial activities are called nanoantibiotics. Nitric oxide - releasing NPs (NONPs) act through many simultaneous antimicrobial mechanisms. NO exerts its antimicrobial activity largely through reactive nitrogen oxide intermediates (RNOS), which are formed after NO reacts with superoxide (O– 2). The RNOS react with amino acid residues of bacterial proteins and plasma membrane proteins, leading to death of bacterial cells. RNOS also directly damage bacterial DNA through strand breaks, formation of basic sites, and deamination of nucleotides. NO - NPs have been shown to inhibit the growth of antibiotic - resistant strains of P. aeruginosa, E. faecalis, K. pneumoniae, and E. coli. When administered at a concentration of 1.25 - 5 mM, NO - NPs successfully killed MRSA, E. faecalis, and E. coli. [18] In addition, nanoantibiotics have advantages

over conventional antibiotics because they interact with multiple biological pathways in bacteria and are stable for a long time in terms of their action and storage. In addition, antibiotic NP polymers enhance the efficacy of traditional antimicrobial agents not only through the additional antimicrobial activity of the NP polymers, but also by increasing the solubility and efficiency of delivery of the antimicrobial. Nylon - 6 nano - fiber incorporated with 5, 5 dimethyl hydantoin (DMH) exhibited strong antimicrobial activity compared with DHM alone.



3. Conclusion

In conclusion, nanotechnology holds immense promise in revolutionizing infectious disease diagnosis and treatment. Through advancements in nanoparticle - based diagnostics, targeted drug delivery systems, and innovative therapeutics such as nanovaccines nanotechnology offers unprecedented precision, efficiency, and safety in combating infectious diseases. While challenges remain, including regulatory hurdles and scalability issues, ongoing research and development efforts are poised to further harness the potential of nanotechnology in addressing global infectious disease challenges, ultimately improving patient outcomes and public health worldwide.

Citations

- Hung YP, Chen YF, Tsai PJ, Huang IH, Ko WC, Jan JS. Advances in the Application of Nanomaterials as Treatments for Bacterial Infectious Diseases. Pharmaceutics.2021 Nov 12; 13 (11): 1913. doi: 10.3390/pharmaceutics13111913. PMID: 34834328; PMCID: PMC8618949.
- [2] Sheikhzadeh E, Beni V, Zourob M. Nanomaterial application in bio/sensors for the detection of infectious diseases. Talanta.2021 Aug 1; 230: 122026. doi: 10.1016/j. talanta.2020.122026. Epub 2020 Dec 17. PMID: 33934756; PMCID: PMC7854185.
- [3] Deng J, Zhao S, Liu Y, Liu C, Sun J. Nanosensors for Diagnosis of Infectious Diseases. ACS Appl Bio

Mater.2021 May 17; 4 (5): 3863 - 3879. doi: 10.1021/acsabm.0c01247. Epub 2020 Nov 19. PMID: 35006812.

References

- [4] Pai, M. Global health technologies: time to re think the 'trickle down' model. *Forbes* https: //www.forbes. com/sites/madhukarpai/2020/02/17/global - health technologies - time - to - re - think - the - trickle down - model/?sh=67a7d67d44d9 (2020).
- [5] A. Sosnik and M. Amiji, Adv. Drug Del. Rev.62, 375 (2010).
- [6] T. S. Hauck, S. Giri, Y. L. Gao, and W. C. W. Chan, Adv. Drug Del. Rev.62, 438 (2010).
- [7] Wang T., Li X., Chen L., Zhang Y., Zheng Y., Yu L., Ye Z., Wang H., Cui X., Zhao S. The preparation of bifunctional hybrid nano - flowers and their application in the enzyme - linked immunosorbent assay for *Helicobacter pylori* detection. *Analyst*.2021; 146: 338–347. doi: 10.1039/D0AN01533D.
 [PubMed] [CrossRef] [Google Scholar]
- [8] Wang T., Li X., Chen L., Zhang Y., Zheng Y., Yu L., Ye Z., Wang H., Cui X., Zhao S. The preparation of bifunctional hybrid nano - flowers and their application in the enzyme - linked immunosorbent assay for *Helicobacter pylori* detection. *Analyst*.2021; 146: 338–347. doi: 10.1039/D0AN01533D.
 [PubMed] [CrossRef] [Google Scholar]

- [9] Pu Y., Hou Z., Khin M. M., Zamudio - Vazquez R., Poon K. L., Duan H., Chan - Park M. B. Synthesis and Antibacterial Study of Sulfobetaine/Quaternary Ammonium - Modified Star - Shaped Poly [2 -(dimethylamino) ethyl methacrylate] Based Copolymers an Inorganic Core. with Biomacromolecules.2017; 18: 44-55. doi: 10.1021/acs. biomac.6b01279. [PubMed] [CrossRef] [Google Scholar]
- [10] Lam S. J., O'Brien Simpson N. M., Pantarat N., Sulistio A., Wong E. H., Chen Y. Y., Lenzo J. C., Holden J. A., Blencowe A., Reynolds E. C., et al. Combating multidrug - resistant Gram - negative bacteria with structurally nanoengineered antimicrobial peptide polymers. *Nat. Microbiol.*2016; 1: 16162. doi: 10.1038/nmicrobiol.2016.162. [PubMed] [CrossRef] [Google Scholar]
- [11] Pirzada M., Altintas Z. Nanomaterials for Healthcare Biosensing Applications. *Sensors*.2019; 19: 5311. doi: 10.3390/s19235311. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- Jiang Z., Feng B., Xu J., Qing T., Zhang P., Qing Z. Graphene biosensors for bacterial and viral pathogens. *Biosens. Bioelectron*.2020; 166: 112471. doi: 10.1016/j. bios.2020.112471. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [13] Schultz A., Knoll T., Urban A., Schuck H., von Briesen H., Germann A., Velten T. Novel Cost -Efficient Graphene - Based Impedance Biosensor for the Analysis of Viral Cytopathogenicity and the Antiviral Effect of Drugs. Front. Bioeng. 9: 718889. Biotechnol.2021: doi: 10.3389/fbioe.2021.718889. [PMC] free article] [PubMed] [CrossRef] [Google Scholar]
- [14] Peng H., Borg R. E., Nguyen A. B. N., Chen I. A. Chimeric Phage Nanoparticles for Rapid Characterization of Bacterial Pathogens: Detection in Complex Biological Samples and Determination of Antibiotic Sensitivity. ACS Sens.2020; 5: 1491–1499. doi: 10.1021/acssensors.0c00654. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [15] Narang R., Mohammadi S., Ashani M. M., Sadabadi H., Hejazi H., Zarifi M. H., Sanati Nezhad A. Sensitive, Real time and Non Intrusive Detection of Concentration and Growth of Pathogenic Bacteria using Microfluidic Microwave Ring Resonator Biosensor. *Sci. Rep.*2018; 8: 15807. doi: 10.1038/s41598 018 34001 w. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [16] M. Look, A. Bandyopadhyay, J. S. Blum, and T. M. Fahmy, Adv. Drug Del. Rev.62, 378 (2010).
- [17] R. P. Allaker and G. Ren, Trans R Soc. Trop Med. Hyg.102, 1 (2008).
- [18] F. Martinez Gutierrez, P. L. Olive, A. Banuelos, E. Orrantia, N. Nino, E. M. Sanchez, F. Ruiz, H. Bach, and Y. Av - Gay, Nanomed. Nanotechnol. Bio. Med.6, 681 (2010).
- [19] M. Rai, A. Yadav, and A. Gade, Biotechnol. Adv.27, 76 (2009)
- [20] N. Cioffi, L. Torsi, N. Ditaranto, G. Tantillo, L. Ghibelli, L. Sabbatini, T. Bleve - Zacheo, M. D'Alessio, P. G. Zambonin, and E. Traversa, Chem. Mater.17, 5255 (2005).

[21] M. J. Hajipour, K. M. Fromm, A. A. Ashkarran, D. J. de Aberasturi, I. R. de Larramendi, T. Rojo, V. Serpooshan, W. J. Parak, and M. Mahmoudi, Trends Biotechnol.30, 499 (2012)