EDITORIAL

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NANOTECHNOLOGY IN INFECTIOUS DISEASES

In this era of evidence-based medicine, diagnostics play a major role in holistic health care. Microscopic world is messy and sometimes a hazardous place as bacteria, viruses and other organisms lurk on every surface. Though a broader view might seem greatly reassuring, a closer look into it reveals that these existing methods have significant drawbacks. Some of the more sophisticated approaches like, gene identification require expensive equipment and specialized operating staff. On the contrary, microbial culture usually takes days rather than hours or minutes that might save lives in a crisis.[1]

Nanotechnology could be a one-stop solution for many issues encountered in diagnostics as well as therapeutics. Advances in the field of nanotechnology and its applications in the field of diagnostics revolutionized the twentieth century. The development in the field of nanotechnology started in 1958 and has reached wider horizons, making medical practice simpler and more precise. Nanotechnology is the study of extremely small structures. The prefix "nano" is a Greek word, which means "dwarf". The word "nano" means, very small or miniature in size. Nanotechnology is the manipulation of individual atoms, molecules, and compounds into structures to produce materials and devices with special properties.[2]

In spite of major advances in diagnostics, infectious diseases caused by viruses [human immunodeficiency virus (HIV-AIDS), hepatitis C and dengue fever], parasites (malaria, trypanosomiasis and leishmaniasis) and bacteria (tuberculosis and cholera) continue to be causes of high morbidity and mortality in developing countries.[3] Thus, there is a great demand for newer diagnostic technologies. In developing countries including India, any new diagnostic device should be cost-effective, portable, and a point of-source detection system that is highly reliable, sensitive, and accurate. Furthermore, detection of multiple pathogens in a single reaction is the need of the hour. Nanotechnology, i.e. DNA microarrays or DNA chips are the newer diagnostic entities in the inventory which equate all the above-mentioned prerequisites and help in rapid diagnosis of infectious diseases.[4]

NANOTECH-BASED DIAGNOSIS OF INFECTIOUS DISEASES

Let us look at a few infectious diseases, where nanotechnology has made huge strides in diagnosis.

Tuberculosis (TB) has been a massive prevailing disease burden in the present as well as past several decades. The emergence of multidrug-resistant strains and the dearth of newer development of anti-TB drugs are threatening future containments of TB. There are several advances in the diagnosis of TB, like interferon gamma release assays (IGRAs), enzyme-linked immunospot assay methods (ELISPOT), the T SPOT.TB test, ELISA-based QuantiFERON test, which measures INF-γ following exposure to PPD in patients with compromised immune systems (e.g., patients co-infected with HIV). But they can give false-negative results as these patients tend to have low T-cell counts. Fluorescent silica Nanoparticles (FSNPs) 98 have now been developed to detect *Mycobacterium tuberculosis (MTB)*. Hence, nanotechnology presents an exciting opportunity for proper identification of mycobacterial strains. The ability of nanoparticles to potentially detect extremely small quantities of pathogens on a stand-alone platform may be particularly useful in rapid detection of TB.

In HIV-infected people, direct detection of viral RNA is possible only 9 days after infection, whereas IgG or IgM anti-HIV antibodies (produced in response to infection) can be detected by western blots by 3–6 weeks after infection. This extremely rapid detection, ideally based on viral RNA, would likely aid in stemming additional viral multiplication. Also, the knowledge of viral load would assist further treatment.

In case of malaria, although there are many tests with high sensitivity and specificity, detection of coinfections, which cause similar symptoms, would lead to a reduction in the overuse of antimalarial drugs which, in turn, leads to drug resistance. Polystyrene nanoparticles (NPs) copolymerized with acrylic acid, have been used to identify *P. falciparum*, the causative agent of malaria.

In the field of microbiology, gold NPs have been used for the detection of DNA since 1996. 116 gold nanowire arrays (GNWA) linked with specific antibodies against *E.coli* have been developed to detect urinary tract infections. 117 Immunogold-silver staining with Au-NPs is a very sensitive method for detection of single molecules that do not require advanced instruments, and has been applied for the detection of hepatitis C virus (HCV) and hepatitis B virus (HBV). Nanomaterials have been used to construct sensors in three different platforms for simple infectious disease diagnostics. These include: (1) nanoparticle labels in immunochromatographic test (ICT) assays, (2) nanoparticle aggregation assays, and (3) nanoparticle labels of whole pathogens.

NANOPARTICLES AS THERAPEUTIC DRUGS AND VACCINE DELIVERY SYSTEMS

Nanoparticles that have been developed to have novel immunotherapeutic properties can themselves be used as drugs. Metallic NPs and their oxides produce reactive oxygen species that possess antimicrobial activity. Metallic NPs incorporating Ag, 96–98 Au, 98–99 Cu,100 Ti,96 Mg, Zn,79 Fe, or metal oxides, 101 have significant antimicrobial, antifungal, and antiviral activities.102 Ag-NPs effectively kill many bacterial species including *E. coli, S. aureus, B. subtilis*, and *S. typhi*. Nanomaterials with inherent antimicrobial activities are called nano-antibiotics. Nitric oxide (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*. In addition, nano-antibiotics have advantages over conventional antibiotics, in that they interact with multiple biological pathways in bacteria and are stable for a long time in terms of their action and storage.

Vaccination is a reliable method of preventing infectious diseases and plays a vital role in controlling mortality and morbidity associated with infectious diseases. Nanoparticles can be used as a vessel to deliver encapsulated vaccines (antigenic proteins) into selective sites and release them over a sustained period in order to boost immune response. In addition, the 51NP formulation when lyophilized into a powder form, prolongs shelf-life of vaccines over wide ranges of temperatures (i.e., 0 °C to –40° C). 51 NPs can therefore allow, safe transportation of vaccines over a long distance without a need for cold chain. Nanoscale aerosol vaccines have been developed for respiratory pathogens which include *Mycobacterium tuberculosis* as well. NPs can also function as adjuvants in order to enhance immunostimulatory properties of traditional vaccines. MF59 is a nanosized oil-in-water emulsion (<250 nm) developed from squalene and two surfactants (polysorbate 80 and sorbitan trioleate). These surfactants are being used as adjuvants along with influenza vaccine in many countries. MF59 is currently the only vaccine adjuvant approved by the FDA. MF59 has also been shown to significantly enhance immune response in HIV/AIDS treatment.[5]

CONCLUSION

"A new wave of 'bio-nanosensors' might make it quicker, cheaper and easier to detect harmful microorganisms, but hurdles remain before they can enter the clinical realm", reports Joe McEntee of Physics World, Bristol. Although advances in nanotechnology have not been fully applied to infectious diseases detection in developing countries, nanotechnology can potentially address numerous challenges outlined by the World Health Organization for rapid and effective delivery of point-of-care diagnostics. Furthermore, nanotechnology-based therapeutics, vaccines, and diagnostics may foster easy, inexpensive, safe, and portable use of end products, which will, in turn, help control infectious diseases, especially those of developing countries, and thereby improve public health.

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REFERENCES

1. https://physicsworld.com/a/nanoparticles-home-in-on%E2%80%AFinfectious-diseases.
2. Nikalje APG. Nanotechnology and its Applications in Medicine. Med chem. 2015;5:081–089. DOI: 10.4172/2161-0444.1000247.
3. Hauck TS, Giri S, Gao Y, Chan WCW. Nanotechnology diagnostics for infectious diseases prevalent in developing countries. Adv. Drug Deliv. Rev. 2010;62(4–5):438–448.
4. Al-Orainey I. Diagnosis of latent tuberculosis: can we do better? Ann. Thorac. Med. 2009;4: 5–9.
5. Qasim M, Lim DJ, Park H, Na D. Nanotechnology for Diagnosis and Treatment of Infectious Diseases, J Nanosci Nanotechnol. 2014;14(10):7374–7387.
6. S. Godreuil, L. Tazi, A.-L. Bañuls Encyclopedia of infectious diseases: modern methodologies.
7. Godreuil S, Tazi L, Bañuls A-L. Nanotechnology diagnostics for infectious diseases prevalent in developing countries – ScienceDirect M. Tibayrenc (ed.), Pulmonary Tuberculosis and *Mycobacterium Tuberculosis:* Modern Molecular Epidemiology and Perspectives, Hoboken: John Wiley & Sons; 2007, p. 1–30.