ISSN: 0976-3376

Available Online at http://www.journalajst.com

ASIAN JOURNAL OF SCIENCE AND TECHNOLOGY

Asian Journal of Science and Technology
Vol. 08, Issue, 09, pp.5771-5773, September, 2017

REVIEW ARTICLE

NANOTECHNOLOGY IN CLINICAL MICROBIOLOGY: A MINI REVIEW

***[1]Mayuri Rani, [2]Tanu Sagar and [3]Shukla Das**

[1]Zoonosis Division, National Centre for Disease Control, 22-Shamnath Marg, Delhi, India
[2]Department of Microbiology, All India Institute of Medical Sciences, Delhi, India
[3] Department of Microbiology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi

ARTICLE INFO

Article History:
Received 08th June, 2017
Received in revised form
26th July, 2017
Accepted 02nd August, 2017
Published online 27th September, 2017

Key words:

Nanotechnology, Quantum(Q)dots, Nanoarrays, Nanocantilever, Nanopore Sequencing, Gold Nanoparticles, Nanoemulsion.

ABSTRACT

Now days there are limitation of current technologies available for diagnosis due to high cost and short shelve half-life of some reagents such as enzymes and DNA primers, limit the application of most conventional pathogen detection techniques in developing nations. Enzyme Linked Immunosorbent Assay (ELISA) and Polymerase Chain Reaction (PCR) , require extensive sample preparation and have long turn around times, which delay prompt response and disease containment. Also decreased availability of newer antimicrobial agents and rise in multi drug resistance among microorganisms, prompt us to explore newer modalities of treatment. Due to unique electrical, magnetic, luminescent, and catalytic properties of nano materials faster, sensitive, economical, simple, and reliable diagnostic assays and newer antimicrobial treatment modalities can be developed. This paper presents the different aspects of use of nanotechnology in microbiological diagnosis and anti microbial treatment.

INTRODUCTION

"Nano " means very small, and it comes from the Greek word "nanos", meaning dwarf . Nanotechnology by definition is the art and science of manipulating matter at the nanoscale, thus encompassing nanoscale science and involves manipulating matter at 1 to 100 nm length scale. At the nanoscale, the physical, chemical, and biological properties of materials differ in fundamental and valuable ways from the properties of individual atoms and molecules. Nanotechnology research & development is directed toward understanding and creating improved materials, devices, and systems that exploit these new properties.

Limitation of current technologies: There are limitation of current technologies available for diagnosis like high cost and short shelve half-life of some reagents such as enzymes and DNA primers, limit the application of most conventional pathogen detection techniques in developing nations. Enzyme Linked Immunosorbent Assay (ELISA) and Polymerase Chain Reaction (PCR), require extensive sample preparation and have long turnaround times, which delay prompt response and disease containment.

****Corresponding author:*** **Mayuri Rani**
Zoonosis Division, National Centre for Disease Control, 22-Shamnath Marg, Delhi, India

The potential of nanotechnology: Due to unique electrical, magnetic, luminescent, and catalytic properties of nano materials faster, sensitive, economical, simple, reliable and user friendly diagnostic assays can be developed without any sample preparation. The properties of the nanomaterials used for pathogen detection can be tailored by changing the size, shape, composition and surface modification of the nanomaterial. Their electronic, spectroscopic (emissive, absorptive), light scattering and conductive properties can be modified by engineering the nanoparticles' structural parameters like size, composition and binding properties.

Nanotechnology tools & their applications in clinical microbiology

***Quantum(Q)dots*:** Qdots can emit light in different wavelengths upon excitation, by modulating their size they can be excited at a given wavelength and have tuneable emission from the ultra-violet (UV) to the near infra-red (NIR) region. Advantage of these Qdots is that it confers target specificity for detection of biomolecules, as it incorporate multiple affinity reagent, in contrast with dye-labeled conjugates, in which multiple dyes are attached to a single affinity reagent. Also they are highly bright and extremely photo stable, so photo bleaching can be avoided. Qdots have been used in

Fluorescent Resonance Energy Transfer (FRET) based Immunoassay for rapid and sensitive detection of *Aspergillus amstelodami*, in confocal nanoscope ,Q dot barcodes have been used for the detection of viruses (HIV), via a sensitive handheld diagnostic system (C. Kaittanis *et al*, 2010) (M.D. Kattke *et al*, 2011).

***Gold and Silver nanoparticles*:** The optical absorption and scattering spectra of gold nanoparticles display a pronounced peak in the the plasmon resonance (the collective excitation of the free electron gas). The surface chemistries of gold nanoparticles can be controlled by grafting thiol molecules or thiol-containing polymers on them, as the gold surface exerts strong affinity towards sulfhydryl groups leading to the formation of relatively strong covalent bonds. Hence, further surface modification can be done simply by using thiolated functional molecules, facilitating conjugation of various probes, including antibodies and nucleic acids. These nanoparticles have been used in resonance scattering confocal microscopy or two-photon luminescence confocal microscopy and as a carriers for drugs (L.A. Dykman *et al*, 2011).

***Nanoarrays*:** Nanochips can be prepared for the fast identification of biomolecules, using gold or silica nanoparticles supported on thin silicon layers. These nanochips due to their small size, can screen samples in a high-throughput format requiring minute sample volumes. A nanoarray system known as Nano eNabler System™ (BioForce Nanosciences) has been developed having advantage of utilizing approximately 1/10,000th of the surface area occupied by a conventional microarray. Over 1,500 Nanoarray spots can be placed in the area occupied by a single microarray spot and very small quantities (0.1µg) of individual proteins can now be effectively screened. It has been used in detection of HIV 1 virus in the plasma (Ki-Bum Lee *et al*, 2004).

***Nanocantilevers*:** The cantilever is made of silicon with a tip(probe) radius of curvature on the order of nm. It is an advanced sensor for biomolecules and can be conjugated with nucleic acids, antibodies. It has been used in Atomic Force Microscopy (AFM) and cantilever based arrays. The AFM consists of a cantilever with a sharp tip (probe) at its end that is used to scan the surface of specimen, when the tip is brought into proximity of surface, forces between the tip and the sample surface lead to a deflection of the cantilever. Forces that are measured in AFM include mechanical contact force, vander Waals forces, electrostatic forces, and magnetic forces. The deflection is then measured, using a laser spot reflected from the top surface of the cantilever into an array of photodiodes. (A. Raman *et al*, 2008)

***Nanopore sequencing*:** A nanopore is a small hole, of the order of 1 nm in internal diameter. Certain porous cellular proteins act as nanopores like alpha-hemolysin of *S. aureus* and *Mycobacterium smegmatis* porin A (MspA). Nanopores have also been made by etching a somewhat larger hole (several tens of nanometers) in a piece of silicon, and then gradually filling it in, forming a much smaller diameter hole. When a nanopore is immersed in a conducting fluid and a voltage is applied across it, an electric current due to conduction of ions through the nanopore can be observed. The amount of current is very sensitive to the size and shape of the nanopore, if a single nucleotide pass through the nanopore, this can lead to a characteristic change in the magnitude of the current passing through the nanopore. Each nucleotide on the DNA molecule may obstruct the nanopore to a different, characteristic degree. Thus the amount of current which can pass through the nanopore at any given moment varies depending on whether the nanopore is blocked by an Adenine, Cytosine, Guanine or Thiamine. Advantage of nanopore sequencing is that it does not require PCR amplification step and chemical labelling step. Also it read genomic DNA at a speed of hundreds to thousands of bases per second (D. Branton *et al*, 2008) (M.T. Basel *et al*, 2009).

Nanomethods can alter Quorum Sensing: The nanofactories could trick the bacteria into sensing a quorum too early, doing so would trigger the bacteria to try to establish an infection before they reach the critical mass, so that a natural immune system response can contain them without the use of drugs. Magnetic nanoparticles are synthesized by first co-precipitating nanoparticles of iron salts and the biopolymer chitosan, *E. coli* AI-2 synthases, Pfs and LuxS, are then covalently tethered onto the chitosan. Chitosan serves as a molecular scaffold and provides cell capture ability and magnet provides stimuli responsiveness. The enzymes *E. coli* AI-2 synthases, Pfs and LuxS synthesize autoinducer-2 (universal bacterial quorum-sensing signal molecule) from metabolite S-adenosylhomocysteine. These magnetic nanofactories are shown to modulate the natural progression of quorum-sensing activity. (R. Fernandes *et al*, 2007)

Application of nanotechnology in treatment of infections

The decreased availability of newer antimicrobial agents and rise in multi drug resistance among microorganisms, prompt us to explore newer modalities of treatment. Nanoparticles can be used for targeted drug delivery, nanoparticles containing drugs are coated with targeting agents (e.g. conjugated antibodies), circulate through the blood vessels and reach the target cells and drugs are released directly into the targeted cells. Some nanoparticles can directly have antimicrobial activity on pathogens.

Liposomes: These nanoparticles are comprised of lipid bilayer membranes surrounding an aqueous interior. Targeting ligands attached to their surface allowing for their accumulation in the target areas for treatment of disease. Hydrophobic chemicals can be dissolved into the membrane, so are able to carry both hydrophobic molecules and hydrophilic molecules, the lipid bilayer can fuse with other bilayers such as the cell membrane, thus delivering the liposome contents to sites of action. It can be used for delivery of antibiotics to the target site of action (Zuzanna Drulis-Kawa *et al*, 2010).

Dendrimers: Branched molecules having high degree of molecular uniformity, specific size and shape characteristics, and a highly- functionalized terminal surface. A lipid-dendrimer hybrid nanoparticle (LDHN) system has been shown to effectively deliver vancomycin against methicillin-resistant Staphylococcus aureus (MRSA) infections (S. J. Sonawane *et al*, 2016).

Nanoemulsion: Composed of oil and water and are stabilized by surfactants and alcohol. Active ingredient and the high energy are essential for its mechanism of action. Reduction of size results in more energy units per volume and is achieved

by a high-pressure microfluidizer. The nanoemulsion particles are driven to fuse with lipid-containing organisms by the electrostatic attraction between the cationic charge of the emulsion and the anionic charge on the target microorganism. When enough nanoparticles fuse with the pathogens, they release part of the energy trapped within the emulsion. Both the active ingredient and the energy released destabilize the lipid membrane of the pathogen, resulting in cell lysis and death. Michigan nanotechnology institute for medicine and biological sciences has developed nanoemulsion with broad spectrum activity against bacteria like *E. coli, Salmonella spp, S. aureus*, some enveloped viruses (HIV, Herpes simplex), fungi (Candida, Dermatophytes) and spores of *B. anthracis*. (P.C. Teixeira *et al*, 2007) (N. Shams *et al*, 2016).

***Gold nanoparticles*:** Possibility of producing a stable complex of vancomycin and gold and the efficacy of such a complex against various strains of Enteropathogenic Escherichia coli (EPEC), *Enterococcus faecium*, *Enterococcus faecalis* (including vancomycin-resistant strains) have also been demonstrated. (H. Gu *et al*, 2003) Similarly a complex of ciprofloxacin with gold nanoshells showed high antibacterial activity towards *E. coli*. (C. Kaittanis *et al*, 2010).

REFERENCES

Basel, M.T., Dani, R.K., Kang, M., Pavlenok, M., Chikan, V., Smith, P.E. Bossmann, S.H. 2009. Direct Observation of Gold Nanoparticle Assemblies with the Porin MspA on Mica*, ACS Nano*, vol. *3, no*. 2, pp. 462–466.

Branton, D., Deamer, D.W., Marziali, A., Bayley, H., Benner, S.A., Butler, T., Schloss, J.A. 2008. The potential and challenges of nanopore sequencing, *Nature Biotechnology,* vol. *26*, no. 10, pp. 1146–1153.

Dykman, L.A. and Khlebtsov, N.G. 2011. Gold Nanoparticles in Biology and Medicine, Recent Advances and Prospects *Acta Naturae,* vol. 3, no. 2, pp. 34–55.

Fernandes, R., C.Y. Tsao, Y. Hashimoto, L. Wang , T.K. Wood, G.F. Payne and W.E. Bentley 2007. Magnetic nanofactories: localized synthesis and delivery of quorum-sensing signaling molecule autoinducer-2 to bacterial cell surfaces, *Metab Eng,* vol. 9, no. 2, pp. 228-39.

Gu, H., Ho, P.L. Tong, E., Wang, L. and Xu, B. 2003. Presenting Vancomycin on Nanoparticles to Enhance Antimicrobial Activities, Nano Lett, vol. 3, pp. 1261–1263.

Kaittanis, C., Santra, S. and J.M. Perez 2010. Emerging nanotechnology-based strategies for the identification of microbial pathogenesis, *Adv Drug Deliv Rev,* vol. 62, no. (4-5), pp. 408–423.

Kattke, M.D., Gao, E.J., Sapsford, K.E., Stephenson, L.D. and Kumar, A. 2011. FRET-Based Quantum Dot Immunoassay for Rapid and Sensitive Detection of *Aspergillus amstelodami,* Sensors, vol. 11, pp. 6396-6410.

Ki-Bum Lee, Eun-Young Kim, Chad A. Mirkin and Steven M. Wolinsky, 2004. The Use of Nanoarrays for Highly Sensitive and Selective Detection of Human Immunodeficiency Virus Type 1, Nano let, vol. 10, pp. 1869-72.

Raman, A., Melcher, J. and Tung, R. 2008. Cantilever dynamics in atomic force microscopy, Nano Today, vol. 3, no. 1–2, pp. 20-27.

Shams, N. and Sahari, M. 2016. Nanoemulsions: Preparation, Structure, Functional Properties and their Antimicrobial Effects, Applied Food Biotechnology, vol. 3, no. 3, pp. 138-149.

Sonawane, S. J., R. S. Kalhapure, S. Rambharose, C. Mocktar, S. B. Vepuri, M. Soliman and T. Govender, 2016. Ultra-small lipid-dendrimer hybrid nanoparticles as a promising strategy for antibiotic delivery: In vitro and in silico studies, International Journal of Pharmaceutics, vol. 504, no. 1–2, pp. 1-10.

Teixeira, P.C., Leite, G.M., Domingues, R.J., Silva, J., Gibbs, P.A. and Ferreira, J. 2007. Antimicrobial effects of a microemulsion and a nanoemulsion on enteric and other pathogens and biofilms, *Int J Food Microbiol*, vol. 118, pp. 15–19.

Zuzanna Drulis-Kawa and Agata Dorotkiewicz-Jach, 2010. Liposomes as delivery systems for antibiotics, *International Journal of Pharmaceutics,* vol. 387, no. 1–2, pp. 187-198.

****