NANOTECHNOLOGY BASED APPROACHES IN DIAGNOSIS AND TREATMENT OF TUBERCULOSIS

K.S. Mithra[1], W.R. Sam Emmanuel[2]

Abstract: Tuberculosis (TB) is one of an infectious threatening disease that kills millions of people all over the world every year. The disease is caused by mycobacterium a tuberculosis bacterium that mostly affects the lungs but sometimes affects other parts of the human body also. The drug resistant TB continues to threaten global TB control, making the existing drugs ineffective, remains a major public health concern in many countries. There are many tools for TB detection such as chest X ray screening, blood specimen culture, skin test but the most widely used one is sputum smear microscopy. All the above methods had its own limitations such as highly expensive, time consuming and low sensitivity in diagnosis etc. There is, therefore, a need for new diagnostic tests that are sensitive, fast, inexpensive and capable of working with unprocessed biological samples. This paper presents a review of various types of nanoparticles for the detection of mycobacterial species in TB diagnosis. Several anti TB drugs have been suggested to arrest the growth of tuberculin bacteria such as nanosuspensions, niosomes, carbon nanotubes, quantum dots, nanoemulsions and aerosolic nanoparticles.
Key words: nanoparticles, tuberculosis, Drug resistance TB, liposomes, quantum dots

1. INTRODUCTION

TB is a contagious disease caused by various strains of mycobacterium species which affects mainly the lung but also expand in various other parts of the body like eyes, bone and blood vessels. While TB is less prevalent in industrialized nations, the death toll in developing countries is high. India has approximately two to three million people infected with Tuberculosis and it remains as one of the largest on India's health and wellness scale [1]. India is the highest TB burden country with World Health Organization (WHO) statistics for 2011 giving an estimated incidence figure of 2.2 million cases of TB for India out of a global incidence of 8.7 million cases [2].

There are many methods available for TB detection such as chest X ray screening, sputum slide based diagnosis, blood specimen culture and TB skin test etc. Each method has its own drawbacks such as high cost, long processing time, low sensitivity and specificity rate in diagnosis etc. The clinical treatment of TB is becoming a difficult task because of the emergence of multidrug-resistant (MDR) tuberculin bacterial strains (MDR-TB). Current estimation indicates that out of all the incidents of TB cases, about 3.6% are reported to have MDR-TB [3].

A suitable way to overcome the drug resistance is the selection of an efficient drug delivery system that delivers drug to the targeted tissues without a loss in their potential strength and effectiveness. Thus, the use of nanoparticles can improve both the detection of specific mycobacterial strains as well as the delivery of anti-TB drugs (ATDs) to the mycobacterium-infected tissues. The focus of this paper is to review various nanotechnology based approaches used, for the detection of tuberculosis bacilli and several ATDs have been suggested, to arrest the growth of tuberculin bacteria.

2. NANOTECHNOLOGY BASED TUBERCULOSIS DIAGNOSIS

Nucleic acid diagnostic tests such as polymerase chain reaction play a crucial role in detection of TB bacilli at an early stage of TB disease progression but nanotechnology is expanding the currently available options which will contribute to better efficiency, especially greater sensitivity.

2.1 Quantum Dots

Nanotechnology uses semiconductor nanocrystals with no larger than 10 nanometers that can be made to fluoresce in different colors depending on their size to overcome the low specificity of fluorescence or electronic microscope to detect TB bacilli. These minute investigations can withstand significant more light emissions and more cycles of excitations than typical organic molecules [6].

2.2 Protein Chips (or Proteomics)

Proteomics plays a vital role in diagnosis of diseases like tuberculosis and its respective drug development. Protein chips can be preserved with small modular protein components of TB bacilli that can specifically bind to proteins containing a certain biochemical or structural motif [4].

2.3 Sparse Cell Detection

Sparse cells are both rare and physiologically distinct from their surrounding cells in normal physiological conditions. This method can take advantages of the unique properties of sparse cells manifested in differences in deformation of intracellular TB bacilli. It is a challenge to identify and subsequently isolate these sparse cells and now nanosystems are capable to effectively sort sparse cells from blood and other tissues [4].

[1] *Research Scholar, Nesamony Memorial Christian College, Marthandam-629165, Tamil Nadu, India.*
[2] *Associate Professor, Dept.of Computer Science, Nesamony Memorial Christian College, Marthandam-629165, Tamil Nadu, India.*

2.4 Individual Target Probes

Nano-gold particles studded with short segments of TB-bacilli deoxyribonucleic acid (DNA) form the basis of the easy-to-read test for the presence of TB-bacilli genetic sequences. It binds to complementary DNA tentacles on multiple nanospheres and forms a dense web of visible gold balls then allows the detection of TB bacilli [4].

2.5 Nuclear Magnetic Resonance (NMR) with Microfluidic System

Iron-based magnetic nanoparticles tagged with antibodies are used for binding the Mycobacterium tuberculosis bacilli while microfluidic system deliver the Mycobacterium tuberculosis and buffer solutions. Concentrating the specimens with the membrane filter can markedly improve the detection sensitivity. Magnetic nanoparticles have high sensitive detection of Bacillus. Integration with quantum dots can detect not only Mycobacterium tuberculosis but also Mycobacterium avium subspecies [5, 7].

2.6 Silica Nanoparticles

In this method the luminescence-based nanoparticles are combined with immunofluorescence microscopy for detection of Mycobacterium tuberculosis. It is observed that silica nanoparticles are of extremely high sensitivity and low false positivity [5].

3. NANOTECHNOLOGY BASED TB TREATMENT

Nanoparticles are very much versatile and diverse with respect to their properties and structural arrangement, which enables them to be used for clinical diagnosis and effective drug delivery purpose in a unique and more reliable manner [8]. Fig.1 shows several nanosized carriers available for drug delivery purposes that include liposomes, polymeric nanoparticles, nanosuspensions, nanoemulsions and many other excellent multifunctional nanosystems, leading to better pharmacokinetics, biodistribution and bioavailability [9]. These are mentioned in the following paragraphs.

3.1 Liposomes

Liposomes are tiny spherical bubbles composed of lipid bilayer membranes with an aqueous core. These serve as common carriers for drugs such as gentamicin, sparfloxacin, amikacin, streptomycin and many others, depending on their sustainable biological compatibility. Phosphatidylcholine is the most commonly used lipid in liposomal preparation besides using cholesterol (for maintaining rigidity and stability), dicetylphosphate, o-stearoyl amylopectin, distearoyl phosphatidylethanolamine and polyethylene glycol (PEG). Studies have revealed that encapsulation of liposomes with PEG considerably enhances their circulatory lifespan in the blood stream [10].

3.2 Polymeric nanoparticles

Polymeric nanoparticles possess very good biocompatible and biodegradable features that make them sustainable candidates for use as drug delivery carriers. Polymeric nanoparticles are structurally much more stable and can be synthesized with various properties (drug release profile, zeta potential) by selecting different polymer lengths, surfactants, monomer dimensions and choice of organic solvents. Polymeric nanoparticles contain emblematic functional groups that can be transformed according to either structural moiety of drugs or targeted ligands [11].
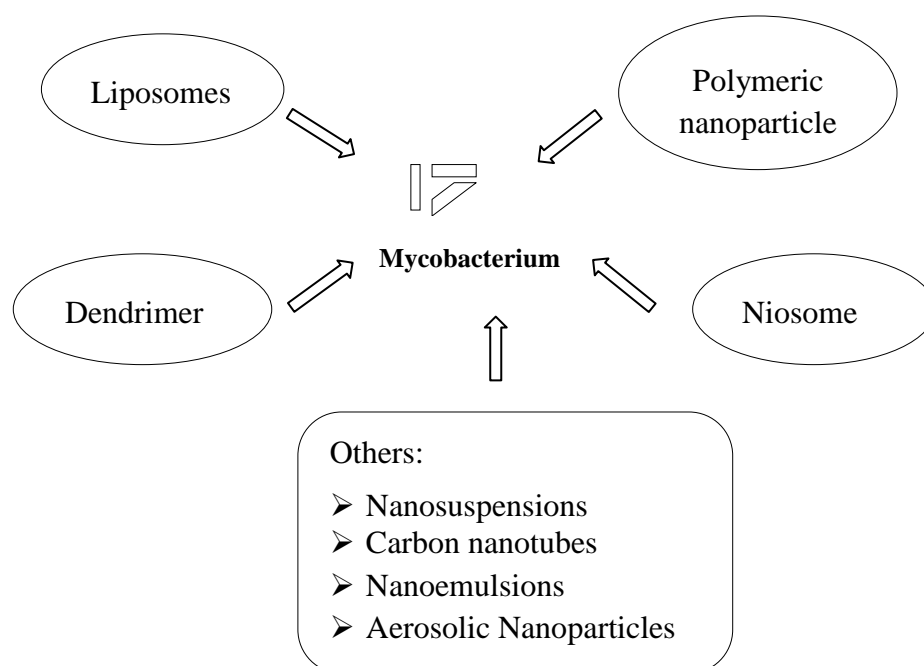

Fig. 1 Various Nano based Drug Delivery Agents

3.3 Dendrimers

Dendrimers are long-chained, repeated three dimensional arrangements of a group of atoms. These are synthetic nanomaterials which are 5–10nm in diameter. They are very versatile molecules with regard to their geometry and multifunctional nature. In a comprehensive review, Cheng et al. in paper [12] discussed the optimized drug delivery considerations for dendrimer synthesis and the different variations and combinations.

3.4 Nanosuspensions

A nanosuspension is commonly defined as a colloidal dispersion of particles in the microscale. For drug delivery purpose, it is normally employed in cases wherein the drug is poorly soluble in water as well as in the organic solvents. Nanosuspension ensures overall efficient absorption and better biodistribution of drug molecules. During the formulation of a nanosuspension, the crystalline particles of the drug are converted into amorphous form. The conversion to amorphous forms can be achieved using X-ray diffraction. Various parameters such as particle size, charge distribution and drug dissolution velocity can also be effectively and easily monitored as well as suitably modified to suit a particular kind of drug delivery mechanism by the use of nanosuspension [13].

3.5 Niosomes

Niosomes are the nanosized, nonionic sac like structural analogues of liposomes but they have some additional advantages over liposomes. These molecules are amphipathic molecules that can be stabilized using surfactants [14]. To date, TB treatment using niosomes has been performed using the conventional ATDs isoniazid, rifampin and pyrazinamide.

3.6 Carbon nanotubes

Carbon nanotubes have lengths of several micrometers and cross-sectional diameter in the range of 1–100nm. They are of two main types: single walled and multi-walled. They can be functionalized with a number of different chemical moieties coupled to their surface and possess wide applications [15].

3.7 Nanoemulsions

Nanoemulsions represent a stable thermodynamic mixture of two immiscible liquids which are combined with the help of surfactant molecules to behave as one phase. In a significant review article, Ahmed et al. [16] have comprehensively illustrated the use of rifampicin-based nano emulsions for TB treatment. They have elaborated the critical design features such as viscosity, solubility and chemical interaction ability for nano emulsion design to become optimized drug delivery vehicles. It has been successfully used for the killing of TB germs at low dosage.

3.8 Aerosolic Nanoparticles

Aerosolic nanoparticles are a suspension of nanoparticles in dry powdered aerosol form. They are used for the development of nanoparticles as potential drug delivery molecules that can be inhaled and treat the subsequent pulmonary infections. TB, being one of such respiratory infections having multidrug resistance, can be therefore very efficiently be dealt with by the use of nanoparticles [17]. Using aerosolic nanoparticles, efficient detection and treatment of the TB is almost sure to be achieved with much less systemic toxicity.

4. CONCLUSION

Over the last few decades, tremendous advancement has been made in nanotechnology in various fields, especially in medicine, by the introduction of new approaches to molecular detection and treatment. The gold standard methods used for detection of mycobacterium tuberculosis have many disadvantages of being less sensitive, time consuming and require skilled professionals. The evident advantages of nano diagnostics involve their ability to produce results in a short time frame, along with the high specificity and sensitivity when compared to conventional method of detection like microscopy and culture. Nanotechnology-based drug delivery has thus proved to be a huge boon in the detection and treatment of TB.

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