Nirma Univ J Pharm Sci; 2019, 6(2) 35-54

ISSN 2348 –4012

ARTICLE

AN EPITOME ON TUBERCULOSIS: A PHASE OF DRUG DISCOVERY TO NANOTECHNOLOGY

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Abstract

Mycobacterium tuberculosis is a chronic infectious disease. It kills approximately 1.7 million people in the world and also has the highest risk of reactivation in the patients with latent infection. Relapse of the disease and drug resistance (MDR-TB/XDR-TB) are the key parameters of too complex tuberculosis therapy. Due to this varied failure treatment on this globe has asked the researchers to identify novel targets and to intercorrelate its mechanism of action. With an ascending growth of the disease and more specifically drug-resistance has signified its emergence for new anti-tuberculosis drugs. Thus, with the prior knowledge and applying it in the drug discovery has led a convincing opportunity for the modification of current inhibitors or to develop new drugs. With the re-arrangement of recognized scaffolds is applied in its core structure which may help in the improvement of bactericidal, pharmacokinetics and pharmacodynamics activities. Along with the surveys carried out, a large number of compounds are screened against Mycobacterium tuberculosis and can be helpful later in the computer databases. The present drug discovery should include an integrative analysis with computational databases. Nanomedicine also plays an important role in the management of the disease. The nano-sensors which help in the detection of infection rate have provoked its role for the rapid and short term diagnosis. Thus, with the current literature review it can be noted that interconnecting computational chemistry with the nanotechnology diagnosis can be helpful for short term therapy as well as lesser side-effects.

Keywords: Nanosensor; dendrimers; chemoinformatics; mycolic acid; nanotechnology

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1. Introduction

The term disease resembles to the abnormal condition or construed as a medical condition that are associated with specific symptoms and signs.[1] With large numbers of increase in bacteria/micro-organisms have caused mankind to global threats. Tuberculosis is one such kind of bacterial infectious disease that has caused a global risk to mankind/manhood.1 Remaining to be one of the most neglecting disease in the world caused by the member of MTBC (mycobacterium tuberculosis complex).3 Kills about 1.7% people in the world as rated by WHO every year. It has also been evaluated that 25% of deaths occurred in HIV-positive people are due to tuberculosis.2 Despite of renovation in sanitation and also in the living conditions has decreased its level of incidence worldwide. Mycobacterium tuberculosis being a successful pathogen dormantly infects active growth of bacteria by various processes like cell wall biogenesis, chromosome replication, etc.6 Emergence in drug-resistant tuberculosis, specifically for the patients who carry latent infection are at a risk of reactivation of tuberculosis.19 Even though devising various therapies for control of bacterial MDR-TB has its highest ratio in its area.7,20 To rule over the targets a cocktail of frontline drugs (isoniazid, rifampin, ethambutol, streptomycin, pyrazinamide) are given for the first two months. Followed by long term therapies which lasts between 6 to 9 months.6 On the other hand increase in therapy leads to patient's non-compliance. Growing at an alarming phase with rise up in statistics has led WHO declaring tuberculosis 'a global emergency'.[2]

With the past decades it has been beheld where treatment is getting more difficult along with severe side-effects. Therefore, in both cases i.e. drug-resistant and drug-sensitive strains, treatment fails because of one or more drug intolerance.[3] As a result, powerful and effective new anti-TB drugs should be given with short therapy and lesser side-effects along with low cost expenditure.11 Furthermore, it is also necessary to develop collaborative approach in drug discovery. Ruling out its development of new targets in drug design has become a main question for designing of new drugs and developing a new and potential drug. To integrate its workflow in computational approaches, chemo-informatics as well as bio-informatics plays an important role. The pathways, enzymes, databases, etc are levarging at an expanding level along with workflow for anti-tubercular in drug discovery.[5] To get the potent form for anti-TB are essentially new and effective therapies are carried out. Later, nanotechnology has increased its tremendous growth for the study of disease, diagnosis of disease, treatment of disease and design of Nano-particles. Nano medicine plays an important role along with bio-sensors for the detection of bacterial strains.[4] As a consequence of it, the present summarizes on characteristics of anti-TB agents along with computational tools and triggering

nanotechnology for advancement of new and cheaper approaches which circumvents rapid and sensitive detection of main etiologic agent.[3,4,5] Thus, the stages of tuberculosis gives the description about the phase of infection in (Figure 1).

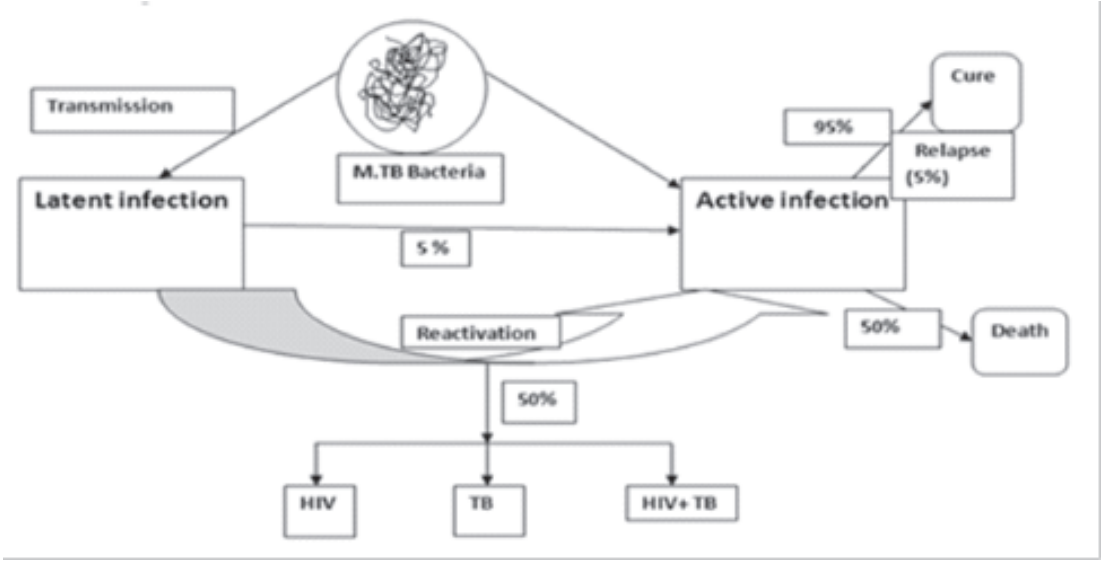


Fig. 1. Stages of Tuberculosis.[18]

2. MDR-TB and XDR-TB surveillance and its emergence

Drug resistant tuberculosis is the result of inadequate tuberculosis therapy. Due to its transmission all over the biosphere has made undetermined effects to control the global TB epidemic. With its increase in ratio on a global scale, MDR-TB as well as XDR-TB has been spread which aggrandizes its emerging level of globe.[6] The flow chart has been described in (Figure 2).

3. Current targets and its mechanism of action

The current elevation in tuberculosis cases and more potently in drug-resistant mycobacteria has indicated an emergence for an advancement of new anti-TB drugs. Because of its prolonged therapy has an upshot for persistent M.TB. They are not effectively killed by current anti-TB agents. Thus, the most happening disease has spread like a virus.5 Thus, by the use of knowledge of biology of organisms and its availability of genomic sequence has led an opportunity for the development of novel targets for drug design.5,20 Therefore, by modern approaches such as structure based drug design and combinatorial chemistry has led to development of new drugs which will not be effective in drug resistant but can also enhance short dose regimen.5,6 The chemical structures as anti-tubercular agents have been described (Figure 3). The enzymatic inhibitors are as follows:

3.1. Inhibitors of cell-wall synthesis

Isoniazid (INH) being a kind of a drug in which it requires an activation of M.TB catalase-per-oxidase (KaTG) has been aided to obtain the range of reactivate oxygen species and reactivated its organic radicals. It also helps to invade the multiple targets in tubercle bacillus. Therefore, the preliminary target is inhibition of cell wall mycolic acid synthesis pathway, where enoyl ACP reductase (Inha) was identified as a target of INH inhibition. The divergent species of Inha inhibitors are found to be isonicotinic acyl radical which reacts with NAD and forms INH-NAD complex. It also helps in inhibition of NAD metabolism. Its effect on multiple targets in tubercle bacillus is due to bactericidal activity of INH. Here, the process of mutation takes place by the involvement of INH activation, its targets and InhA and NDH-II causes INH resistance. Thus, KatG mutation plays an important role for the resistance of INH.[6]

3.2. Nucleic acid synthesis inhibition

Rifampin possessing a broad spectrum has a semi-synthetic rifamycin B derivative. Interference with RNA synthesis gets bind with bacterial DNA dependent RNA synthesis gets binds with bacterial DNA dependent RNA polymerase sub-unit encoded by rpoB. Similarly, for fluoroquinolones various derivatives were also synthesised like ofloxacin, levofloxacin, etc. And has possessed good potent activity against M.TB. Thereby, targeting DNA gyrase A and B subunits helps in inhibition. It acts on cell wall bio-synthesis and is GDP dependent process. Being a type-II DNA topoisomerase here enzymes acts as a tetramer and forms sub-units of 2A and 2B. They both gets bind to DNA molecules. The enzymes here bind to 140 base pairs, wraps at C-terminal tail domain of gyr A protein to form a positive coil. Here, sub-unit A carrier breakage reunion at active site, whereas sub-unit B promotes ATP hydrolysis. They form the A2B2 tetramer in holoenzyme and acts as a distinct function. Later, all amino acids get positively charged with two active sites tyrosine residues which are located at the centre. A region gets bind to G segment and forms DNA gate. The process of mutation takes place and leads to quinolone resistance named as QRDR (quinolone resistance determining region) gets functionally characterised by ATP hydrolysis. It gets stable reconstitute into its fragments and supercoils it by activities. Thus, M.TB develops resistance to fluoroquinolone by mutation in gyrase A and gyrase B subunit.[6]

3.2. Protein synthesis inhibition

Benzimidazole being a potent drug for an inhibition of protein on cell wall synthesis. It is ATP dependent process and is temperature sensitive mutant Z gene. Formed of cytoskeleton protein and relates to tubulin forms nucleotide exchange i.e. GDP-FtsZ monomers. The monomers are inhibited and undergoes polymerization process i.e. FtsZ-GTP monomers. These monomers get hydrolysed and

interconnected and retains its capacity forms a dynamic, restructure to fragments and anneal. Later, condense laterally developed genes.[6]

3.3. Peptide deformylase inhibition (PDF)

Bacterial peptide deformylase which belongs to mettaloproteases subfamily. Catalyses its removal of N-terminal and forms group from newly synthesised protein. Later, it was found to be reported that both the synthesis and bio-activity occurs of highly potent inhibitors. The SAR and crystallographic data clarified its required highly potent enzymes. Thus, developing potent inhibitors of H37Rv and MDR TB strains can be helpful to it.[6]

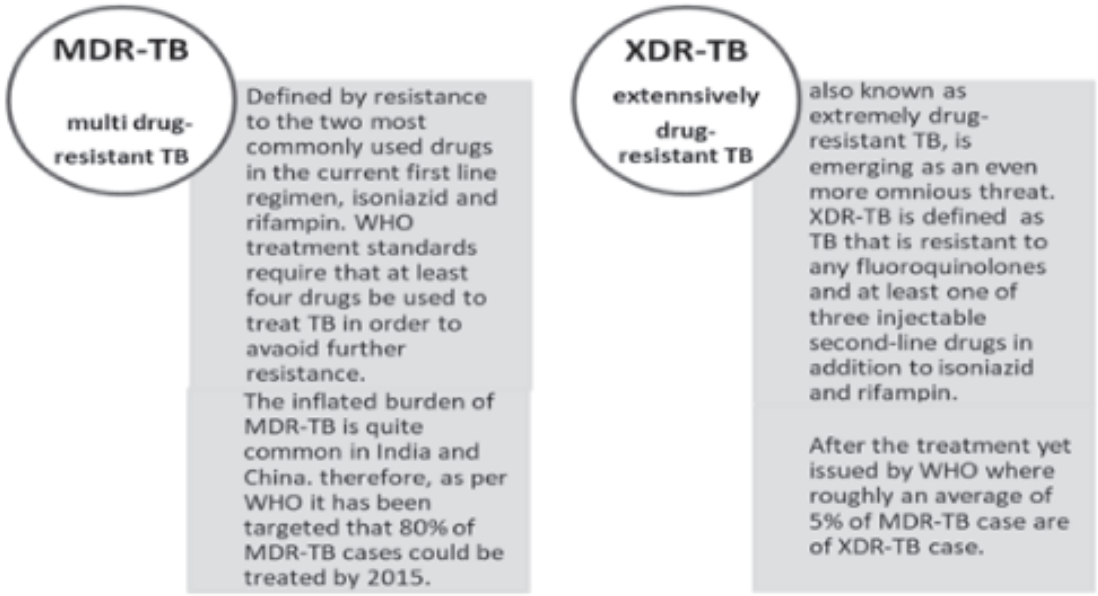
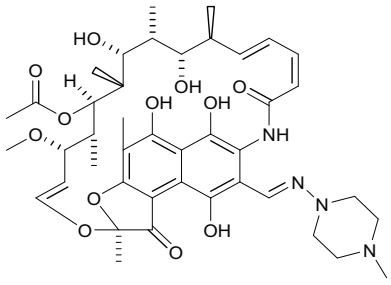
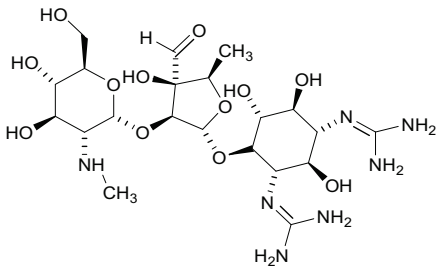


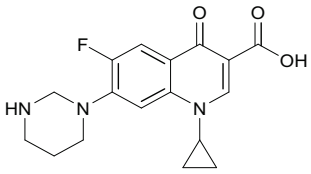
Fig. 2. Flow chart of MDR-TB and XDR-TB21



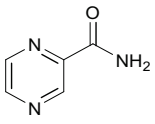
Rifampicin



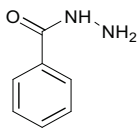
Streptomycin



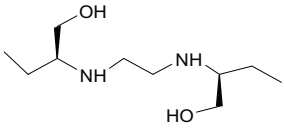
Ciprofloxacin



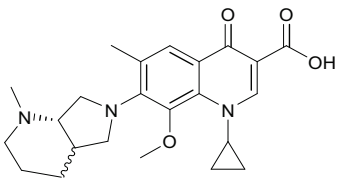
Pyrazinamide



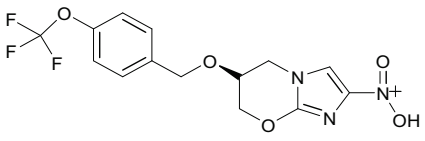
Isoniazid



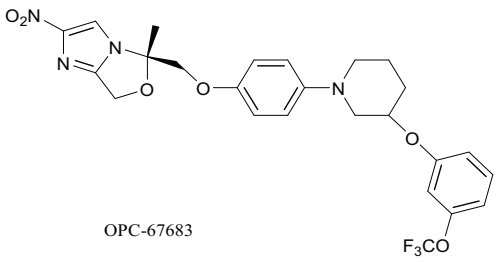
Ethambutol



Moxifloxacin



PA-824



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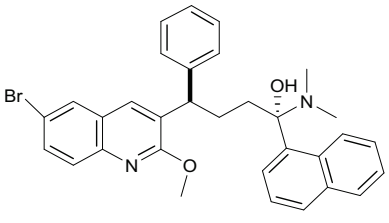

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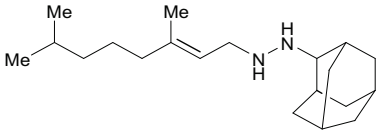

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Fig. 3. Chemical Structures of Anti-Tubercular Agents.

4. Tuberculosis: its challenge in drug discovery

Tuberculosis being a chronic disease which results into infection from M.TB is growing at a slow rate. Having its complex therapy now-a-days has become a threat for the patients acquiring with this disease. Therefore, the discovery of new targets or modifying existing targets with shorten duration of action has become a big challenge for the researchers. Earlier were the days when patients with TB and HIV where resistant strains took place. Here it included both MDR as well as HIV induced reactivation occurred. The treatment used to fail because of resistance effects. Now-a-days due to change in lifestyle, effective for both the patients (MDR-TB/ XDR-TB) and (HIV-patients) compatible with other disease, short term therapy, development of new compound attributes and effective in both cases can be helpful in tuberculosis therapy.

5. Development of new chemical scaffolds

Due to poor potency effect an identification of new tuberculosis drugs has been screened by pharmaceutical like collections which are linked to limited chemical diversity collections. Therefore, it was found that most of tuberculosis drugs don't follow lipinski's rule of five. Here, it was obtained that optimal drug-like features and pharmaceutical compound collections are found to be biased towards these properties. Due to constant development and accepting new challenges the current TB pipeline are expanding very slowly. But yet there is an inadequate development of novel regimen.[18]

6. Arrangements of new existing scaffolds

Over the past decades, it was found that many anti-biotic candidates are the chemical molecules that are re-engineered from older drug classes. Therefore, a new TB drugs from existing anti-bacterial drug classes involve re-designing of scaffolds which helps in the improvement of TB drugs that are under clinical trials. With the modification of known scaffolds, introduced into core structure aids for the advancement of bactericidal activities, good resistant action as well as pharmacodynamic and pharmacokinetic properties. For e.g. Having the modified version of oxazolidones like linezolid has led to new structures like PNU-100480 and AZD-5847 shows good activity against M.TB. The inhibition of mitochondrial protein synthesis, thrombocytopenia and myelosuppression was noted when patients were treated with oxazolidones for more than 14 days.

In case of nitroimidazoles used for the treatment of anaerobic bacteria and parasitic infections, identifies its establishment of scaffolds for synthetic modification and has been introduced for increase in anti-mycobacterial potential. Transformation of nitroimidazoles relates to unique mechanism of action, mimics its host defence strategies which can be

achieved through bio-activation and is flavin-dependent nitro-reductase. The other two candidates PA-824 and OPC-6768 are currently under clinical phase and can be helpful for shortening of the treatment. Presently, the main approach is to improve its activity its distribution in tissue and bio-availability. The current drug meropenen requires parenteral administration and thereby helpful in more serious MDR-TB/XDR-TB cases.

Thus, due to good improvement of existing scaffolds a proper statististics should be made in order to fill the drug development pipeline. It can also be helpful to improve some existing classes like fluoroquinolones, benzimidazoles and can be aided in the discovery of new chemical scaffolds for attractive approach. Hence, with proper understanding a new chemical scaffold can be facilitated along with physicochemical properties with an existing TB drugs.[18]

7. Chemo informatics and its role in Tuberculosis

Cheminformatics (also known as chemoinformatics, chemioinformatics, and chemical informatics) is the use of computer and informational techniques applied to a range of problems in the field of chemistry. It is widely used in the field of chemistry which is applied in computers and information techniques. It is largely used in the drug discovery process.[10]

8. Computational databases associated with TB

According to the surveys it was found that over 300,000 compounds were screened against M.TB in a laboratory. Therefore, it was noted that commonly millions of compounds were scanned by several numbers of the groups. The main advantage is that by gathering various data can prevent its repetition from screening by use of different groups which allows large scale of analysis of molecular properties of compounds with anti-TB activity. The database which helps for different data different aspects are developed by TB research[5] The following are the databases as below:

8.1. Bio health base: It is incorporated into PATRIC where it includes approximately 1850 to 2000 complete bacterial genomes. This website also provides some genome browser, some metabolic pathways (KEGG pathway maps), phylogenetic tree pathway, blast searches, etc.[5]

8.2. CDD TB (Collaborative drug discovery tuberculosis database): It is a kind of database which is focused mainly on small molecule libraries of compounds which acts against MTB. It is also used to find out the compounds having similar molecules to know the MTB drugs. It has also been aided in the development of novel computational machine learning and also in the identification of potent inhibitors by the development of pharmacophore models.[5]

8.3. GenoMycDB: It is also a kind of database where the tools for functional classification as well as analysis of genome structure organization and evolution can be carried out. It is also helpful in the comparative analyses of completely sequenced mycobacteria genomes.[5]

8.4. TB browses: It is a kind of a database where the resources for integrative analysis of TB genome. It is also the part of open source drug discovery.[5]

8.5. TDR target database: The database where includes all together genome sequencing, functional genomics projects, protein data. Its importance is that it includes computational evaluation of target, drug‘s ability and as well as integration of some large screening of compounds with manual data and its assembly associated with tuberculosis resistant drugs.[5]

8.6. Tuberculist: It is one of the widely recognized databases which is mainly focused on the M.TB genomes and can be aided in collating and integrating various kinds of aspects for the genomic information. It is also gives the datasets of DNA as well as protein sequences which is obtained from the strains of H37Rv. It is also connected with the annotations and functional assignments.[5]

8.7. The tuberculosis database (TBDB): It is a kind of a database where information regarding genomic data can be retrieved. It also helps the researchers to deposit their data before the publications and also helps them to carry out comparative analytical studies using genome map tools, genome synteny map or opera map browser.[5]

8.8. Web TB.org: It is a tool which contains the TB genomes, MTBreg database of proteins which is sometimes up-regulated or down-regulated in TB and also contains many more tools associated with it.[5]

9. Pathway tools for anti-TB screening

As suggested by various pathways and tools it was noted that the screening efforts for anti-TB has been facilitated by an integrative analysis of metabolic pathways, small screen and structural database. It is also helpful in the computer aided drug discovery approach. The target selection as well as drug discovery approach can be helpful in the target selection methods. The area of target selection in TB plays a difficult role in drug discovery process. Therefore, a group of researchers as well as theoreticians has been created for the collaborative approach in order to develop the transitional system of biology approach for tuberculosis.[5]

10. Applications associated with biology approaches

There are various types of databases that are helpful for identifying the stress and knowing the gene expression data. The pathways like KEGG (Kyoto Encyclopedia

of Gene and Genomes), BioCyc metabolic pathway databases and a k-shortest algorithm. Therefore, it is helpful in developing the expression related to the drug used and also for knowing the mechanism of action. Recently, an initiative was taken for a system biology program which aims to detect the regulatory and metabolic networks. It also includes the integration of profiling, high through put promoter, bioinformatics and comparative sequence analysis. Thus, provides its liberty by giving the combination in the field of chemo informatics and hereby, gives larger historical views in tuberculosis research.[5]

The databases for system biology are as follows:

10.1. BioCyc, MetaCyc (SRI):

It is a kind of database where a combination of suite tools is supported for the generation of pathways and querying of them. It consist of various organisms for specific pathway as well as genome databases. It is also specific for pathway/genome database which includes both virulent as well as drug susceptible of two MTB strains. The collection of BioCyc database also includes MetaCyc where it contains a non-redundant, exemplifies the metabolic pathways, development of experimental surveys. Largely, it was found that MetaCyc contains somewhere about 1200 pathways from more than 1600 different organisms. It is therefore, used to create the new PGDB where contains the predicted metabolic pathways of an organism, also gives interpreted genome as an input. Prediction of metabolic pathways and operons are also carried out. Thus, there is a computational analysis tool which acts as a pathway tools omics viewer.[5]

10.2. KEGG (Kyoto Encyclopedia of Genes and Genomes):

It is a database which is used as an academic resource. It consists of 16 databases which covers genome and chemical information. It is also used as a reference for many compounds and metabolites for biological pathways.[5]

11. Role of nanotechnology in the field of tuberculosis

In order to counteract its effect in the field of the bacterial world, especially in tuberculosis by applying the knowledge and giving the potentials in Nano-medicine. By aiding Nano-medicines help in the improvement of intracellular disease therapy, which offers different kinds of properties like targeting, sustained drug release and drug delivery by targeting intracellular pathogens. Thus, nanotechnology has now-a-days provoked its development for orientation of new and cheaper approaches. Hence, Nano-diagnostics will be helpful in the rapid and sensitive detection of M.TB.

12. Current Scenario

Nanotechnology gives a good chance for the detection and identification of mycobacterial strains. It also helps in the

improvement of potential drugs helpful in the treatment of tuberculosis. Nano science has given a unique and comparatively more effective drug delivery carrier, liposomal-mediated drug delivery, solid-lipid Nano particles, dendrimers, Nano suspensions, etc. Hence, the Nanoparticles, which act as drug carriers shows higher stability as well as carrier capacity with enormous improvement in drug bio-availability that later leads to reduction in dosage frequency.[3,13]

12.1. Liposomes

They are tiny spherical bubbles which are composed of the lipid bilayer membrane with an aqueous core. They act as carriers for various drugs like gentamicin, sporfloxacin, amikacin, etc. Here, it depends upon their sustainable biological compatibility. Various studies have revealed that when liposomes are encapsulated with PEG it enhances its circulatory life span in the blood stream. Thus, it is also noted that a large number of liposome-based variants if formulated it can be helpful for curing tuberculosis infection.[1] Table 1 presents liposomal-mediated drug delivery and its effect on M.TB species

Table 1 Liposomal-mediated drug delivery[4]

Drug	Liposome Formulation	M.TB Species	Effect	Animal Model
Isoniazid, Rifampicin	Multialmellar liposomes containing ePC, CH, DCP and DSPE-PEG.	Mycobacterium Tuberculosis	Controlled drug release and site directed delivery	Mouse
Pyrazinamide	Dipalmityl PC (7): CH (2) neutral and dipalmitoyl PC (7): CH (2): DCP (1) negatively charged.	Mycobacterium Tuberculosis	High therapeutic efficacy	Mouse
Clofazinamine	DMPC-DMPG (7:3) and clofazimine (drug: lipid, 1:15) in 80% tertiary butanol.	Mycobacterium Tuberculosis	Decreased cfu with no toxicity	BALB/C, Mouse

Where, DCP: dicetylphosphate, cfu: colony-forming unit, DMCP: dimyristoylphosphatidyl choline, DMPF: dimyristoylphosphatidyl glycerol

12.2. Dendrimer

They are long-chained, repeated three dimensional arrangements of a group of atoms. Being a synthetic Nano material possesses 5 to 10 nm in a diameter. In case of mycobacterium tuberculosis it was known that the cell wall of tuberculosis is similar to that of gram negative bacteria's cell wall. This cell-wall is made up of a good amount layer of mycolic acid where it renders its potency for anti-TB medicinal preparation and enters into the infected cells. Here, it acts into the latent period for curing of the disease. When a drug enters into the cell, forms complex with polymeric drug complex gets cleaved by lysosomal compartments of drug and results into drug release at high concentration in the cell. As a result of this presently mixture of drugs rifampicin, isoniazid and ethambutol is used for treatment of tuberculosis.1 Table 2 presents dendrimer-mediated drug delivery system and its effect on M.TB species:

Table 2 Dendrimer-mediated drug delivery system[4]

Drug	Formulation	M.TB Species	Effects	Animal Model
Rifampicin	Mannosylated dendrimer	Mycobacterium Tuberculosis	Biocompatibility, site-specific delivery	-

12.3. Polymeric nanoparticles

It possesses good bio-compatible and biodegradable properties for the use of drug delivery carriers. They are more stable, structured and can be synthesised with different properties like zeta potential, drug release profile, etc. These particles contain emblematic functional groups which can be transformed to structural moiety of drug or targeted ligands. The main advantage of PNP's is high stability, high loading capacity of hydrophilic and hydrophobic drugs and can be administered through different routes. The main approach of PNP's is considered to be one of the most extensively investigated with respect to anti-TB drug-loaded alginate by means of ionotropic gelatin.1 Table 3 presents Nano-Particle mediated drug delivery system and its effect on M.TB species:

Table 3. Nano-Particle mediated drug delivery system[4]

Drug	Formulation	M.TB Species	Effects	Animal Model
Moxifloxacin	Poly(butyl cyanoacrylate) Nano-particle	Mycobacterium Tuberculosis	High drug payload	-
Isoniazid	Polyactic-co-glycolic acid (PLGA) co-polymer	Mycobacterium Tuberculosis	Drug remains for prolonged period.	Rabbit
Rifampicin, Isoniazid, Pyrazinamide and Ethambutol	Alginate Nano-particle	Mycobacterium Tuberculosis	High drug payload, Improved pharmacokinetic, High therapeutic efficacy	Murine mouse
Ethionamide	PLGA Nano-particles	Mycobacterium Tuberculosis	Improved pharmacodynamics	Mouse
Rifampicin	PLGA Nano-particles dried in powdered form porous Nano-particle aggregate particle	Mycobacterium Tuberculosis	Shelf stability, Effective dispersibility and Extended release with local lung and systemic drug delivery	Guinea pig
Streptomycin	PLG Nano-particle	Mycobacterium Tuberculosis	Suitable oral dosage form	Murine mouse

12.4. Solid lipid nanoparticles

They are the promising carrier systems which are helpful for drug delivery applications. Its size ranges from 50-1000 nm. Composed of lipids and surfactants. For eg: it was noted that extra pulmonary tuberculosis considerably affects adverse immune response. These systems can be aided where it affects various conditions like they can effectively deliver drugs formulation to control lymphatic system.1 Table 4 presents Solid lipid nanoparticle-mediated drug delivery system and its effect on M.TB species:

Table 4: Solid lipid nanoparticle-mediated drug delivery system[4]

Drug	Formulation	M.TB Species	Effects	Animal Model
Rifampicin, Isoniazid, Pyrazinamide,	SLNs prepared by emulsion solvent diffusion	Mycobacterium Tuberculosis	Decreased dosing frequency	Mice
Rifabutic	Mannose coated SLNs	Mycobacterium Tuberculosis	Sustained delivery, Decreased side effects	-

13. Advantages of Nano-particles[4]

- Long shelf-life.
- Good carrier capacity.

Beneficial of both hydrophilic and hydrophobic substances.

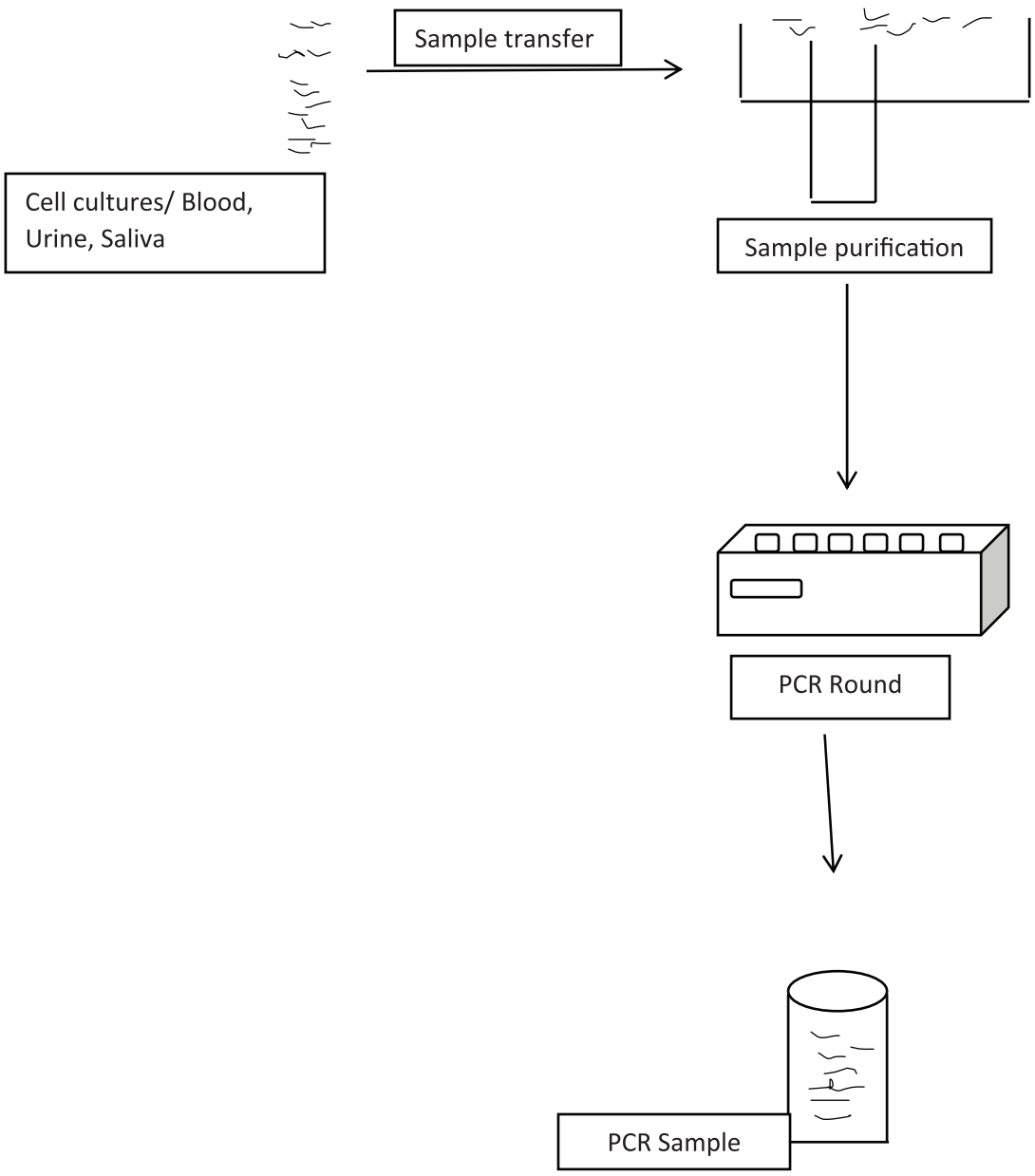
14. Drawbacks of Nano medicine in TB therapy

The main apprehension with nanoparticles as a presumed drug for tuberculosis therapy is its toxicity. The main drawback is that the physicochemical properties of nanoparticles like aggregations where the pH changes with it. The various issues like the redox potential of mitochondria, size dependent permeability of nuclear, etc. Thus, in order to remove its toxicity the carrier molecules should be treated with the utmost importance. As the size of Nano-particles are extremely small rendering its ability to cross with biological barriers like blood-brain barrier, blood-testis barrier, its regard with human health which can later cause caution and can be applied under some guidance.4

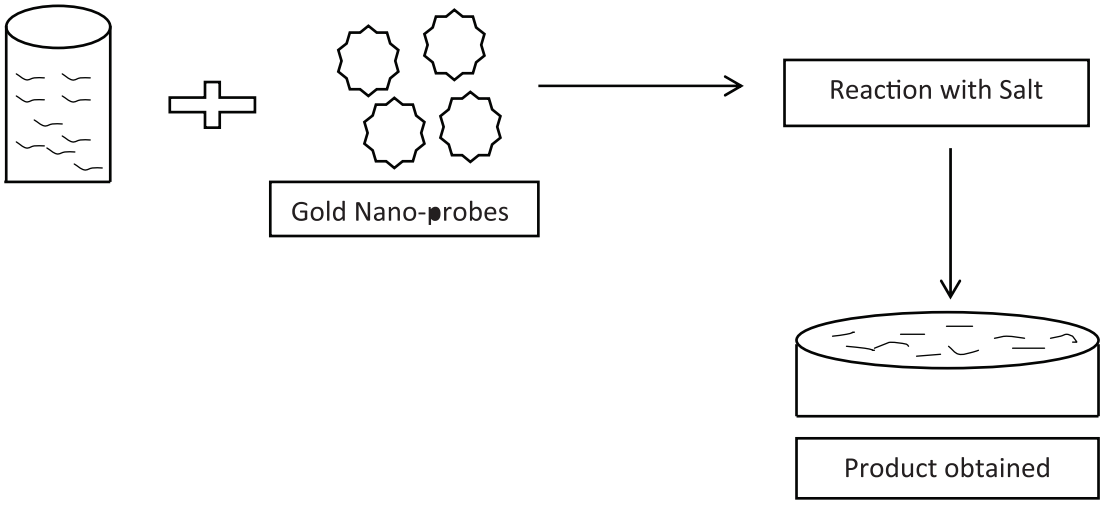
15. Nanosensors

"The term Nano sensors are defined as any biological, chemical or sensory points which are useful for passing the matter about nanoparticles in the macroscopic world." 20 Thus, the modified figure has been designed and is described in figure 4.19

a) Sample Preparation



b) Sample Preparation



c) Data Analysis

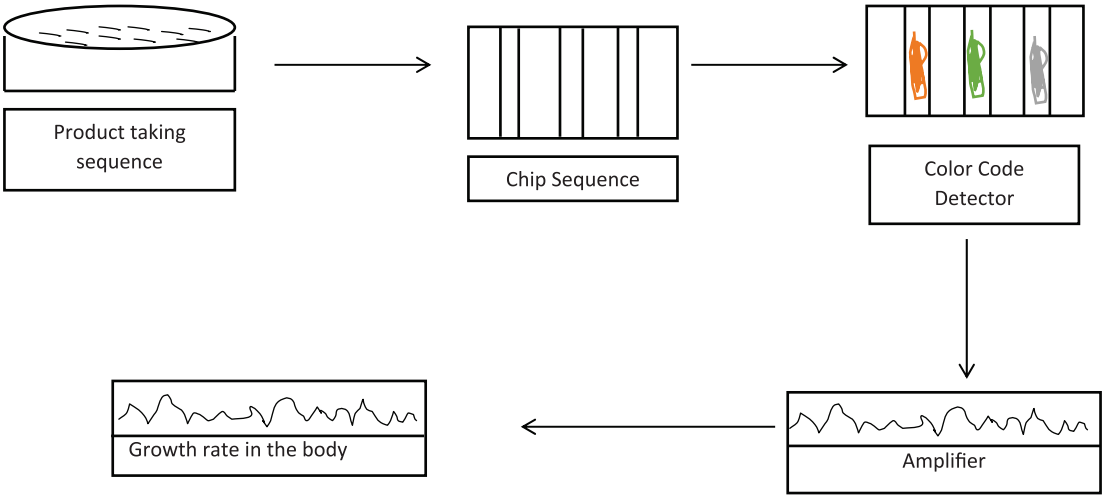


Fig. 4.Schematic representation of diagnosis using Nano sensor.[19, 20]
a) Sample Preparation, b) Sample Detection, c) Data Analysis

The following are the steps for detecting the bacterial growth rate using Nano-sensors as shown in figure 4:

1) Sample preparation.

2) Sample purification is carried out.

3) Purified sample and gold Nano-probes are taken in one plate.

4) Combined with salt and undergoes reaction.

5) The Product is obtained along with gene sequencing

6) Added to chip sequencing using Nano-sequences.

7) Detection of bacteria through color code.

8) Amplifier present, which gives a graphical growth rate of bacteria in the body.

   Note: red- indicates the major growth rate of bacteria in the body.

   Orange- indicates the average growth rate of bacteria in the body.

9) Green- indicates the minor growth rate of bacteria in the body

Anti-tuberculosis drug induce liver injury is observed in 40% of patients. Single nucleotide polymorphism and mutation account for the major contribution to drug resistance.21 The detection of resistance related mutations through the drug resistance diagnosis could improve the patient care.22 The drug resistance tuberculosis poses a serious challenges to the existing anti-TB therapies. Therefore, there is an unmet need for combination therapy.23

Conclusion

Many new anti-TB drugs have been developed in several years. But due to lack of knowledge of a novel mechanism of action, sometimes it fails to act against bacterial resistance. To reduce the duration of therapy potent drug development against M. TB should be carried out. Various dosage forms like suspension or emulsions using nanoparticle for tuberculosis can be considered for effective treatment. Taking the nanosenors by attaching it with human veins and detecting it through color code detector can be helpful in knowing its bacterial growth rate in the body. Considering all the aspects of drug discovery potential anti TB molecule can be developed with short term dose regimen with fewer side effects.

Conflicts of Interest: Authors disclose no conflicts of interest

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