

A review on modern patterns toward treatment of infective diseases in the antibiotic resistant era by utilizing nanoparticles

Asif Nawaz¹, Maria Shoukat², Shumaila Yousaf³, Huma Murtaza⁴, Hafiz Saboor ul Hassan², Muhammad Farhan Zafar Chaudhry⁵, Mehwan Riaz⁷, Zoha Sarfraz⁸, Sarfaraz ali²

¹Abbottabad university of Science and Technology

²National Institute of Health Islamabad

³Nuclear institute for Agriculture and Biology (NIAB)

⁴Department of Biotechnology, Quaid-I-Azam university Islamabad

⁵Department of Microbiology, Government College University Faisalabad

⁶Department of Bioinformatic and Biotechnology, Islamic international university Islamabad

⁷Gulab Devi Educational Complex, Lahore

Corresponding Author's Email: sarfraz.ali@org.pk

ABSTRACT:

We are living in period of cutting edge and current advances with the improvement of anti-infection agents 70 years prior however from the most recent decade there is a proceeds with increment in the microbial obstruction because of decreased explanation in instrument of malady and atomic planning of new medications, with the progression of time irresistible ailments have gets impervious to various medications, creating in one of the best wellbeing challenge all through the world. Medication obstruction bring about high portion of prescription conveyance of anti-microbials ordinarily produce terrible harmfulness, different medication opposition (MDR) is an unmistakable general wellbeing concern, representing 25000 passings worldwide consistently. Nano innovation itself created in late decennaries. Later the development of high goal microscopy there is advancement in sub-atomic sciences. These all got potential in beginning of twentieth century once the ways to the nanocosmos was blasted open with the creation of inventive magnifier. In 1902 structure under four nm were with progress distinguished in ruby channel exploitation dim field magnifying instrument created by Richard Zsigmondy and Henry Siedentopf with help of extra developments. Nanomedicine without a doubt flexibly a method of prior finding; progressively down to earth, more secure, and customized medicines also as marked down human services costs. A few experts concur that nanomedicine can deliver a change in outlook that upsets medicinal services at stretches future ten years. Nonetheless, for significant achieve be made toward this objective, rather more work is required to decide testing standards, approve viability, and aggregate wellbeing data for various nanotherapeutic operators and materials.

1. INTRODUCTION:

As the truth that humans are living in time of progressed and modern innovations with the development of antibiotics 70 years ago but from the last decade there is a continues increase in the microbial resistance due to reduced clarification in mechanism of disease and molecular designing of new drugs, with the passage of time infectious diseases have becomes resistant to multiple drugs, developing in one of the greatest health challenge throughout the world. Medication obstruction leads to elevated amount of antimicrobial drug dosage and usually generates unbearable toxicity, multiple drug resistance (MDR) is a clear universal health concern, accounting for 25000 deaths worldwide every year. Inside the timespan non-conventional antimicrobial agents provides marvellous attraction in defeating the opposition that is evolved by various infectious microbes against most ordinary utilized antimicrobial agents. Various class of antimicrobials especially nano-particles appears to have

imaginable role in overcoming and modernizing the diagnosis and treatment of microbial infections, particularly caused by multiple drug resistant strains. (Ae Jung Hu et al., 2011).

Nano technology produces materials that have particulate substance that have one dimension but 100nm a minimum of. The importance of this nano material are recognized at the point when researchers found that size can impact the physio-chemical behaviour of the component. (Dreaden et al., 2012).

Nano particles are straight forward atoms itself and consequently made up of three layers for example. (a) A surface layer with a number of minute atoms, metal ions, surfactants and polymers that can be functionalized. (b) The shell layer, which, from all points of view, is synthetically different from the middle. (c) The core, which is actually the middle part of the nano particle, typically alludes to the nano particles themselves. (Shin et al., 2016). Having these deviate properties researchers showed great interests for using these nanoparticles in multidisciplinary fields. According to the antibacterial properties of nano particles, metallic nano particles shows effective results in surpassing bacterial resistance. Metallic nanoparticles are toxic in nature therefore reducing their use in human cells. Solution to this problem is the combination of the metallic nanoparticles with antibiotics which results in declining the toxicity of these two agents concerning to the human cells. This reduction in the toxicity is because of lowering high dosage needs and also by amplifying bactericidal activity. Combination of antibodies with nanoparticles also reimpose the capacity to destroy bacteria. (Adil M Allahverdiyev et al., 2011).

2. HISTORY AND DEVELOPMENT OF NANO MEDICINE:

Nano medicine is a young science. Therapeutic innovations and pharmacology has just been investigated about since 1990's. Nano technology itself developed from few decennaries. With the innovation of elevated determination micro-scope there is an evolution within molecular sciences. For nano-medicine, Nano biotechnology that examine the composition as well as performance about cell likewise intra – living procedures and cells crosspondance is of foremost significance. These all composed a potential in starting of twentieth century when the ways to the nano-cosmos was blown out to open with the creation of inventive magnifier. In 1902 structure less than four nm were with success detected in ruby filter victimization dark field microscope established by Richard Zsigmondy, Henry

Siedentopf. With aid of additional inventions like voltage clamp, understanding the structure and performance of plasma layer, dissemination method moreover efficient cell crosspondance which implies that of receptors and antibodies in keeping with secured laws got to be ever higher within the next decennaries . Mechanism which maintains as well as regulates metabolic process, the part of enzyme, proteins moreover the working of immunesystem. (Mappes T et al., 2012).

3. RESISTANCE TO CONVENTIONAL ANTIMICROBIAL DRUGS:

Penicillin was the essential anti-microbial to be found in 1928 that denoted the beginning of the advanced period of anti-microbials. Anti-toxins is characterized on the reason of their method of activity, range of activity, or their concoction structure. For instance, anti-infection agents will either be germicidal (deadly to microorganisms) or organic procedure (causing development restraint of microbes). The wide range antibiotics. Target each the gram-negative and gram-positive microorganism, though the thin range anti-microbials target just 1 of them. Bolstered their atomic structures, anti-infection agents is grouped as β -lactams, macrolides, antibiotic medications, quinolones, aminoglycosides, sulphonamides, glycopeptides, and oxazolidinones. The β -lactam anti-microbials meddle with the cytomembrane combination in microorganism by authoritative to anti-microbial restricting super particle (PBP). The job of PBPs is to cross-connect the amide units inside the peptidoglycan Layer. Authoritative of β -lactams to PBPs brings about the restraint of the last mentioned, and a short time later celllysis. The β -lactam anti-microbials are extra isolated into penicillins,

cephalosporins, monobactams, and carbapenems. Inside the late Nineteen Sixties, the development of microorganisms was found out.

These microorganism had the option to ready to, compounds that may that may anti-infection agents. The disclosure of carbapenems bypassed this drawback, as this new class of β -lactams was heartless toward the β -lactamases. Among all the incredible, carbapenems display the broadest range of movement. Unfortunately, the development of carbapenem obstruction was moreover reputed in microorganism. Glycopeptides also focus on the microorganism cytomembrane blend, anyway moreover to hindering the PBPs, they moreover restrain peptidoglycan blend. A nearby record of ongoing advancements in glycopeptide anti-infection agents has been uncovered somewhere else. The macrolides, antibiotic medications, aminoglycosides, and oxazolidinones repress the microorganism development by focusing on super particle combination inside the cells. Macrolides tie to the 50S ribosomal money related unit and hinder the lengthening of mRNA all through interpretation, in this manner stopping super atom amalgamation. Oxazolidinones furthermore tie to the 50S ribosomal fiscal unit, dislike the macrolides, hinder super atom amalgamation by safeguard the arrangement of 70S interpretation commencement progressed. Together, these two classifications kind the 50S inhibitors bunch. Antibiotic medications and aminoglycosides, the 30S inhibitors group, tie to the 30S ribosomal fiscal unit denying aminoacyl-tRNAs access to the organelle and a short time later hindering super particle union. While macrolides and antibiotic medications are commonly natural procedure, aminoglycosides are extensively germicidal in their method of activity. Super particle (DNA and RNA) blend is prime to a cell's endurance.

Quinolones hinder microorganism development by impendance the activity of deoxyribonucleic corrosive helicases that are irreplaceable for moving the twofold spiraling structure of deoxyribonucleic corrosive before deoxyribonucleic corrosive replication or fix. Moreover, quinolones also meddle with the elements of topoisomerase II and topoisomerase IV in microorganism prompting a negative outcome on ribonucleic corrosive catalyst, in this way restraining ribonucleic corrosive amalgamation. Sulfonamides fundamentally mirror para-aminobenzoic corrosive (PABA), a substrate for the blend of folate in bacterial cells. Folate is fundamental for super atom (DNA) combination, in this manner by competitory with PABA and impendance folate union; sulfonamides hinder natural procedure and cause development hindrance in microorganism. Tragically, protection from those regular anti-toxins has been supposed in microorganism, making it intense to treat the diseases brought about by these microorganism (Adzitey et al., 2015).

4. NANO MEDICINE FUNCTIONALIZING:

Functionalization includes fixing properties of a NP through compound or physical changes that square measure applied to achieve an ideal effect. (Bhaskar S, et al., 2010) This strategy will give local or coordinated conveyance, drag out medication impacts, encourage transport into target cells, discover a neoplasm or space of disease, give input identifying with effectivity or medication conveyance, or scale back blood stream shear impacts. (Godin B, et al., 2010). A conversation of the varying ways to deal with functionalizing NPs follows.

4.1 TARGETING:

NPs are regularly managed provincially or are frequently effectively focused on abuse cell-explicit ligands, attractive limitation, as well as size-based property (Galvin P, et al., 2012). A few components got the opportunity to be thought of once building focused on NPs, along with size, biocompatibility, target fondness, dismissing of the RES, and security inside the blood, moreover in light of the fact that the capacity to encourage controlled medication unharness. Attractive compound Nano composites or magneto liposomes joined with sedate atoms have decent potential for focused medication conveyance (Bhaskar S, et al., 2010).

These NPs have without a doubt positive bio dissemination and pharmacokinetic profiles, which may be expanded by the outside utilization of a static power field at the area of activity. For example, in one examination, X-ray affirmed that attractive NPs had relocated toward neodymium/iron/boron (NdFeB) magnets that had been put outside the substantial pit, on head of unions of a person's sex organ dangerous neoplastic ailment (Galvin P, et al., 2012). NPs are frequently worked to incorporate a decent sort of treatment operators which will be focused on legitimately and explicitly to the development site for higher adequacy and security (Bharali DJ et al., 2010). NPs may likewise be loaded with unique excellence specialists for imaging capacities. When contrasted with little particle differentiation specialists, multifunctional NP edifices or NPs utilized in symptomatic imaging have the benefit of a larger than usual span that grants focusing through surface changes and furthermore the capacity to simultaneously convey helpful operators (Poirot et al., 2011).

4.2 SURFACE CONJUGATION:

One path during which NPs might be functionalized for explicit applications is through surface conjugation (Taylor E et al., 2011). Nanoparticle surfaces might be conjugated with a decent fluctuate of analytic or restorative specialists (Poirot et al., 2011) Some applicant biomolecules for NP surface conjugation square measure cell-entering peptides (CPPs) that improve intracellular conveyance, fluorescent colors for imaging, and operators for hereditary clinical guide like minimal harsh polymer (siRNA) (Bhaskar S, et al., 2010).

Nanoparticle surfaces, conjugated with a focusing on particle that ties to amazingly communicated tumor cell receptors, can even encourage the vehicle of imaging qualification specialists that give accumulated affectability and particularity, that guide in tumor identification (Sajja HK et al., 2009). The surfaces of NPs can even be conjugated with tranquilize treatments. Three Surface conjugation with ligands that explicitly tie to the objective site will improve the adequacy of NP tranquilize conveyance frameworks while significantly diminishing poisonousness (Bharali et al., 2010). In disease treatment, tumor focusing on might be accomplished by conjugating a particle or biomarker, (for example, amide, protein, or nucleic corrosive) that is eminent to tie to tumor cell receptors on the NP surface (Sajja HK et al., 2009).

4.3 BIOAVAILIBTY:

NPs are commonly cleared from dissemination by framework proteins known as opsonins that enact the insusceptible supplement framework and imprint the NPs for annihilation by macrophages and various phagocytes. Nonpartisan NPs are opsonized less significantly than charged particles, and hydrophobic particles are cleared from course snappier than hydrophilic particles NPs will along these lines be intended to be unbiased or conjugated with hydrophilic polymers, (for example, PEG) to draw out flow time (Galvin P, et al., 2012).

The bioavailability of liposomal NPs can even be swelled by functionalizing them with a PEG covering in order to stay away from take-up by the RES. Liposomes functionalized during this implies are known as "covertness liposomes." NPs are typically covered with a PEG covering as a general implies that of forestalling opsonisation, diminishing RES take-up, improving biocompatibility, as well as expanding course time. SPIO NPs can even be made dissolvable on the off chance that they're covered with a hydrophilic compound, (for example, PEG or dextran), or they will be made amphophilic or hydrophobic in the event that they're covered with non-cyclic surfactants or liposomes to gracefully magnetoliposomes (Sajja HK et al., 2009). Supermolecule coatings can even improve the biocompatibility of various particles (Galvin P, et al., 2012).

4.4 CONTROLLED RELEASE :

NPs can even be structured so they'll be enacted to release remedial or indicative stacking because of a site-explicit or remote trigger (Galvin P, et al., 2012). Properties that might be wont to functionalize NPs for controlled release typify hydrogen particle fixation, temperature, field of power, impetus action, or elective choices like light-weight or radiofrequency signals (Seigneuric et al., 2010).

NPs made with hydrogen particle focus responsive materials will be intended to trigger medication release at an objective site after distinguishing a change in pH. For instance, the delicately acidic setting inside provocative and neoplasm tissues (pH 06-08) and cell vesicles, as endosomes (pH 5.5–6.0) and lysosomes (pH 4.5–5.0), will be abused to trigger medication release.

Thermally responsive linkers, comprising of nucleic acids, peptides, proteins, lipids, starches, or polymers, can even be wont to join one or extra specialists for controlled release from the NP. Once the thermally responsive linker is presented to a specific temperature or temperature shift (the "trigger temperature"), the linker is broken and in this manner the specialist is released (Galvin P, et al., 2012). For instance, DNA particles with heat-labile gas holding between corresponding strands will go about as a warmth delicate linker. A NP can even be intended to fuse numerous thermally responsive linkers that square measure intended to upset at very surprising temperatures, sanctionative medication conveyance to happen in an exceedingly explicit request over fluctuated times of your time (Sajja HK et al., 2009).

The arrival of operators from NPs can even be accomplished through the fuse of bonds that corrupt underneath elective explicit conditions at the objective site. For instance, tumor-explicit procedures could likewise be abused to interfere with a bond and trigger the release of a helpful operator. Neoplasm site-explicit conditions would possibly} be wont to trigger release may typify unusual component levels, particular biomarkers, or presentation to concoction activity catalysts that square measure overexpressed in tumors (Sajja HK et al., 2009).

5. PHYSICAL FEATURES:

The physical attributes of NPs will contradict from various perspectives that impact work. A conversation of a considerable lot of those physical choices follows.

5.1 SIZE:

NPs region unit inalienably little, with at least one measurement inside the shift of one to a hundred nm, however they'll even be micrometer (μm)- estimated particles. NPs have novel basic, optical, and electronic properties that a ton of bigger particles or mass solids need (Godin et al., 2010).

They even have improved dissolvability, with the goal that they could likewise be acclimated reinvestigate mass medication partners that territory unit popular to have helpless solvency (Seigneuric et al., 2010).

This property could offer the ability to change over insoluble or ineffectively dissolvable medication into solvent twofold compound suspensions, so killing the need for venomous natural solvents. Another key benefit related with the little size of NPs is an intensified bioavailability and flow time. Studies have indicated that particles underneath 200 nm have longer flow times, contrasted and bigger particles, paying little mind to any surface adjustments blessing (Galvin P, et al., 2012).

5.2 SHAPE:

NPs are accessible a spread of shapes, along with circles, plates, sides of the equator, chambers, cones, cylinders, and wires. NPs additionally can be empty, permeable, or strong. These attributes of NPs are frequently hand-singled out the possibility of intuitiveness, stacking capacity, and transport abilities. For example, an empty NP could likewise be a wonderful bearer for medicate treatments or imaging qualification specialists (Galvin P, et al., 2012).

5.3 SURFACE AREA:

One element of NPs that gives them unmistakable physical properties might be a goliath degree comparative with size. As molecule size declines, complete degree will increment exponentially. An ascent in territory unit, region scope, degree suggests that a greater extent of iotas are determined to the molecule surface comparative with the center. This improvement makes NPs extra responsive

contrasted and commonplace bigger atoms, or mass strong partners. Swelled degree is also responsible for the improved water dissolvability and bioavailability that consistently happen with NPs (Bawa R et al., 2011).

The huge breadth of NPs also allows them to be intended to join a wide change of surface attributes, along with conjugation with power charges or biomolecules (Seigneuric et al., 2010).

Such surface alternatives is deliberately tip top for focusing on and various capacities and territory unit so decided on it premise (Godin et al., 2010).

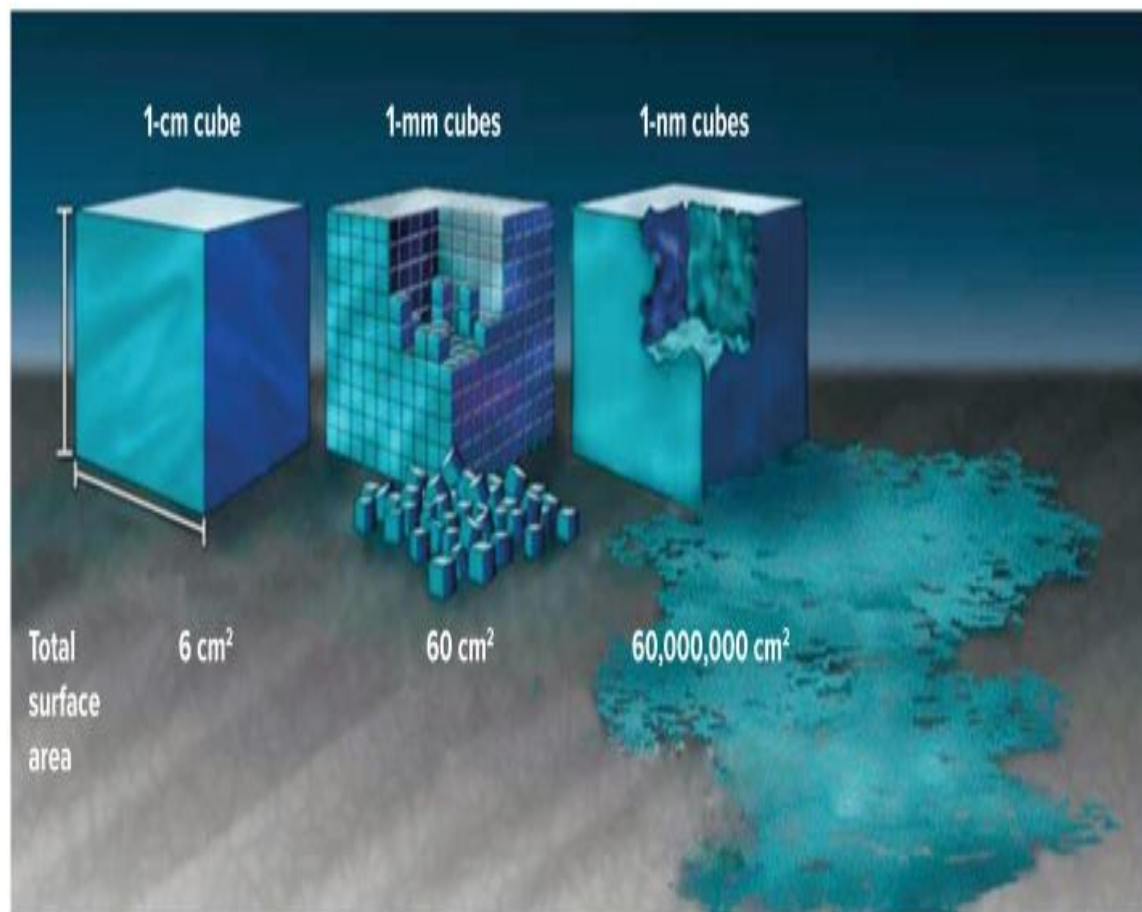


Figure 2 Illustration depicting the exponential increase in surface area that occurs with nanoscale materials. (Adapted from the National Technology Initiative.)

PERMIABILITY:

Appropriately designed NPs square measure, their small size would turn them to cross physiological obstructions to transmit prescription to locations that do not appear to be normally accessible by old recommends that (Seigneuric et al., 2010). For example, A NP 's collected porosity could enable it to transfer prescription of malignant growth into tumours by passing through new vessel pores that still measure square in breadth. (Sajja HK et al., 2009). The amassed porosity of NPs may moreover empower them to cross the blood–mind hindrance through the use of different take-up systems (Seigneuric et al., 2010).

FUTURE DEVELOPMENT OF NANO MEDICINE:

In the returning decade innovation and Nanobiotechnology applications can pick up significance in medications and clinical innovation. This pattern is now obviously noticeable at present: For the essential and half. This decade (2010-2014) the net of information (Center Assortment) records the titles of three, 438 distributions beneath the watchword "nanomedicine" (as against 857 passages for the total earlier decade of 2000-2009).

Nanomedicine can possibly extensively improve the standard of life of patients. Withal, the new possibilities moreover include dangers and raise sociology and good inquiries that ought to be investigated and discussed. Figure four shows the four investigation and advancement zones that will no doubt get the best catalyst from nanomedicine inside the coming decades. The Nano treatment vision of the more drawn out term is treatment of patients with independently bespoke prescriptions ("customized medication") at the sub-atomic level as after a short time on the grounds that the disorder is inside the improvement stage (McDermott U et al., 2011).

The planning of nano drugs and furthermore the various methods of focused vehicle of dynamic substances (tranquillize conveyance) can assume an exceptional job here. With these it might get potential to create powerful and very much endured medicines for so far hopeless infections. Nanotechnologies give ways by that organic information can be non heritable basically, rapidly and cheaply and dissected, and consequently gigantically increment the probabilities of training of medication. Treatment also, nosology region unit dynamically transforming into mixed into the new authority clinical field of theranostics, because of the designing ways and medications serve demonstrative and remedial capacities simultaneously.

Models region unit the balance material that carries with it legitimately the dynamic substance inside the occasion of an obsessive tissue alteration (Lu Zr et al., 2007) .and transporter frameworks that stream into preventively inside the living being and respond to endogenous signs and precisely discharge dynamic substances if necessary (Patel K et al.,2008).

The get together of nano materials that recognize cells and cell constituents, just as individual qualities, of weakened perform furthermore, fix them willingly inside the life form is also being investigated (Xeu et al., 2010).

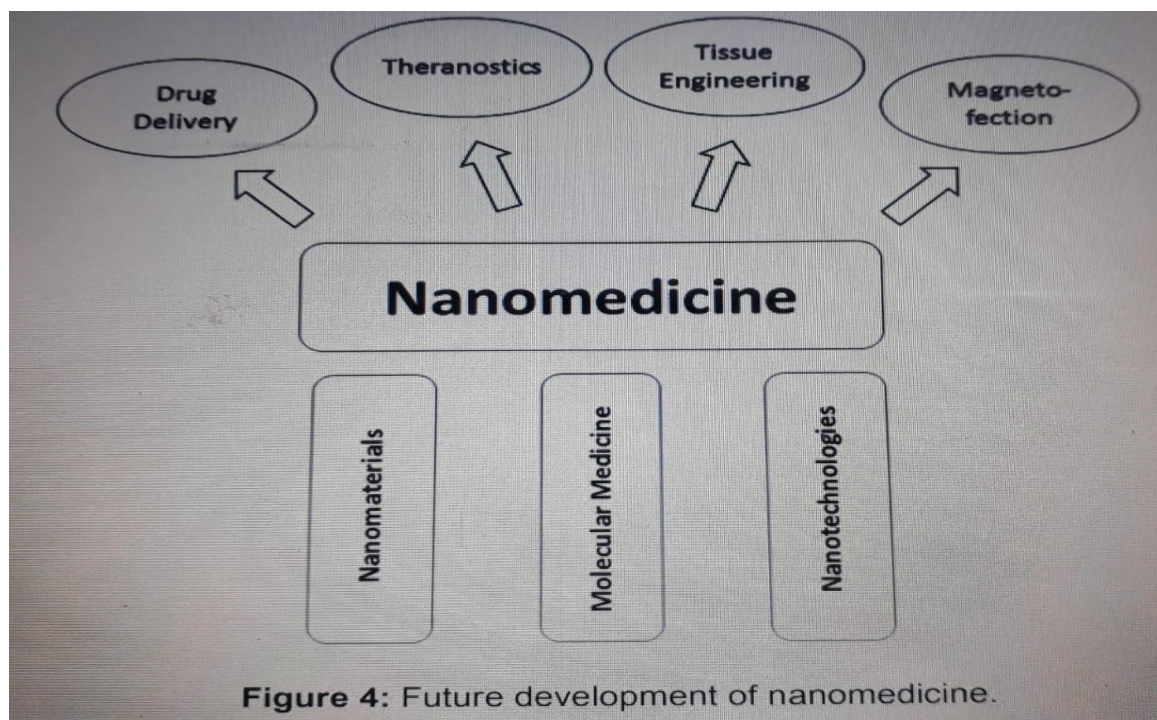


Figure 4: Future development of nanomedicine.

As of late, a promising theranostic application has been self-tended to in adjusting AN on-switch illusory substance Receptor (Vehicle) against chemotherapy-safe sorts of lymphocyte malignant growth (Wu CY et al., 2015). By presenting little particles a switch-on-switch-off instrument may with progress been set up in an exceedingly draconic fabricated lymphocyte restorative methodology, in this manner maintaining a strategic distance from nephrotoxic impacts of the cell executioner work.

Nanobiotechnology uncovered new possibilities explicitly inside the field of regenerative medications. By incitement and focused on the executives of cell development, broken or missing tissue – from hair, cartilage and bone, by means of muscles and organs, through to nerve cells – may be recovered or delivered by fake methods with the assistance of nanomaterials (tissue engineering). Nanoporous transporter materials ar as of now presently getting utilized in wound recuperating and in corrective medical procedure as grids on that controlled cell development happens (Zang L et al., 2009). Whenever focused on development of nerve cells were conjointly to be effective, new potential medicines for so far hopeless neurologic maladies as parkinson Alzheimer's, mind issue and different sclerosis might be created. What's more, will focused on control of grown-up immature microorganisms even be lucky, endogenous tissue that causes no dismissal responses might be developed, and in this manner the utilization of early stage undeveloped cells might be relinquished.

6. CHALLENGES FOR NANOMEDICINE:

Notwithstanding the points of interest that nanomedicine ought to give, a great deal of investigation stays expected to pass judgment on the assurance and poisonousness identified with a few NPs (Galvin P, et al., 2012). A ton of nano clinical examination has focusing on medicate conveyance, with relatively hardly any investigations represent considerable authority in the pharmacological medication or harmfulness of NPs.7 examination NP pharmacological medication, pharmacodynamics, and potential since quite a while ago run poisonousness in vivo is imperative to perception the aftereffects of NPs on quiet populaces. Validating each nano remedial operator for wellbeing and effectivity, regardless of whether sedate, gadget, biologic, or mix item, presents a huge test for scientists and furthermore the FDA, that is by and by grieved to detail testing models and amass security data (Galvin P, et al., 2012).

Studies additionally are required to survey the immunogenicity of NPs. Nano therapeutics and nosology may blessing unexpected ototoxic impacts because of overstated reactivity contrasted and their mass partners (Bawa R et al., 2011).

The premier regularly reportable aspect result once infusion of a nano remedial specialist has all the earmarks of being an excessive touchiness, which can be brought about by initiation of the invulnerable supplement framework. The most atomic system for in vivo NP poisonousness is thought to be the acceptance of aerophilic worry through the development of free radicals (Galvin P, et al., 2012). In overabundance, free radicals will make injury lipids, protein, DNA, and option natural parts through response. Numerous creators have reportable that natural attributes of NPs, similar to proportion and degree, is master oxidant and expert provocative (Bhaskar et al., 2010).

Notwithstanding, the development of free radicals in light of partner degree NP may likewise create different causes, similar to the response of vegetative cell cells to outside material, lacking cancer prevention agents, the nearness of change metals, ecological elements, and option characteristic synthetic or physical properties (Galvin P, et al., 2012).

Exploration to pass judgment on the measurements and surface properties of NPs may moreover encourage to recognize the imperative measurements at that they have a tendency to significantly aggregate inside the body. NPs have partner degree overstated capacity to cross organic obstructions thus can possibly amass in tissues and cells because of their little size (Bawa R et al., 2011). The possible tissue gathering, stockpiling, and moderate leeway of those presumably free radical-delivering particles, comparably in light of the fact that the pervasiveness of different phagocytes inside the RES, may make organs like the liver and spleen the most focuses of aerophilic pressure (Galvin P, et al., 2012).

This absence of information concerning potential harmfulness issues powers nano clinical examination to concentrate prevalently on compound NPs, that security and effectivity data exist as of now. Indeed, numerous nano medications containing compound NPs region unit previously affirmed by FDA (Galvin P, et al., 2012). Rather than elective materials that will get ototoxic in NP kind, the macromolecule NPs likewise are thought of to be biocompatible and passable (Galvin P, et al., 2012).

Thusly, short-lived, dissolvable, nontoxic NPs, similar to polymers, liposomes, and IO particles, territory unit undeniably more captivating to use in nanomedicine than bio determined parts zone unit. The work of NPs like carbon nanotubes, QDs, and a couple of metal like nano bearers that aren't short-lived can be extra hazardous. This trademark needn't demoralize nano clinical investigation with these NPs anyway should strengthen endeavors to spot further transient shapes, materials, and surface medicines (Bhaskar et al., 2010).

CONCLUSION:

In spite of the fact that nanomedicine keeps on being at beginning phase of advancement, many medication that use Nano sciences are endorsed and advertised, and loads of others zone unit being contemplated. Nanomedicine without a doubt flexibly a method of prior conclusion; increasingly functional, more secure, and customized medicines moreover as scaled down social insurance costs. A few masters concur that nanomedicine can deliver a change in outlook that alters social insurance at spans future ten years. In any case, for significant achieve be made toward this objective, rather more work is required to decide testing rules, approve adequacy, and gather security data for various Nano therapeutic operators and materials.

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