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Nanotechnology in Pharmaceutical Science: A Concise Review

Shivraj Popat Jadhav[1]*, Himmatsingh Chawra[1], Khanderao Rajaram Jadhav[2], Deepak Devidas Sonawane[2]

[1]School of Pharmacy, Suresh Gyan Vihar University, Jaipur.

[2]Shrishakti Shaikshanik Sanstha's, Divine College of Pharmacy, Satana, Maharashtra.

ABSTRACT

Nanotechnology indicates use of material at nanoscale (10^{-9} meter). Nanotechnology is multidisciplinary field covering areas like engineering, electronics, physics, molecular biology, biophysics, medical and pharmaceuticals. The properties of material at nanoscale are different than macro scale. Nanotechnology in dosage form development have many advantages like enhanced solubility, increased dissolution rate, enhanced stability, reduction in dosage, increase in bioavailability and rapid onset of action. Various nano based technologies are used in pharmaceutical sciences like Quantum dots, Dendrimers, Carbon nanotubes, Liposomes, Polymeric nanoparticles, Metallic nanoparticles, Polymeric micelles, Nanocomposites and many more. Various applications of nanotechnology include oral drug delivery, pulmonary drug delivery, ocular drug deliver, gene therapy, cancer treatment, brain targeting, as a diagnostic tool and many more. This review includes different nanopharmaceuticals and there applications in drug delivery system.

Keywords: Nanotechnology, Nanoparticles, Liposomes, drug delivery system, nanotubes

INTRODUCTION

Nanotechnology word indicates use of technology at nanoscale. Over the past couple of decades nanotechnology is proving its importance in drug delivery. In Latin language, meaning of word nano is dwarf (small). In 1974, Tokyo science university Professor Norio Taniguchi coined the word nanotechnology and since then it is being used. [(1)] Any technology

which deals at nanoscale is called as nanotechnology. Nano word indicates size of 10^{-9} meter. Nanotechnology is multidisciplinary field covering areas like engineering, electronics, physics, molecular biology, biophysics, medical and pharmaceuticals. The properties of material at nanoscale are different than macro scale. [2] These changed particles of drug molecule in nano scale can lead to increased performance in different dosage form. If we trace back the use nanotechnology in medicine, we can find the use of colloidal gold in ancient time. The growth of nanoscience can be drawn to the time of the Greeks and Democritus in the 5th century B.C. [3] Nanotechnology in dosage form development have many advantages like enhanced solubility, increased dissolution rate, enhanced stability, reduction in dosage, increase in bioavailability and rapid onset of action. [4] Nanotechnology is playing vary important role to fight against various life-threatening diseases like cancer.

It helps in detection of various neurodegenerative diseases like Alzheimer's disease and Parkinson's disease, diabetes mellitus, sensing viruses and microorganism. Nanotechnology can be used in pharmaceutical sciences like development of nanomedicines, diagnosis, tissue engineering and development of biomarkers, biosensors, targeted drug delivery. [5] Various nano based technologies are used in pharmaceutical sciences like Quantum dots, Dendrimers, Carbon nanotubes, Liposomes, Polymeric nanoparticles, Metallic nanoparticles, Polymeric micelles, Nanocomposites and many more.

NANOTECHNOLOGY IN PHARMACEUTICALS:

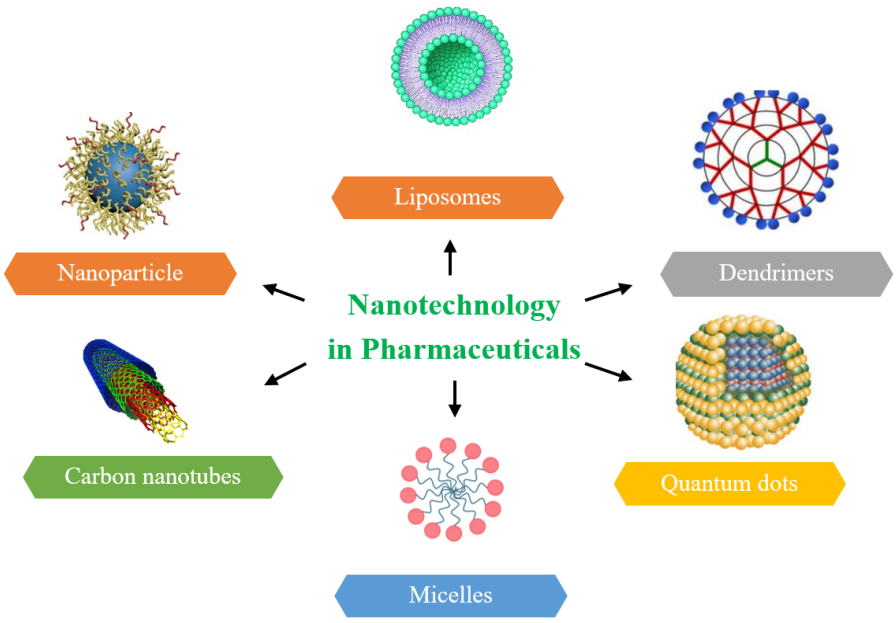


Figure 1: Different nanotechnology applications in pharmaceutical sciences.

Quantum dots:

Quantum dots are made up of semi-conducting material having improved optical properties having a semi-conductor core coated by a shell. Size of quantum dots ranges from 10-100A^0 in radius which gives them unique physical characteristics. Quantum dots are used in various techniques like in-vitro, in-vivo analysis, imagining, immunoassay, analysis of biomolecules, DNA hybridization and in non-viral vectors for gene therapy. Quantum dots are primarily used for labelling of cells and in cancer treatment as therapeutic tool. (6)

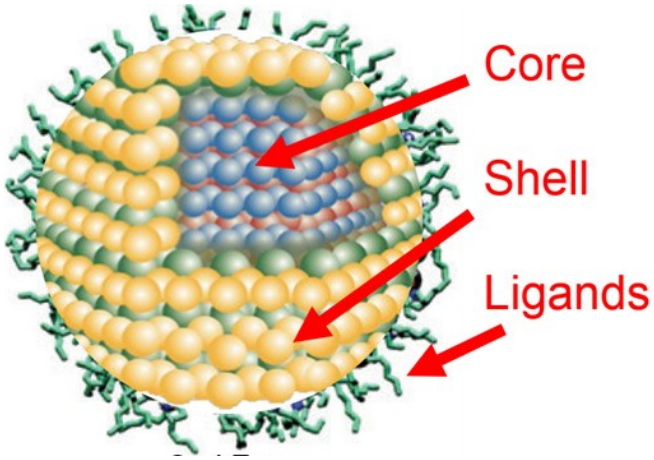
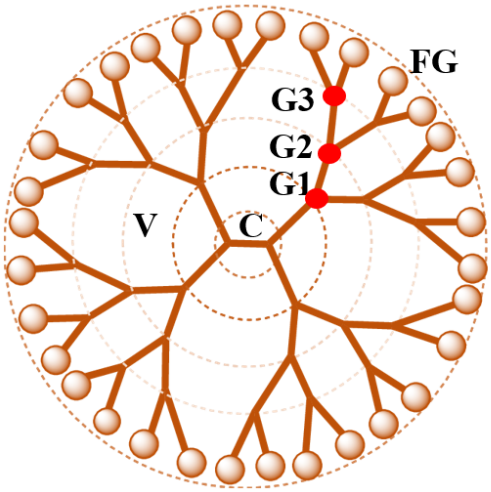


Figure 2: Basic structure of quantum dot

Dendrimers

Dendrimers are nanosized macromolecules having hyper-branched spherical structure and are extensively used for drug delivery system. In difference with traditional polymeric nano-vehicles, dendrimers have monodispersity and well recognized chemical structures. One of the advantages of dendrimer is due to specific structure, drugs can be loaded in dendrimer structure by either covalent conjugation or electrostatic adsorption. (7) Dendrimers is mainly made up of three parts, 1st part is a fundamental core consisting of single atom or group of atoms, 2nd part consists of building blocks of dendrimers called as generations attached to central core and 3rd part is functional groups present on surface of dendrimer. Dendrimer consist of huge void space in which drug molecules can be entrapped which helps in improvement in solubility of drug molecule.



C= Core, **G1**= First generation, **G2**= Second generation,
G3= Third generation, **V**= Void space, **FG**= Functional group

Figure 3: Basic structure of dendrimer

Dendrimers are typically manufactured by using two tactics. First technique known as divergent method in which dendrimers are constructed from core to border and in second method dendrimers are constructed from border to core and known as convergent method. [8] The peripheral functional groups may have positive, negative, and neutral charges depending upon which, appropriate dendrimer can be used for preferred drug delivery system. [9]

Carbon nanotubes:

sp^2 hybridized carbon have different structures. Graphite is well known example. Apart from graphite, carbon can form honeycomb like closed cages. Graphene is known as 2D single layer of graphite. Because of sp^2 hybridization graphene is stronger material than diamond which is sp^3 hybridized. Carbon nanotubes have generated interest in area of research in recent years. As name indicates carbon nanotubes are made up by rolling graphene into cylindrical form. [10] Diameter of these tubes in nano scale. Carbon nanotubes have many structures depending upon length, thickness, number of tubes rolled up and type of helicity. Depending upon number of tubes coiled to form tube, carbon nanotubes can be classified as single walled carbon nanotube (SWCTs) and multi walled carbon nanotube (MWCTs). Single walled carbon nanotubes have simple structure and can easily be twisted. These nanotubes have poor purity and less complex structure. SWCTs require catalyst for synthesis and diameter can is from 0.5 to 1.5 nm. MWCTs doesn't require any kind of catalyst for synthesis. These are more complex in nature, can't be easily twisted and have high purity. Diameter of MWCTs is up to 100 nm.

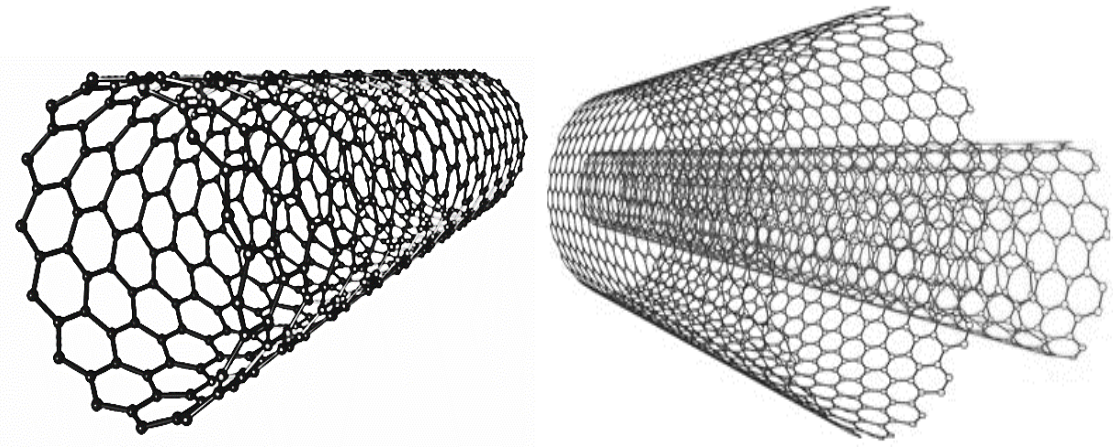


Figure 4: Single walled and multi walled carbon nanotubes.

Carbon nanotubes can be prepared by various techniques like arc discharge method also known as plasma-based synthesis method, chemical vapor deposition and laser method. These tubes have various applications like drug targeting to cancerous cell, for tissue generation, can act as bone substituent, for DNA delivery, for preservation of drugs which are easily oxidized, etc. [(11)]

Liposomes:

Liposomes are the vesicles which are made up of phospholipids and cholesterol having bilayers or multilayers surrounding an aqueous compartment. Aqueous as well as lipidic drugs can be entrapped within the liposome. Liposomes have discovered in 1960 and since then it has gained lot of attention in drug delivery because of its unique properties and have been used in delivery of various biologicals, anticancer drug as well as cosmetics. Liposomes are colloidal transporters, having a diameter of 0.01–5.0 μm. Liposomes have several advantages like increase in bioavailability of certain drugs, helps in drug targeting, biocompatibility, provide sustain release action, can be encapsulate to use biodegradable drug, can be administered through various route and helps to reduce toxicity of certain drugs. [(12)] Liposomes are of various types. Depending upon method of preparation, size, number of layers, composition liposomes are classified into different types. Based on upon number of layers present in liposomes they are classified as multilamellar vesicle (MLV), large unilamellar vesicle (LUV), small unilamellar vesicle (SUV). Based upon material from which liposomes are made, they are classified as conventional liposomes (CL), pH-sensitive liposomes, cationic liposomes, long circulating liposomes (LCL) and immuno-liposomes. Various methods are used for formulation of liposome such lipid film hydration, freeze drying, micro emulsification, sonication, French pressure cell, membrane extrusion, ethanol

injection, ether injection, double emulsification method, lyophilization, etc. [13] Liposomes have several applications in drug delivery like gene therapy, as carrier for vaccines, pulmonary drug delivery, topical drug delivery and ophthalmic drug delivery. [14]

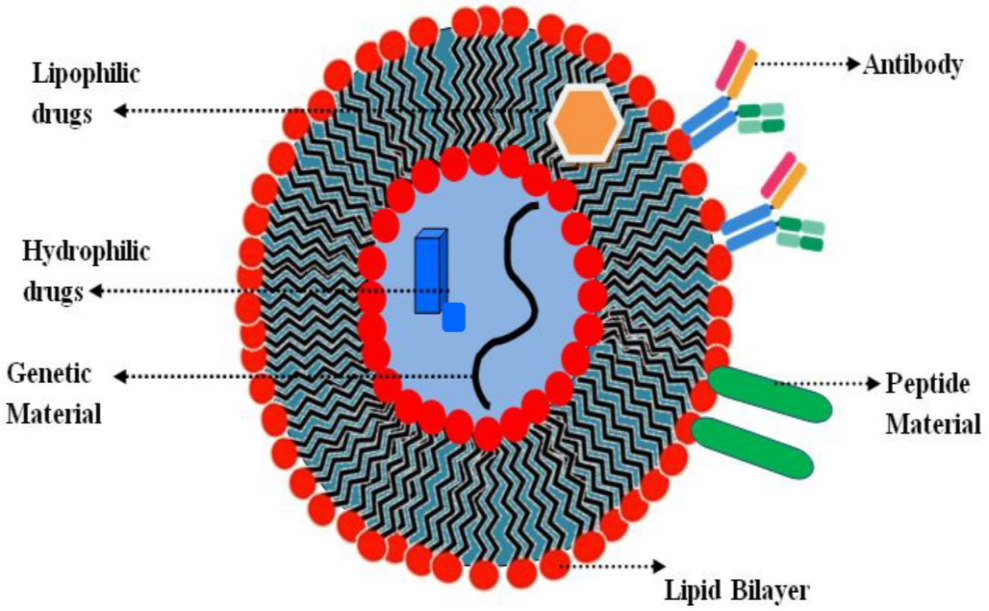


Figure 5: Structure of liposome

Polymeric nanoparticles:

Polymeric nanoparticles are synthetic nano sized colloidal particles having size range of 10 nm- 1000 nm. These nanoparticles have several advantages like biocompatibility, non-immunogenicity, non-toxicity and biodegradability. Nanocapsules and nanosphere are the two types of polymeric nanoparticles. In nanocapsules drug is present in central core surrounded by polymeric capsule and in nanospheres dug is dispersed throughout in polymeric matrix. Natural as well as synthetic polymers are used for preparation of polymeric nanoparticles. Natural polymers like gelatin, albumin and alginate while synthetic polymers like polyesters are used in preparation of nanoparticles. [15] There are various advantages of polymeric nanoparticles like active and passive targeting, control as well as sustain release of drug, high drug loading, can be administered by various routes. Various methods are used for manufacturing of nanoparticles like solvent evaporation method, solvent diffusion method, polymerization method, ionic gelation method and supercritical fluid technology. Various application of polymeric nanoparticles includes oral drug delivery of protein and peptides, delivery of genes and delivery of drugs to brain. [16]

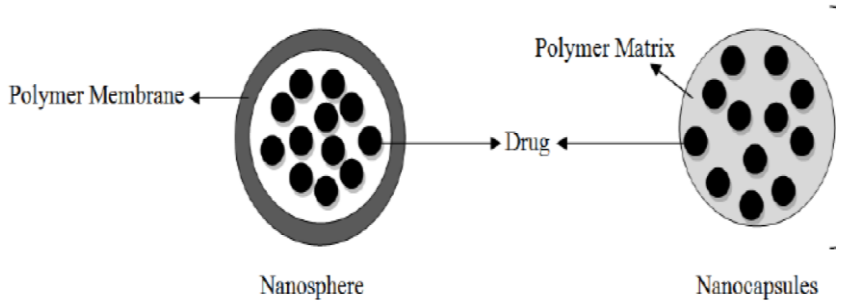


Figure 6: Polymeric nanoparticles

Metallic nanoparticles:

Metallic nanoparticles are majorly made up of silver and gold though other material can be used. Gold and silver nanoparticles are of prime importance. Metallic nanoparticles are used for drug delivery as well as biosensor. Large number of biomolecules like sugar, peptides, proteins and DNA can be linked to metallic nanoparticles and can be targeted. Biomolecules and ligands can be easily attached on the surface of metallic nanoparticles. Due to this unique ability of surface attachment of biomolecules, polymeric nanoparticles are used for active delivery of biomolecules, in bioassays, detection, imaging and many more other applications. Metallic nanoparticles have vast therapeutic applications like delivery of anti-infective agents, anti-angiogenic agents, anti-tumour agents, anti-leukaemia drugs and anti-rheumatoid drugs. [(17)]

Polymeric micelles:

Micelles are spherical structure where lipid molecules or polymers orient themselves in such a manner that hydrophilic end orient towards aqueous phase and lipophilic end towards oily phase. In polymeric micelles, amphiphilic end copolymers orient into nanoscopic supra molecular core shell structure known as 'polymeric-micelles'. Size of polymeric micelles is less than 100 nm. Hydrophilic surface of polymeric micelles protects them from nonspecific uptake by reticuloendothelial system. These micelles are used for systemic delivery of aqueous insoluble drugs. Drug molecules can be linked covalently to polymeric micelles or entrapped within hydrophobic core. Polymeric micelles have several advantages like have high loading capacity, stability in physiological conditions, slower rate of dissolution, high accumulation of drug at target site. [(18)]

Nanocomposites:

The word composite indicates any material made up of two or more different material. If among these materials any one material is in nano range then it is called as nanocomposite. Nanocomposite material have properties of all the material from which it is made.

Nanocomposite consist of one or more discontinuous phase dispersed through continuous phase. The continuous phase is called as matrix while discontinuous phase is called as reinforcing material. Nanocomposites have several advantages like uniform distribution of active component in matrix, sustain release of active ingredient, reduced frequency of administration and increase in stability. [19]

APPLICATIONS OF NANOTECHNOLOGY IN DRUG DELIVERY:

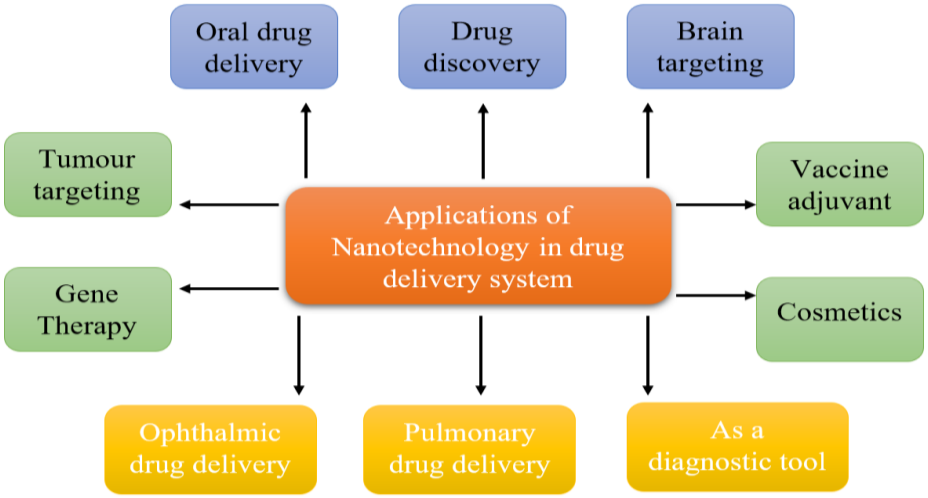


Figure 7: Different applications of nanotechnology

Tissue Engineering:

Nanotechnology has vast applications in tissue engineering. It can be used for tissue repair, as tissue replacement, generation of tissues, as surgical aids and in bone repair. Cells are surrounded by extra cellular matrix (ECM). ECM is natural nanofiber structure surrounding cell. This ECM provide cell support and decides cell behaviour. ECM also helps in activity of various biological factors. Successful generation of engineered biomaterial can be used as replacement of ECM which can be utilized for regeneration of tissues. (20) Tissue engineering of bones also require complex formation of cell types such as osteoblasts, osteoclasts and osteocytes. This complex environment can be created by application of carbon nanotubes. Multiwalled carbon nanotubes has been proven to produce bone repair. Also, carbon nanotubes can be utilised for cardiac tissue engineering. [21, 22]

Oral drug delivery:

Oral drug delivery remains one the prominent route of drug administration. It is oldest as well as commonest route of drug administration owing to its several advantages. However, this route fails to deliver certain category of drugs like water insoluble drugs, protein and peptides, drugs which gets destroyed by gastric environment. In such cases nanotechnology

can play a vital role. Drugs loaded in nanoparticles will be protected from gastric environment as well as solubility of such drugs can be increased which in turn increases the bioavailability. Also, protein and peptide delivery through oral route is possible by use of nanotechnology. [23]

Parenteral drug delivery:

In case of parenteral drug delivery nanosuspension is considered on of the best approach. Nanosuspensions increase solubility of aqueous insoluble drugs. [24] Nanosuspension can be targeted to particular site as well as sustain release effect can be obtained. Etoposide is an anticancer drug. Nanosuspension of etoposide was prepared with bovine serum albumin in order to reduce its toxicity and obtain drug targeting into lungs. [25]

Ocular drug delivery:

One of the disadvantages of drug delivery through ocular route is rapid precorneal elimination and drainage of dosage form. For increasing permeation of drug through cornea and reduce frequency of administration drug can be formulated in dosage form by using nanotechnology. There are many nanotechnology-based drug delivery systems such as liposomes, nanoparticles, nanosuspensions, polymeric colloids which are being tried for ocular drug delivery system. [26] Lai et. al. prepared liposomes of berberine hydrochloride and chrysophanol using third polyamide dendrimer. The prepared dendrimer showed effective use for ocular drug delivery system. [27]

Pulmonary drug delivery:

Size reduction of drug plays a vital role in improvement of drug efficiency. If drug is converted into nanopharmaceuticals then it an be directly targeted to lungs by mechanically intervention of capillary bed of the lungs. Different types of nano based formulations are utilised for pulmonary drug delivery such as beclomethasone lipid nanocarriers, budesonide solid lipid nanoparticles and liposomes, curcumin polymeric nanoparticles, indomethacin nanoparticles, fluticasone dried nanoparticles, amikacin liposomes, tacrolimus nanoparticles, etc. [28]

Brain targeting:

For targeting drugs to the brain, Blood Brain Barrier (BBB) plays an important role. [29] It creates a firm blockade between brain and molecules entering into blood. It prevents entry of potential toxic chemicals into brain but this also prevents entry of desired drug molecules into

brain. Nanotechnology can be used to overcome this hurdle. Nanopharmaceuticals can penetrate inside the brain along with drug.

Gene therapy:

Gene therapy is used for treatment of various genetic disorders like haemophilia, cystic fibrosis and tumours. Delivery of gene at desired site is still a herculean task. Genetic material is unstable and get easily destroyed by biological environment as well as genetic material fail to cross various biological membranes. Viral vectors are being utilised for delivery of genes conventionally. But major problem associated with viral vectors is that they may induce immunological response. [30] This problem can be overcome by using non-viral vectors such as liposomes, nanoparticles, nanocarriers, etc. genetic material can be encapsulated inside the carriers. PLA and PLGA nanoparticles can be effectively used for delivery of plasmid DNA. Chitosan, gelatine, poly-1-lysine and silica nanoparticles are used in gene therapy. [31]

Marketed preparations based on nanotechnology: [32]

Table-1: Marketed preparations based on nanotechnology

Nanosystem	Drug	Brand Name	Marketed by	Use
Nanoparticles	Paclitaxel	Pacliall	Panacea	Lung cancer
Liposome	Cytarabine	DepoCyt®	SkyePharma	Lymphomatous meningitis
Liposome	Amikacin	MiKasome	NeXstar Pharmceutical	Tuberculosis
DepoFoam	Aprepitan	Emend	Merck	Antiemetic
Nanoimplants	hydroxyApetite	Vitoss	Orthovita	BoneGraft
Crosslinked polyallylamine resin	Sevelamer hydrochloride	Renagel	Genzyme	Renal failure
Nanopowders	Zinc	clinical trial	Zincox	Sun screen
Nanogel	Metronidazole	Elyzol	Camurus	Dental
Lipid nanoemulsion	Cyclosporine A	Restasis®	Allergan	Ophthalmic
Liposomal DNA/Lipidic complex	Plasmid DNA	Allovectin -7	VICAL	Melanoma

CONCLUSION

Nanotechnology is the future of medicines. It has enormous potential as drug delivery system. It propositions novel apparatuses, openings and opportunities, which are projected to have a prodigious influence on countless zones in disease, diagnostics, prognostic and treatment of diseases through nano-engineered tools. Nanotechnology is used to deliver therapeutic and pharmacological agents. Desired properties of therapeutic agents can be enhanced by use of nanotechnology. Various nanotechnology-based formulations like liposomes, nanoparticles, solid lipid nanoparticles, polymeric nanoparticles, metallic nanoparticles, micelles, are being utilised for treatment of various disorders and diseases. To be precise nanotechnology holds a potential to solve majority of health-related problems.

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