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Nanostructures in Drug Delivery System

Sham V. Ingole*, Sumedh N. Moharil, Prajakta K. Bansod, Sohal A. Jadhav
D. R. G. College of Pharmacy, Malkapur, Dist.-Buldhana, Maharashtra, India

Review Article

***Corresponding author**
Sham V. Ingole

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Abstract: The technology used for to design, characterization and synthesis of smallest particulate system term as nano called nanotechnology and having diamension has monometer. Nanotechnology should not be viewed as a single technique that only affects specific areas. Advances in nanotechnology were utilized in medicine for therapeutic drug delivery and treatment for variety of diseases and disorders. The various type of Nanostructured Drug Delivery System are available like liposomes, Dendrimers, GNP, SLN, PN, MN, Metalic nanoparticles, CM, SM, ME and NE, NT, NC, NF, and QD etc. The reason review gives all details information about all the system which is important in Nanostructered Drug Delivery System. So it is advantege and gives reduce the doses required that type of advantage.

Keywords: Nanostructured Drug Delivery. Nanostured dosage forms.

INTRODUCTION

Nanotechnology is manipulation of matter on an atomic, molecular and super molecular scale. Eg- nanoparticles thus delivers chemotherapy drug directly to cancer cell are developed.

The technology used for to design characterization and synthesis of smallest particulate system learns as nano called nanotechnology and having dimension as nanometer. Various unique different surprice effects of atom and molecule is only by size which is nano.

Nanotechnology deals with the creation of useful materials, device and systems and systems through control of matter on the nanometer length scale and exploitation of novel phenomena and properties at that length scale. With advancements in nano science and technology, a large number of materials and improved products may be available with a change in the physical properties when their sizes are shrunk. Nanotechnology-based delivery systems can also protect drugs from degradation. These properties can help reduce the number of doses required, make treatment a better experience and reduce treatment expenses. The drug which are previously rejected due to their various properties, the drugs which having solubility problems and drug having administration problem are overcome of nano-system. e.g. paclitaxel. At present these systems are generally used for existing, fully developed off-patent drugs, the so called "low-hanging fruit" of nanotechnology-based delivery. Nanoparticles like polymeric nanoparticles, nanostructure lipid carriers, solid lipid nanoparticles, nanosensors, nano-devices, nano-emulsion, and all other involve in nanotechnology. Gold NPs and quantum dots (semiconductors) are the most widely used, but new materials are becoming available as more molecular entities are discovered as amenable to nanoscale design and fabrication. Crystal materials like those of gallium, phosphate, quartz, and ceramic are chosen for their durability and piezoelectric properties of developing and retaining an electric potential (charge) when subjected to mechanical stress. Another area of development is Nano biosensors, in which antibody based piezoelectric Nano biosensors are well developed. Nanoparticles take advantage of their dramatically increased surface area to volume ratio. Their optical properties become a function of the particle diameter. When brought into a new material, Nanoparticles can vastly influence the material, like stiffness or elasticity. The various products like commercial, household, engineered involve in technology, It's not a single technique, it's catch all the areas which is beneficial to humans.

Nanotechnology is a rapid expanding field, encamp-passing development of materials with 5-200 nanometers in size. It has a wide range of applications in the fields of engineering, medicine and life sciences. Advances in nanotechnology were utilized in medicine for therapeutic drug delivery and treatment for a variety of diseases and disorders. The drug is dissolved and entrapped into biodegradable nanoparticles which are specially designed to absorb drug and protecting it against chemical and enzymatic degradation. To achieve the site specify, designing of nanostructured

materials is a better from and it's a goal of a nanotechnology. In current years, several biodegradable polymeric nanostructures have attracted the notice with their inherent capacity to target particular organ/tissue to deliver the drug. The base revolution / development in pharma field is a versatility in drug delivery, targeting, tissue targeting, doses forms another etc. The present review details the recent developments of nanostructure drug delivery systems and their applications [1].

Types of Nanostructure Drug Delivery System

- Liposomes
- Dendrimers
- Gold nanoparticles
- Solid lipid nanoparticles
- Polymeric nanoparticles
- Magnetic nanoparticles
- Metalic nanoparticles
- Carbon material
- Silica materials
- Microemulsions and Nanoemulsions
- Nanotubes
- Nanocrystals
- Nanofibers
- Quantum dots

Liposomes

Liposomes have been the first to be investigated as drug carriers. They are nano/micro-particular or colloidal carriers, usually with 80–300 nm size range. They are spherical vesicles composed of phospholipids and steroids (e.g., cholesterol), bilayers, or other surfactants and form spontaneously when certain lipids are dispersed in aqueous media where liposomes can be prepared, e.g., by sonication. Liposomes have been reported to increase the solubility of drugs and improve their pharmacokinetic properties, such as the therapeutic index of chemotherapeutic agents, rapid metabolism, and reduction of harmful side effects and increase of in vitro and in vivo anticancer activity. A drug is incorporated in liposomes by the encapsulation process. The release of a drug from liposomes depends on the liposome composition, pH, osmotic gradient, and the surrounding environment. Modified liposomes are an interesting type of such lipid structures. The multifunctional liposomes, containing the specific proteins, antigens, or other biological substances, can be used to design drugs which act selectively on a particular tissue. It is a promising approach for targeted delivery of therapeutics. Biswas et al. presented hydrazine-functionalized poly-(ethylene glycol)-phosphatidylethanolamine (PEG-PE)- based amphiphilic polymer which can conjugate a variety of ligands. In addition, cationic liposomes (CLs) can be used as a gene delivery carrier. For gene transfer it is better than natural and anionic liposomes. Modified cationic liposomes were studied by kim and co-workers either by polyethylene glycol or PEG assing method as a transfection complexes or plasmid DNA. In a recent study, Biswas *et al.* have examined polyethylene glycol-phosphatidylethanolamine (PEG-PE) conjugate with the TPP group as drug carriers. They used paclitaxel (PTX) as a standard drug and studied them for their toxicity, mitochondrial targeting, and efficacy in delivering. As a result, they advised that TPPPEG- PE can be used as non-toxic, mitochondria targeted drug delivery systems. These liposomes are the most commonly used antimicrobial drug delivery system. Several procedures for the encapsulation of drugs into liposomes have been described. Preparation of drug loaded liposomes in size range that makes them vulnerable for a phagocytosis. These liposomes can be digested within the microphage's phagosome, thus releasing their drug contents. Opsonins and ligands that activate endocytosis in other cell types can also be incorporated into liposome membranes. One of the distinguishing features of liposomes is its lipid bilayer structure, which mimics cell membranes and can readily fuse with infectious microbes. By directly fusing with bacterial membranes, the drug can be released inside the directly bacteria [2].

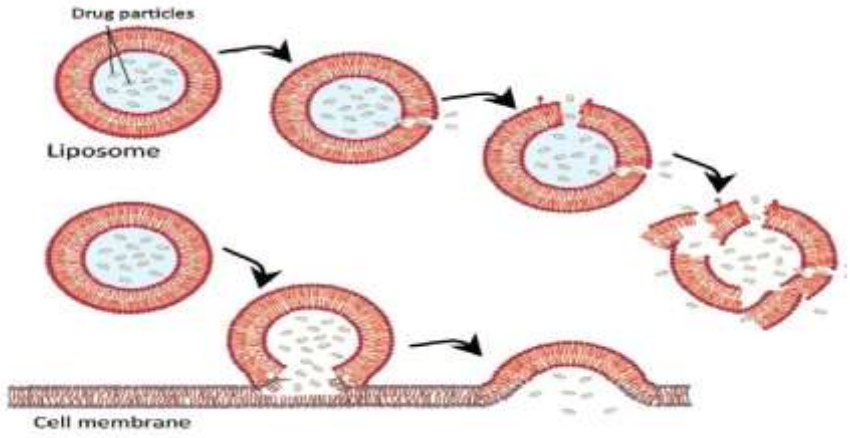


Fig-1: Liposomes

Dendrimers

Dendrimers are well-structured globular macromolecules. They consist of three regions: a core, layers of branched repeat units emerging from the core, and functional end groups on the outer layer of repeat units. The highly-branched nature of dendrimers provides large surface area to size ratio and allows great reactivity with microorganisms in vivo. Drug molecules can be included into dendrimersbyeithercomplexation or encapsulation. Both hydrophobic and hydrophilic agents can be loaded into dendrimers. Dendrimers are unique polymers with well-defined size and structure. Dendritic architecture is one of the most popular structures observed throughout all biological systems. Some of the examples of nanometric molecules possessing dendritic structure include: glycogen, amylopectin, and proteoglycans [16]. In the structure of dendrimer, in contrast to the linear polymer, the following elements can be distinguished: a core, dendrons, and surface active groups. A core is a single molecule having two identical functional groups where Dendron's are attached. The dendrons (dendrimer arms) are molecules of monomer linked with the core, forming layers and building successive generations (their growth is spatially limited). Biocompatibility and physicochemical properties of dendrimers are determined by surface functional groups. Dendrimers cytotoxicity depends on the core material and is strongly influenced by the nature of the dendrimers surface. For example, changing the surface amine groups into hydroxyl ones may result in lower levels of cytotoxicity. The term polyvalence defines the number of active groups on a dendrimers surface. The presence of several surface functional groups enables a simultaneous interaction with a number of receptors, thus, it enhances biological activity.

Dendrimers are synthetic, branched macromolecules with a well-defined chemical structure, consisting of an initiator core and multiple layers with active terminal groups Swami *et al*.

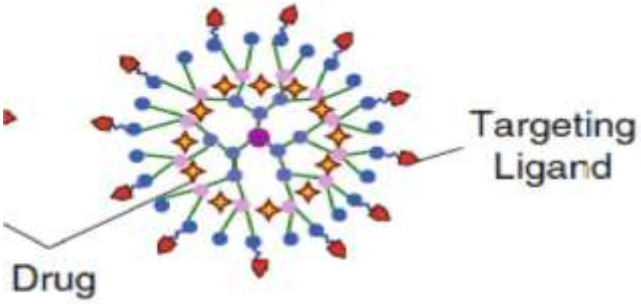


Fig-2: Dendrimers

Gold Nanoparticles

Gold nanoparticles were used for have some applications in drug delivery system. The loading of gold nanoparticles with drugs through covalent and non-covalent bonding offers increased therapeutic efficacy. The combination of gold nanoparticles and laser irradiation to control the release of drugs give useful therapeutic benefits. The gold nano-shell-antibody complex is broadly used in cancer treatment. The gold nanoparticles incorporated with have also shown a selective transportation of drugs to cancer cell nucleus specially when incorporated with RGDand PEG shows specific transportation of drug to cancer cell nucleus. When getting the tumor cells, they can induce hyperthermia using non-invasive radiofrequency [1].

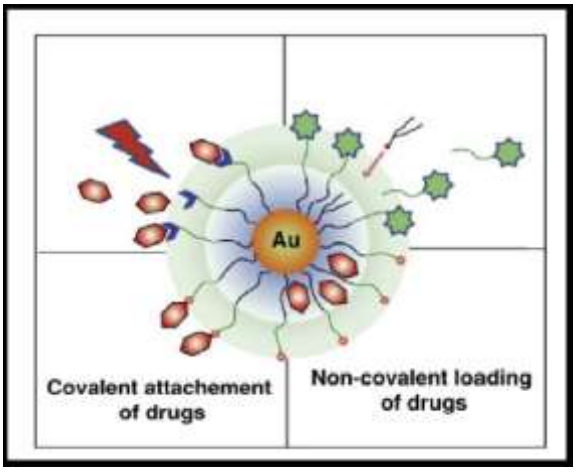


Fig-3: Goldnanoparticleswith drugs through covalent and non-covalent bonding

Solid Lipid nanoparticles

SLN is colloidal system or carrier it's lipid base system. Widely used lipids are palmitostearate, lecithin, triglyceride etc. They need high amount of surfactants for stability. They can be used by different routes like oral, topical or pulmonary and stable for a long period. Proteins and antigens intended for therapeutic purposes may be incorporated or adsorbed onto these nanoparticles and further administered by parenteral routes or by alternative routes such as oral, nasal and pulmonary. Application in anti-cancer and antiviral therapy show good results. Solid lipid nanoparticles can improve the ability of the drug to penetrate through the blood-brain barrier and is a promising drug targeting system for the treatment of central nervous system disorders. Because of entrapment of drug in solid lipid nanoparticles, permeability was enhanced 4-11 times than traditional delivery. Drugs like Indomethacin, Ketoprofen, Isoniazid and pyrazinamide has been reported to be targeted to the pulmonary system. Delivery of important peptides such as cyclosporine A, insulin, calcitonin and somatostatin have also currently under research.

SLN (solid lipid nanoparticles), NLC (nanostructured lipid carriers) and LDC (lipid drug conjugates) are types of carrier systems based on solid lipid matrix, i.e., lipids solid at the body temperature. They have been exploited for the dermal, peroral, parenteral, ocular, pulmonary, and rectal delivery. The main characteristics of SLN include a good physical stability, protection of incorporated drugs from degradation, controlled drug release, and good tolerability.

Disadvantage

Additionally, some disadvantages have been observed, such as low loading capacity (limited by the solubility of drug in the lipid and the structure and polymorphic state of the lipid matrix), drug expulsion after crystallization, and relatively high water content of the dispersions [1].

Polymeric nanoparticles

Polymeric nanoparticles (PNPs) are structures with a diameter ranging from 10 to 100 nm. The PNPs are obtained from synthetic polymers, such as poly-e-caprolactone, polyacrylamide and polyacrylate, or natural polymers, e.g., albumin, DNA, chitosan gelatin. Based on in vivo behavior, PNPs may be classified as biodegradable, i.e., poly (L-lactide) (PLA), polyglycolide (PGA), and non-biodegradable, e.g., polyurethane.

PNPs are usually coated with nonionic surfactants in order to reduce immunological interactions (e.g., opsonization or presentation PNPs to CD8 T-lymphocytes) as well as intermolecular interactions between the surface chemical groups of PNPs (e.g., van der Waals forces, hydrophobic interaction or hydrogen bonding).

Polymeric micelles have attracted substantial attention for their remarkable potential as therapeutic carriers. Polymeric micelles can be formed by selfassembly of amphiphilic polymers with two or more polymer chains of different hydrophobicity. In aqueous environments, these block copolymers can spontaneously self-assemble into core-shell nanostructures, with a hydrophobic core and a hydrophilic shell. In the various stages of clicles developments, several polymeric micells system on hences deposition of therapeutic agent at target site and reduce advese effects of therapeutic agent.

The conjugation of polymeric nanoparticles with targeting ligands could also enable drug delivery in a spatially and temporally controlled manner, which may further enhance the therapeutic efficacy of drugs and reduce their toxic side effects. Our group important for aptamer-targeted nanoparticles polymeric has been developed for cancer therapy. For example, we have developed A10 RNA aptamer-conjugated poly(lactide-co -glycolide)- poly(ethylene glycol) (PLGA–PEG) nanoparticles that can recognize PSMA (prostate-specific membrane antigen), expressed on the cancer cell surface.

Nanoparticles are advantageous in many ways since they use the unique micro-anatomy of the inflamed tissue blood capillaries, which have gaps between the linings of endothelial cells causing vessel leakiness. Moreover, they show high encapsulation efficiency and protection of instable drugs against degradation of the external environment in comparison to liposomes. Several methods have been described and nanoparticles can be obtained by polymerization of a monomer or from pre-formed polymers but recent methods make use of safe solvents with industrial application. Synthetic polymers from the ester family such as poly(lactic acid) (PLA), poly(cyanoacrylates) (PACA), poly(acrylic acid), poly(anhydrides), poly(amides), poly (ortho esters), poly(ethylene glycol), and poly(vinyl alcohol) (PVA) and other like poly(isobutylcynoacrylate) (PIBCA), poly(ethylene oxide) (PEO), poly(ε-caprolactone) (PCL) are suitable for drug delivery due to their biodegradability [3]

MAGNETIC NANOPARTICLES

Magnetic nanoparticles exhibit a wide variety of attributes, which make them highly promising carriers for drug delivery. In particular, these are: easy handling with the aid of an external magnetic field, the possibility of using passive and active drug delivery strategies, the ability of visualization (MNPs are used in MRI), and enhanced uptake by the target tissue resulting in effective treatment at the therapeutically optimal doses. Magnetic Nano-carriers shows difficulty to achieve appeared objectives. It is most likely

associated with improper features of magnetic nanoparticles or imperfect magnet system. Magnetic nanoparticles, for instance, tend to aggregate into larger clusters losing the specific properties connected with their small dimensions and making physical handling difficult. In turn, magnetic force may not be strong enough to overcome the force of blood flow and to accumulate magnetic drugs only at target site. Depending on magnetic properties, MNPs can be divided into pure metals (such as cobalt, nickel, manganese, and iron, their alloys and oxides. However, confining the area of MNPs applications only to biomedicine less significantly the choice of magnetic material. Such a restriction results from the lack of knowledge of the negative effects which the majority of these nanomaterials have on the human body. Iron oxide nanoparticles having good and acceptable features are approved by FDA. These attributes are: facile single step synthesis by alkaline co-precipitation of Fe2+ and Fe3+, chemical stability in physiological condition and possibility of chemical modification by coating the iron oxide cores with various shells, i.e., golden, polymeric, silage, or dendrimer. In addition, iron oxides – magnetite and magnetite – occur naturally in human heart, spleen and liver, which indicate their biocompatibility and non-toxicity at a physiological concentration. It is essential to estimate a safe upper limit of MNPs for biomedical use.

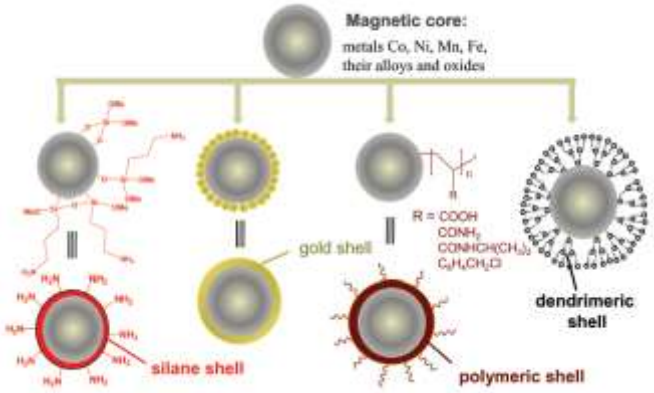


Fig-3: Magnetic nanoparticles with various shells

MNPs have been also tested as carriers for the treatment of in-stent thrombosis. Traditional thrombolytic therapy is associated with severe side effects, such as hemorrhagic complications. In order to eliminate these issues, a tissue plasminogen activator (tPA) – a protein involved in dissolving blood clots – was covalently coupled to salinized and chitosan-modified magnetic nanoparticles. The preliminary studies indicate that such conjugates can be useful in magnetically targeted lysis of in-stent thrombosis and can improve clinical aspects of thrombolytic therapy [2].

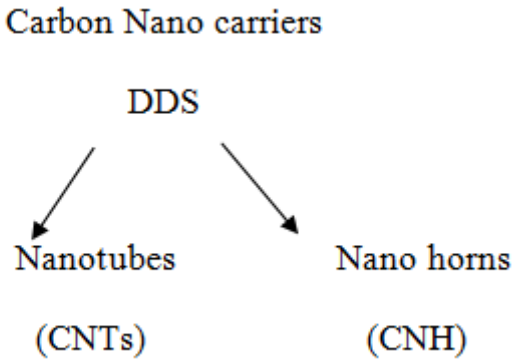
Drug	Therapeutic activity	Nanocarrier (core@shell)
Ciprofloxacin	Anti-infective agents (antibiotic)	Fe3O4@poly(vinyl alcohol)-*g*-poly(methyl methacrylate)
Gemcitabine	Antimetabolites, cancer chemotherapy	Fe3O4@poly(ethylene glycol)
Doxorubicin	Antineoplastic agent	Fe3O4@gelatin
5-Fluorouracil	Antimetabolites, anticancer drug	Fe3O4@ethylcellulose
Daunorubicin	Chemotherapeutic leukemia drug	Fe3O4
Anti-*b*-HCG monoclonal Antibody	Choriocarcinoma-specific gene vector	Fe3O4@dextran
Cisplatin	Chemotherapeutic drug	Fe3O4@poly *e*-caprolactone
Paclitaxel	Mitotic inhibitor used in cancer Chemotherapy	Fe3O4@poly[aniline-co-sodium *N*-(1-butyric acid)
1,3-Bis(2-chloroethyl)-1-nitrosourea (BCNU)	Anti-cancer chemotherapy drug	Fe3O4@poly[aniline-co-*N*-(1-butyric acid) aniline]
t-PA	Tissue plasminogen activator, thrombolytic therapy	Fe3O4@tetraethyl orthosilicate Fe3O4@chitosan

Metalic nanoparticles

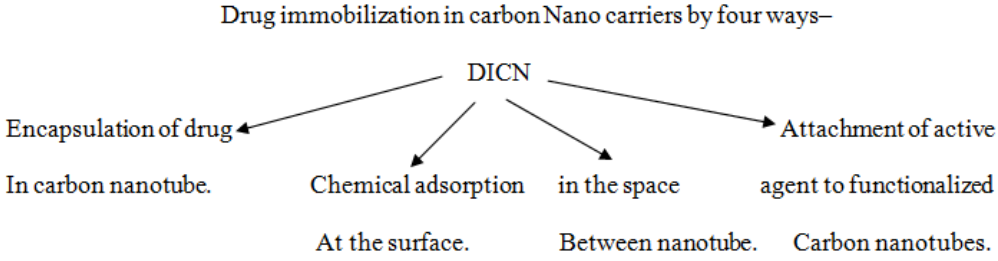
Inorganic nanoparticles have emerged a few years ago as drug and gene delivery systems, imaging agents and diagnostic biosensors. Magnetic drug targeting (such as the use of iron) is characterized by conjugating a magnetic material under the action of the external magnetic field, which can accumulate in target tissue areas under the action of the external magnetic

field. However, magnetic particles alone are not suited for drug vehicles because of limitations in the controlled release. A mixed composition of a magnetic nucleus and a polymeric shell could take advantage of the two components [3].

Carbon materials



CNTs are characterized by unique architecture formed by rolling of single (SWNCTs – single walled carbon nanotubes) or multi (MWCNTs – multi walled carbon nanotubes) layers of graphite with an enormous surface area and an excellent electronic and thermal conductivity. Biocompatibility of nanotubes may be improved by chemical modification of applications. The structure of MSNs enables the incorporation of both small and large molecules, adsorption of DNA, and gene transfer. This gives a possibility of using these nanomaterials in a combined therapy their surface. Such adjustment can be implemented by covalent anchoring of PAMAM dendrimers, amphiphilicdiblock copolymers, or PEG layers on CNTs surface or dispersion within a hyaluronic acid matrix. Due to their mechanical strength, SWCNTs have been used as a support to improve properties of other carriers, e.g., polymeric or non-polymeric composites.



Encapsulation has the advantage over the two remaining methods as the drug is protected from degradation during its transport to the cells and is released only in specific conditions. The examples of drugs that were attached to CNTs are listed in Table.

Type of nanotubes	Drug	Method of immobilization
MWCNTs	Cisplatin	Encapsulation via capillary forces
f-CNTs	Amphotericin B	Conjugated to carbon nanotubes
SWCNTs	Gemcitabine	Encapsulation
MWNTs	Epirubicinhydrocloride	Adsorption
MWCNTs@poly(ethylene glycol-b-propylene sulfide)	Doxorubicine	Adsorption
F –CNTS	Sulfamethaxazole	Adsorption
SWNTs-PL-PEG-NH2	Pt(lV) prodrug-FA	Covalent amide linkage
SWENTs	Cisplatin-EGF	Attachment to carbon nanotube via amide
MWCNTs	Dexamethasone	Encapsulation

Drug release from carbon nanotubes can be electrically or chemically controlled. To prevent the unwanted release of the drug, the open ends of CNTs were sealed with polypyrrole (PPy) films (94). Homing devices, i.e., folic acid and epidermal growth factor, were attached to improve selectivity of such drug

delivery systems. Nanohorns – single-wall nanotubes – give similar properties to nanotubes. Their formation process does not require a metal catalyst, thus, they can be easily prepared with very low cost and are of high purity. The immobilization of drugs may rely on adsorption on nanohornswallsor nanoprecipitation of drugs with Nano horns. A comparison of these two paths of cisplatinincorporationinto Nano horns showed that nanoprecipitations much more effective (almost 3 fold increase in the number of molecules entrapped in Nano horns) than adsorption. The toxicity of carbon nanomaterials also depends on their unique well-defined geometric structure. The toxic potential of carbon nanotubes can result from the high length to diameter ratio and the toxicity of the sole material, which is graphite. In addition, some impurities, such as residual metal and amorphous carbon, contribute to the level increase of reactive oxygen species (ROS), thus, inducing the oxidative stress in cells. Recent studies have pointed out the similarity in carcinogenic potential between CNT and asbestos. Carbon nanotubes have been shown to cause necrosis or apoptosis of macrophage cell lines and changes in cell morphology. Radomski *et al*. studied the effects of engineered carbon nanoparticles (MWCNT and SWCNT) on human platelet aggregation in vitro and rat vascular thrombosis in vivo. Incubation of platelets with carbon nanomaterials caused platelet aggregation with little or no granular release. Incubation of bronchial epithelial cells and keratinocytes with highdoses of SWCNT resulted in oxidative stress, including ROS generation, lipid peroxidation and mitochondrial dysfunction [2].

Silica materials

Silica gel mainly used in a controlled drug delivery system. It's classified into two classes-

- Xerogel
- Mesoporous silica nonoparticles

They exhibit several advantages as carrier systems, including biocompatibility, highly porous framework and an ease in terms of functionalization. Among inorganic nanoparticles, silica materials are the carriers which most often are chosen for biological purposes. Silica xerogels possess an amorphous structure with high porosity and enormous surface area. A porous structure (shape and pore dimensions) depends on synthesis parameters. Sol-gel technique is frequently used to form silica xerogels loaded with drugs. A modification of the synthesis conditions, such as the ratio of reagents, temperature, concentration of the catalyst, and pressure of drying, allows altering properties of xerogels used in controlled drug release. Phenytoin, doxorubicin, cisplatin, metronidazole, nifedipine, diclofenac, and heparin are examples of drugs which have been loaded into xerogels using this technique. The best known types of mesoporous silica nanomaterials are MCM-41 with a hexagonal arrangement of the mesoporous and SBA-15 with a well-ordered hexagonal connected system of pores. TheMSNs, in comparison with xerogels, possess more homogenous structure, lower polydispersity and higher surface area for adsorption of therapeutic or diagnostic agents. The mechanism loading of drug into mesoporous silica material is a physical or chemical adsorption. By these processes, diverse types of drugs, including anticancer drugs, antibiotics, and heart disease drugs, have been embedded into MNSs. The drug release is usually controlled by diffusion. The silicates and mesoporous silica nanoparticles potential application in photodynamic therapy has been also studied. The MSNs properties make them an excellent material for various pharmaceutical and biomedical applications.

Some data indicate that nano-sized silica particles (SNPs) are biocompatible and have a great potential for a variety of diagnostic and therapeutic applications in medicine. However, recent studies have revealed in vitro and in vivo toxicity and certain hazards of using Nano silica. Most of the in vitro studies of silica nanoparticles show the adverse effect in investigated cells. Cell type and nanoparticles size is important for effects which are investigated. Silica nanoparticles have an effect on a generation of oxidative stress in cells via formation of reactive oxygen species , elevated production of malondialdehyde, decreasing glutathione level, and induction of antioxidant enzymes, including superoxide dismutase (SOD) and hem oxygenase 1 (OH-1). All of these events are responsible for lipid peroxidation and cell membrane damage [2]

Micro emulsions and Nano emulsions

Micro- and Nano emulsions are isotropic mixtures of oil/ water stabilized by surfactants frequently in combination with co-surfactants. They have shown high solubilisation and dissolution properties, thermodynamic stability and the stabilizers prevent particle agglomeration and/or drug leakage. Thus, they have improved permeation enhancement ideal for transdermal delivery as they act in synergy. Micro emulsions may work by enhanced disruption of skin-lipid structure or by improving the stability of the drug in the formulation [3].

NANOTUBES

Nanotubes are self-assembling sheets of atoms in order in tubes. They can be classified into two common categories based on their structure: single walled carbon nanotubes (SWCNTs) with a single cylindrical carbon wall and multiwall carbon nanotubes (MWCNTs) with multiple walls cylinders nested within other cylinders. They have unique electronic, thermal, and structural characteristics and suggest a promising approach for drug delivery for cancer therapy. Carbon nanotubes are being hugely researched in the field of better and efficient drug delivery and bio sensing methods for disease treatment. These materials have shown potential in targeting specific cancer cells with a

dosage lower than conventional drugs used. Even though these are potentially promising candidates for pharmaceutical applications, the tolerance on human remains unidentified [1].

NANOCRYSTALS

Nanocrystals are aggregates of molecules that can be combined into a crystal form of drug surrounded via a thin coating of surfactant. These crystals are broadly used in materials research, chemical engineering, and in biological imaging, but comparatively less in nanomedicine for drug delivery. Nanocrystal line species are prepared using a hydrophobic compound coated with a thin hydro review on role of nanostructures in drug delivery system 115 philic layers. Chemical nature of hydrophilic coating important for biological reaction OR nanocrystals. This hydrophilic layer also aids in the biological distribution and bioavailability of the crystalline drug material. These factors combine to enhance the efficiency of overall drug delivery. In order to show their merits in vivo, these drug nanocrystals require being muscle into the right dosage form. Nano suspensions can be directly used as oral suspensions to overcome the difficulties of swallowing tablets by pediatric or geriatric patients [1].

NANOFIBERS

Nanofibers for drug delivery applications are prepared by electrospinning process. As a fibrous scaffold, nanofibers are able to entrap drugs with a large loading capacity and high encapsulation efficiency because of their low weight and inherent large surface to volume ratio. They have been designed as promising carriers for delivering anticancer drugs, especially in postoperative local chemotherapy using surgical implantation of the scaffold. This allows the encapsulation of bioactive molecules and protects them against enzymatic and hydrolytic degradation. For instance, it was found that insulin-loaded nanoparticles have preserved insulin activity and produced blood glucose reduction in diabetic ratsfor up to 14 days following the oral administration [1].

QUANTUM DOTS

Quantum dots are inorganic fluorescent semiconductor nanoparticle composed with 10 to 50 atoms 2-10 nm diameters. The achievement of using these quantum dots in biological imaging, sensing and detection has encouraged scientists to further improve this technology in other application of medicine. One of the most significant emerging applications is drug delivery. Quantum dots have potential for better treatment of cancer by targeted drug delivery systems. Apart from targeting of anticancer drugs, Quantum dots are also useful to deliver other biomolecules such as RNA. Due to concerns about long-term in vivo toxicity and degradation, quantum dots are currently limited to cell and small animal uses [1].

OTHER NANOTECHNOLOGIES FOR DRUG DELIVERY

Cyclodextrin nanosponges

Cyclodextrinnanosponges are complex networks of cross-linkedcyclodextrins cross-linked and formed into a roughly spherical structure, about the size of a protein, with channels and pores inside. The surface charge density, porosity and pore sizes of sponge can be controlled to attach different molecules. Nano sponges have been used for removal of organic impurities in water.

Drug carrying implantable thin films

These are nanoscale thin films that can be precisely controlled to release chemical agents by applying an electrostatic field. Hammond et al. reported the development of a thin film of approx. 150 nm thicknesses using a layer by layer approach. It is made up of the negatively charged material Prussian blue and a positively charged drug molecule, or a positively charged molecule enclosing a drug.

The advantages of the layer by layer approach include ease ofpreparation, versatility, capability of incorporating high loading of biomolecules into films, fine control over the structure, and robustness of the products under ambient and physiological conditions. The film can be implanted in the body and can carry discrete packets of drugs that can be released separately, which could be particularly useful for chemotherapy.

Nano suspensions & nanocrystals

Nano suspensions of an insoluble material stabilized by surfactant. Nano suspensions can be used to maintain these drugs in a preferred crystalline state of sufficiently small size for intravenous administration. Their advantages are similar to those of Nano emulsions. The solid nature of drug is highly loaded in it. Several studies have demonstrated the use of Nano suspensions for drug delivery with improved efficacy and release.

Nanogels

Nano gels are cross-linked nanoscale particles made of flexible hydrophilic polymers. They are soluble in water and allow spontaneous loading of drugs in aqueous media. The nanogelcollapses to form dense nanoparticles after adding the drug molecules. Large surface area, small size, allow to incorporate a molecule are the best qualities of angels. They have been used to incorporate drugs, DNA/RNA and inorganic molecules such as quantum dots. Nano gel particles comprised of PEG and polyethylenimine (>100nm) have been used to cross the blood-brain barrier (BBB) and deliver oligonucleotides to the brain. Nanogelshave also been used for pH-dependant release of doxorubicin and incorporation of an insoluble small molecule anticancer drug.

Nanodiamonds

Diamond nanoparticles or Nano diamonds have the capability for surface functionalization. This has been used to immobilise proteins and deliver drug molecules. Recently, Nano diamonds bound to doxorubicin were embedded into a polymer microfilm to achieve slow release of the drug over one month. This system could potentially be used for tumour patches. Fluorescent nanodiamondscan enter cells, and may have applications in cell tracking and imaging. The Nano diamond-insulin clusters hold promise for wound-healing applications and could be incorporated into gels, ointments, bandages or suture materials.

Nano emulsions

Nano emulsions can be defined as oil-in-water (o/w) emulsions with mean droplet diameters ranging from 50 to 1000 nm. Usually, the average droplet size is between 100 and 500 nm. Submicron emulsion (SME) / mini-emulsion are used as synonyms. Emulsions which match this definition mostly used in parenteral nutrition for a long time. Usually, SMEs contain 10 to 20 per cent oil stabilized with 0.5 to 2 per cent egg or soybean lecithin. Nano emulsions are dispersions of nanoscale droplets of one liquid within another. There are a number of high and low-energy methods of formation. Nano emulsions have a number of advantages over larger scale emulsions. They can be stabilised to increase the time before creaming occurs. They are transparent or translucent, and have a larger surface area due to the small particle size.

Nanocrystals

Nanocrystals are aggregates comprising several hundred to tens of thousands of atoms that combine into a "cluster". Typical sizes of these aggregates are between 10-400 nm and they exhibit physical and chemical properties somewhere between that of bulk solids and molecules. By controlling the size and surface area, other properties such as bandgap, charge conductivity, crystalline structure and melting temperature can be altered. The crystals must be stabilised to prevent larger aggregates from forming. Nanocrystals are produced by Nano sonication. First, a Nano suspension is formed by high speed stirring, followed by wet milling, high pressure homogenisation, Nano crystallisation and spray drying to create Nano sized crystals. The advantages of Nano crystallisation are the ability to solubilise poorly soluble drugs, high bioavailability, major decrease in dosage volume, and an increase in tolerated dose.

LIPID NANOCAPSULES (lncs)

These systems can be thought of as a cross between liposomes and Nano emulsion particles. Their outer wall is thicker than a traditional Nano emulsion particle allowing functionalisation and more controlled delivery. LNCs are composed of a liquid, oily core (medium-chain triglycerides) surrounded by hydrophilic and lipophilic surfactants. Stealth LNCs have also been synthesised using PEG to improve circulation time. LNCs have been used to deliver anticancer drugs LNCs have been used to deliver therapeutic molecules and radionuclides across the blood brain barrier by conjugation of antibodies or antibody fragments. Polymeric nanoparticles and liposomes send which their structure due to their oily core which is surrounded by a tensioactive rigid membrane. They have a lipoprotein-like structure. Their size can be adjusted below 100 nm with a narrow distribution.

Particle size for different nanotechnology techniques

Particle size range for different nanotechnology techniques are shown in Table.

Table-1: Particle size range for different Nanotechnology techniques

Techniques	Size range
Nanoparticle	10 to 1000 nm.
Liposomes	15 nm to several μm
Micelles	10-80 nm.
Solid Lipid Nanoparticle	50 nm to 1000 nm.
Nanoemulsion	50 to 1000 nm.
Lipid Nanocapsule	Less than 100 nm
Nanocrystals	10-400 nm
Carbon nanohorns	Less than 100 nm

Advantages of nanotechnology techniques

- Nanotechnology-based delivery systems can also protect drugs from degradation.
- Improved products may be available with a change in the physical properties when their sizes are shrunk.
- Reduce the number of doses required.
- Make treatment a better experience and reduce treatment expenses.
- Nano-based systems allow delivery of insoluble drugs.
- Allowing the use of previously rejected drugs or drugs which are difficult to administer.
- Drug targeting can be achieved by taking advantage of the distinct pathophysiological features of diseased tissues.
- An ideal targeting system should have long circulating time, it should be present at appropriate concentrations at the target site.

- It should not lose its activity or therapeutic efficacy while in circulation.
- Tumors allow an enhanced permeability and retention effect.
- Passive targeting of drugs to the macrophages present in the liver and spleen.
- Nanotechnology offers a solution for using the numerous chemical entities for treating brain disorders that are not clinically useful because of the presence of the blood-brain barrier.
- Improve the oral bioavailability of the agents that are not effectively used orally [1].

Challenges of nano drug delivery

Although nanotechnology in drug delivery has been successful, as evidenced by some nano drug products in the market, not all approaches have met with the same success. New nanomaterial being developed come with challenges which have to be surmounted. However some of the challenges encountered have been and are still being tackled by modification of the physicochemical characteristics of the nanomaterial to improve on properties such as long circulation in the blood, increased functional surface area, protection of incorporated drug from degradation, crossing of biological barriers and site-specific targeting. Despite the number of patents for Nano drug delivery technologies, commercialization is still at its early stage. This is Students due to the fact that most of the research studies in Nano drug delivery are carried out by researchers in academia. Therefore, for these technologies to get to the market there has to be increased partnership with the pharmaceutical companies.

Advances in nano drug delivery technology also give unic challenges for regulatory control. There is an increasing need to have regulations that would account for physicochemical and pharmacokinetic properties of nano drug products, which are different from conventional drug products. The United States' Food and Drug Administration (FDA) and the European Medicines Evaluation Agency (EMEA) have taken the initiative to identify some possible scientific and regulatory challenges.82 Furthermore, the International Organization for Standardization has set up a technical committee (TC 229) for the field of nanotechnologies to develop standards pertaining to terminology and nomenclature; measurement and characterization; and ealth, safety and environment amongst other standards. These standards are still under development [4].

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