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NANOTECHNOLOGY IN DEVELOPMENT OF DRUG DELIVERY SYSTEM

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ABSTRACT

Nanotechnology is science of matter and material that deal with particle size in nanometers. Nanotechnology has received a lot of attention with never-seen-before enthusiasm because of its future potential. It has provided fine lined diagnosis and focus treatment of disease at molecular level. This technology offers the advantage of protecting drugs from degradation; reduce the number of doses required. In this review, a discussion was carried out on different techniques for the preparation of nanodrug delivery systems like nanoparticles, solid lipid nanoparticles, nanocrystals, nanosuspensions, nanoemulsions. The concept of nanotechnology is widely expanded and applied to many drugs to the present. The ultimate application goal of nano drug delivery system is to develop clinically useful formulation for treating diseases in patients.

INTRODUCTION: Nanotechnology is science of matter and material that deal with the particle size in nanometers. The word' nano' is derived from latin word, which means dwarf ($1nm=10^{-9}m$). Nanomedicine deals with comprehensive monitoring, control, construction, repair, defense and improve human biological system at molecular level using engineered nanostructures and nanodevices.

Pharmaceutical nanotechnology embraces applications of nanoscience to pharmacy as nanomaterials, and as devices like drug delivery, diagnostic, imaging and biosensor materials. Pharmaceutical nanotechnology has provided more fine tuned diagnosis and focused treatment of disease at a molecular level. It helps in detecting the antigen associated with diseases such as cancer, diabetes mellitus, neuro degenerative diseases, as well as detecting the microorganisms and virus associated with infections. In pharmacy size reduction has an important application as drugs in the nanometer size range enhance performance in a variety of dosage forms.

Nanotechnology provides number of advantages in pharmacy by;

1. Increased surface area
2. Enhanced solubility
3. Increased rate of dissolution
4. Increased in oral bioavailability
5. Less amount of dose required & reduces the number of doses
6. Protection of drug from degradation
7. More rapid onset of therapeutic action
8. Achievement of drug targeting
9. Passive targeting of drugs to the macrophages present in the liver and spleen [1]

Some important Drug Delivery Systems developed using Nanotechnology Principles are:

1. Nanoparticles.
2. Solid lipid nanoparticles
3. Nanocrystals
4. Nanosuspensions
5. Nanoemulsions

Nanoparticles: Nanoparticles are defined as particles less: than 100nm in diameter that exhibit new or enhanced size-dependent properties compared with larger particles of the same material. These enable the drug with;

- Increased bioavailability Dose proportionality
- Decreased toxicity
- Smaller dosage form (i.e., smaller tablet) and stable dosage forms of drugs which are either unstable or have unacceptably low bioavailability in non-nanoparticulate dosage forms [2]

Preparation of Nanoparticles: Numerous methods are available for the manufacturing of nanoparticles. The choice of manufacturing method depends on the raw material intended to be used and on the solubility characteristics of the drug. The raw materials are selected depends on biocompatibility, degradation behavior, choice of administration route, desired release profile of the drug, the type of biomedical application.

These nanoparticles include nanospheres and nanocapsules. The difference between these forms lies in the morphology and body architecture. Nanocapsules are composed of a liquid core (generally an oil) surrounded by a polymeric membrane, whereas nanospheres are formed by a dense polymeric matrix.

Nanospheres are prepared by;

a) *In-situ* polymerization
b) Emulsion-evaporation method
c) Salting out method
d) Emulsification-diffusion method
e) Precipitation procedure
f) Precipitation solvent evaporation technique

a) ***In-situ* polymerization*:*** In *in-situ* polymerization, two different approaches are considered for the preparation of nanospheres.

   i. Emulsification polymerization
   ii. Dispersion polymerization.

i. **Emulsification Polymerization:** Incase of conventional emulsification polymerization the continuous phase is aqueous (o/w emulsion), where as in inverse emulsification polymerization the continuous phase is organic (w/o emulsion). In both cases the monomer is emulsified in non-solvent phase with surfactant molecules, leading to the formation of monomer-swollen micelles and stabilized monomer droplets. The polymerization reaction takes place in the presence of a chemical or physical initiator. The drug to be associated to the nanospheres may be present during polymerization or can be added to preformed nanospheres, so that the drug can be either incorporated in to the matrix or simply adsorbed at the surface of the nanospheres.

ii. **Dispersion Polymerization:** Incase of dispersion polymerization the monomer is no more emulsified but dissolved in aqueous medium. This method was developed for the production of very slowly biodegradable poly methyl methacrylate [PMMA] nanospheres.

In this method, water soluble methyl methacrylate monomers are dissolved in an aqueous medium and polymerized by gamma-irradiation or by chemical initiation combined with heating to temperatures above 65^0C. Thus oligomers are formed which may or may not be stabilized by surfactant molecules. Finally nanospheres are obtained by the growth or fusion of primary particles in aqueous phase. These poly (methyl methacrylate) nanospheres are suitable for vaccination purposes.

b) **Emulsification-evaporation procedure:** In this technique, the polymer is dissolved in chlorinated solvent e.g.; CH_2Cl_2, $CHCl_3$ and emulsified in an aqueous phase containing a surfactants like polysorbates, poloxamers, sodium dodecyl sulfate. Emulsification can be achieved by mechanical stirring, sonication or microfluidization (high pressure homogenization through narrow channels). The organic solvent is then removed under reduced pressure. Under these conditions, the organic solvent diffuses into the aqueous phase and progressively evaporates. Polylactic acid nanospheres are prepared by emulsification-evaporation for parenteral drug delivery [3].

c) **Salting-out Procedure:** In this method the use of potentially toxic solvents is avoided. Here only acetone is used and it can be easily removed in the final step by cross-flow filtration. The preparation method consists of adding, under mechanical stirring, an electrolyte saturated solution containing a hydrocolloid, generally poly (vinyl alcohol) as a stabilizing and viscosity increasing agent to an acetone solution of polymer. After the preparation of an oil-in-water emulsion, sufficient water or an aqueous solution of PEG is added to allow complete diffusion of acetone into the aqueous phase, thus inducing the formation of nanospheres.

d) **Emulsification-Diffusion Procedure:** This method is derived from the salting-out procedure, to overcome the problem of using large amount of salts in aqueous phase. Here, an aqueous gel of stabilizing hydrocolloid e.g Poly vinyl alcohol or gelatin is added to a solution of polymer dissolved in benzyl alcohol under mechanical stirring. Due to the partial miscibility of benzyl alcohol with water, a water-in-oil emulsion is obtained first.

The emulsion undergoes phase inversion upon complete addition of the aqueous gel. After complete diffusion of the organic solvent into the water, precipitation of the polymer occurs resulting in formation of nanospheres. Cytostatic drug chlorambucil as an active compound have shown a good over all weight yield (91%) and relatively high drug loading (8.5%) [3].

e) **Precipitation Procedure:** In this method, the polymer D, L-PLA (raceamic poly lactic acid) is dissolved in water-miscible solvent (acetone). Then, solution is poured under mechanical stirring into a non solvent (usually water containing a surfactant), which leads to precipitation of nanospheres.

f) **Precipitation Solvent Evaporation Technique:** This is an alternative method for producing nanospheres that avoids the use of chlorinated solvents. A non-solvent mixture of water and ethanol is added drop wise through a needle into a polymer solution, stirred by a magnetic stirrer, until turbidity, indicative of polymer precipitation is visually observed. The suspension of these preformed nanospheres is then added to an aqueous solution of Poly lactic acid-Poly ethylene glycol copolymer or poloxamine in order to coat the particles with hydrophilic molecules. Subsequently the suspension is agitated at ambient temperature to allow evaporation of solvents.

g) **Interfacial Polymerization** [4]: Nanocapsules are prepared by interfacial polymerization technique. In this technique, the alkyl cyano acrylate monomers and the drug, are dissolved in ethanol phase containing an oil, a phospholipid mixture or benzyl benzoate. This phase is slowly injected into water containing a non ionic surfactant (e.g., poloxamer 188) under magnetic agitation. Dispersion of the organic phase in the aqueous phase occurs simultaneously and leads to the formation of nanocapsules having an oily core and a polymeric shell.

Different types of Nanoparticles used for drug delivery include gold nanoparticles, magnetic nanoparticles, ceramic nanoparticles & protein nanoparticles.

Gold Nanoparticles [5]: Gold nanoparticles can provide effective carriers for biomolecules such as DNA, RNA, proteins and drugs, protecting these materials from degradation and transporting them across the cell-membrane barrier without effective toxicity.

Magnetic Nanoparticles (MNPs) [6]**:** These are a class of engineered particulate materials of < 100nm that can be manipulated under the influence of an external magnetic field. MNPs commonly composed of

magnetic elements such as iron, cobalt and their oxides like magnetite, maghemite, cobalt ferrite, and chromium dioxide. Applications of MNPs include targeted drug delivery, gene delivery cell separation and cell labeling.

Ceramic Nanoparticles [1]: Nanoparticles of silica, titanium, alumina etc. are normally called as ceramic nanoparticles. The advantages of ceramic nanoparticles are preparation is very simple and they are unaffected by change in pH or temperature.

Protein Nanoparticles [7]: Protein nanoparticles are biodegradable, non-antigenic, metabolizable and can also be easily amenable for surface modification and covalent attachment of drugs and ligands. The proteins used for the preparation of nanoparticles are albumin, gelatin, gliadin and legumin.

Solid Lipid Nanoparticles (SLNs): These are a new generation of submicron-sized lipid emulsions where the liquid lipid (oil) has been substituted by a solid lipid. SLNs offer unique properties such as small size, large surface area, high drug loading and the interaction of phases at the interfaces, and are attractive for their potential to improve performance of pharmaceuticals, Nutraceuticals and other materials.

Solid lipid nanoparticles provide the following advantages[8, 9]**:** 1) Control and target drug release 2) Improves the stability of pharmaceuticals 3)High and enhanced drug content when compared to other carriers 4) Feasibility of carrying both lipophilic and hydrophilic drugs 5) Water based technology 6) Easy to scale-up and sterilize 7) Good biocompatibility 8) Low toxicity 9) SLNs particularly those in the range of 120-200nm are not taken up readily by the cells of the reticulo endothelial system and thus bypass liver and spleen filtration.

Preparation of Solid-Lipid Nanoparticles [9]: SLNs are made up of solid lipid, emulsifier and water/solvent. The lipids used may be triglycerides, partial glycerides, fatty acids, steroids and waxes. Various emulsifiers and their combinations like pluronic F68, F 127 can be used to stabilize the lipid dispersion.

Different methods used to prepare the SLNs are:

I. High shear homogenization
II. Hot homogenization
III. Cold homogenization
IV. Ultrasonication/high speed homogenization
V. Solvent emulsification/evaporation f) Micro emulsion based SLNs preparations
VI. SLNs preparation by using supercritical fluid
VII. Spray drying method
VIII. Double emulsion method
IX. Hot homogenization followed by ultrasonication.

a. High Shear Homogenization: This technique was initially used for the production of solid-lipid nanodispersions. Dispersion quality is often compromised by the presence of microparticles. Lipids used in this study are tripalmitin, mixture of mono, di glycerides (witepsolW35) with glycerol behenate and poloxamer 188 as steric stabilizers (0.5% w/w). By using Witepsol W35 dispersions the best SLNs quality was obtained after stirring for 8min at 20,000 rpm followed by cooling for 10min and stirring at 5000 rpm at a room temperature.

b. Hot Homogenization [8]: In this method, lipid is melted to approximately 5^{o}C above its melting point, the drug is dissolved or solubilized in the melted lipid, and the drug containing lipid melt is dispersed in an aqueous surfactant solution of the same temperature. The obtained pre-emulsion is then passed through a high pressure homogenizer. The product of this process is hot o/w emulsion and the cooling of this emulsion leads to crystallization of the lipid and the formation of solid lipid Nanoparticles.

c. Cold Homogenization: In this method, drug is incorporated into melted lipid and the lipid melt is cooled upto solidification. Solid material is ground by a mortar mill. Obtained lipid microparticle is dispersed in a cold surfactant solution at room temperature or even at temperature distinctly below room temperature. The solid state of the matrix mimics partitioning of the drug to the water

phase. It has merit over cold homogenization since even during storage of the aqueous solid lipid dispersion, the entrapment efficiency remains unchanged.

d. Ultrasonication or High Speed Homogenization: In this method the SLNs are produced by high speed stirring or sonication. Bath and probe sonicators are used for production of SLNs. The main disadvantage of this method is physical instability like particle growth upon storage.

e. Solvent Emulsification/Evaporation Method: In this method, lipophilic material is dissolved in water immiscible organic solvent (e.g., cyclohexane) that is emulsified in an aqueous phase to give oil/water (o/w) emulsion. On evaporation of the solvent by reduced pressure, solid lipid nanoparticles dispersion is formed.

f. Microemulsion based SLNs preparation: A warm microemulsion is prepared by stirring, containing typically 10% molten solid lipid, 15% surfactant and upto 10% co-surfactant. This warm microemulsion is then dispersed under stirring in excess cold water (typical ratio 1:50) using thermostated syringe. The excess water is removed either by ultrafiltration or by lyophilization in order to increase the particle concentration.

g. SLN preparation by using Supercritical Fluid: This is a new technique for SLNs production. SLNs can be prepared by the rapid expansion of supercritical carbon dioxide solutions (Rapid Expansion of Supercritical Solution) method. Carbon di oxide (99.99%) was the good choice as a solvent for this method.

h. Spray Drying Method: It's an alternative procedure to lyophilization in order to transform an aqueous SLNs dispersion into a drug product. This method causes particle aggregation due to high temperature shear forces and partial melting of the particle.

i. Double Emulsion Method: It is used for the preparation of hydrophilic loaded SLNs. The drug is encapsulated with a stabilizer to prevent drug partitioning to external water phase during solvent evaporation in the external phase of w/o/w double emulsion.

j. Hot Homogenization followed by Ultrasonication [10]: Drug, triglyceride and lipid are dissolved in an organic solvent. Organic solvents are completely removed using a rotoevaporator. The drug-embedded lipid layer is melted by heating 5^0c above the melting point of the lipid. An aqueous phase is prepared by dissolving polymer in double distilled water and heating to the same temperature as the oil phase. The hot aqueous phase is added to the oil phase, and homogenization is performed using a homogenizer. The coarse hot-oil- in-water emulsion so obtained is ultrasonicated using a ultra homogenizer. Then SLNs are obtained by allowing the hot nanoemulsion to cool to room temperature.

Characterization of Nanoparticles and SLNs [2, 12]: Nanoparticles and SLNs are characterized for various parameters by different methods as shown in **table 1**.

TABLE 1: PARAMETERS AND METHODS FOR CHARACTERIZATION OF NANOPARTICLES AND SLNS

Parameter	Characterization method
Particle size/size-distribution	Photon correlation spectroscopy (PCS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), atomic force microscopy (AFM), scanning tunneling microscopy (STM), or freeze fracture electron microscopy (FFEM).
Charge determination	Laser Doppler anemometry, zeta potential meter.
Surface hydrophobicity	Water contact angle measurements, rose Bengal (dye) binding, hydrophobic interaction chromatography, X-ray photo, electron spectroscopy.
Chemical analysis of surface	Static secondary ion mass spectrometry sorptometer.
SLNs dispersion stability	Critical flocculation temperature.

Nanocrystals [13]: Drug Nanocrystals are crystals with a size in the nanometer range, which means they are nanoparticles with a crystalline character. A further characteristic is that drug nanocrystals are composed of 100% drug; there is no carrier material as in polymeric nanoparticles. Nanocrystals also possess

advantages of increased bioavailability and increase in saturation solubility.

Preparation of Nanocrystals: Basically, three methods are used for preparation of Nanocrystals;

a. Milling

b. Precipitation

c. Homogenization methods as well as a combination of the above

a. Milling Method: Bead or pearl mills are used to achieve particle size diminution. Milling media, dispersion medium, stabilizer and the drugs are charged into the milling chamber due to shear forces of impact, generated by the movement of the media, leads to particle size reduction.

b. Precipitation Method: In this method the drug is dissolved in a solvent and subsequently added to a non-solvent, leading to the precipitation of finely dispersed drug nanocrystals. A problem associated with this technology is that the formed nanoparticles need to be stabilized to avoid growth in micrometer crystals.

c. **Homogenization Method:** Three technologies are used for preparation of nanocrystals by homogenization methods which are microfluidizer technology, piston gap homogenization in water, piston gap homogenization in water mixtures or non aqueous media.

Characterization of Nanocrystals: Nanocrystals are characterized for various parameters by different methods as shown in **table 3**.

TABLE 2: PARAMETERS AND ITS METHODS FOR CHARACTERIZATION OF NANOCRYSTALS

Parameter	Characterization Method
Particle size and shape	Laser diffraction (LD), scanning electron microscopy (SEM)
Crystalline state evaluation	Differential scanning calorimetry (DSC),PXRD

Nanosuspensions: Pharmaceutical nanosuspension is defined as very finely dispersed solid drug particles in an aqueous vehicle. The particle size in nanosuspension ranges between 200 and 600nm. Dispersion of drug nanocrystals in liquid media leads to "nanosuspensions".

Dispersion media can be water, aqueous solutions or non aqueous media (e.g., liquid polyethylene glycol (PEG), oils).

Nanosuspensions possess advantages of [13]:

1) Increase in the dissolution velocity and saturation solubility of the drug
2) Improved biological performance
3) Ease of manufacture and scale-up
4) Long-term physical stability
5) Versatility
6) Increase in the oral absorption
7) Improved dose proportionality

Preparation of nanosuspensions: Two techniques are used for the preparation of nanosuspensions which are

a. Bottom-up technique by;

I. Microprecipitation,

II. Microemulsion

III. Melt emulsification.

b. Top- down technique by;

I. High pressure homogenization,

II. Milling method

a. Bottom up Technique: The bottom-up technology is an assembling method from which molecules to nano-sized particles are formed. Different preparation methods of these include as follows;

I. **Microprecipitation*:*** Similar to method discussed in Nanocrystals.

II. **Emulsion and microemulsion Method [14]:** Drug nanosuspensions by the emulsification method are prepared by;

a. Precipitation of particles by evaporating low–medium boiling point solvents with negligible water solubility

b. Quenching technique- using partially water-miscible solvents, such as benzyl alcohol and butyl lactate.

c. Extracting technique -using supercritical CO_2 (SC CO_2) as extraction agent. Such solvents are used as the dispersed phase of the emulsion to load the solute.

iii. **Melt Emulsification Method:** There are four steps in the production of nanosuspensions by melt emulsification method. Firstly, drug was added to aqueous solution containing stabilizer. Secondly, the suspension was heated above the melting point of the drug and homogenized with high-speed homogenizer to form an emulsion with melted liquid drug as the dispersed phase. Thirdly, it was transferred to a high-pressure homogenizer for homogenization. Finally, the emulsion was cooled at a suitable temperature and the drug particles precipitated and eventually formed the nanosuspensions.

b. Top down Technology: The top-down technology is a disintegration approach from large particles, microparticles to Nanoparticles by high pressure homogenization, milling method as explained previously.

Characterization of Nanosuspensions [15]: Nanosuspensions are characterized for various parameters by different methods as shown in table 4.

TABLE 3: PARAMETERS AND METHODS FOR CHARACTERIZATION OF NANOSUSPENSIONS

Parameter	Characterization method
Mean particle size and particle size distribution	Laser diffractometry (LD), photon correlation spectroscopy (PCS), microscope and coulter-counter
Surface charge (zeta potential)	Electro-acoustic technique
Crystalline state and morphology	X-ray diffraction analysis and supplemented by differential scanning calorimetry scanning electron microscopy (SEM), atomic force microscope or transmission electron microscopy (TEM)
Saturation solubility and dissolution rate	Paddle and basket methods (USP30) and film-dialysis

Nano Emulsions [16]: Nanoemulsions may be defined as oil-in-water (O/W), water- in-oil (w/o) emulsions with mean droplet diameters ranging from 50 to 1000nm. Usually, the average droplet size is between 100 and 500 nm. The particles can exist as water-in-oil and oil-in-water forms, where the core of particle is either water or oil, respectively.

Nanoemulsions provide number of advantages like

1. Higher surface area and free energy than macroemulsions that make them an effective transport system
2. Do not show the problems of inherent creaming, flocculation, coalescence, and sedimentation, which are commonly associated with macroemulsions.
3. These can be formulated in variety of formulations such as foams, creams, liquids, and sprays
4. These are non-toxic and non-irritant, hence can be easily applied to skin and mucous membranes
5. Since NEs are formulated with surfactants, which are approved for human consumption, they can be taken by enteric route
6. Do not damage healthy human and animal cells, hence are suitable for human and veterinary therapeutic purposes

Nanoemulsions are prepared by three methods:

a. High-pressure homogenization

b. Microfluidization

c. Phase inversion method.

a. High-Pressure Homogenization: This technique makes use of high-pressure homogenizer/ piston homogenizer to produce NEs of extremely low particle size (up to 1nm). This mehod is performed by applying a high pressure over the system having oil phase, aqueous phase and surfactant or co-surfactant. With this method only oil in water (o/w) liquid nanoemulsion of less than 20% oil phase can be prepared.

b. **Microfluidization:** For the preparation of nanoemulsion by microfluidization, the device called microfluidizer is used. The two solutions (aqueous phase& oily phase) are combined together and processed in an inline homogenizer to yield a coarse emulsion. The coarse emulsion is then passed into a microfluidizer where it is further processed to obtain a stable nanoemulsion. The coarse emulsion is passed through the microfluidizer until obtain the desired particle size. The bulk emulsion is then filtered through a filter under nitrogen to remove large droplets resulting in a uniform nanoemulsion.

c. **Phase inversion method:** In this method fine dispersion is obtained by chemical energy resulting of phase transitions taking place through emulsification path. The adequate phase transitions are produced by varying the composition at constant temperature or by varying the temperature at constant composition.

Characterization of Nanoemulsion: Nanoemulsions are characterized for various parameters by different methods as shown in **table 4**.

TABLE 4: PARAMETERS AND METHODS FOR CHARACTERIZATION OF NANOEMULSIONS

Parameter	Characterization method
Morphology	Transmission electron microscopy
Droplet size and size distribution	Photon correlation spectroscopy
Viscosity	Brookfield viscometer
Refractive index	Abbes type Refractometer
Thermodynamic stability of nanoemulsions	Heating cooling cycles, centrifugation, freeze thaw cycle

Some other new delivery systems developed by nanotechnology are [1];

Nanogels: Nanogels are cross-linked nanoscale particles made of flexible hydrophilic polymers. These are soluble in water. Nanogels possess large surface area, tuneable size and a network to allow incorporation of molecules. These are used to incorporate drugs, DNA/RNA and inorganic molecules such as quantum dots. These are also used for pH dependent release.

Nanoshells: A nanoshell comprises of a spherical core made from silica or other similar materials, surrounded by a coating of few nanometers thickness. The coatings comprise a metal such as gold or silver. In cancer applications, antibodies or other biomolecules are attached to the gold surface to target at tumor site.

Dendrimers: Dendrimers are unimolecular, monodisperse, micellar nanostructures with a well defined regularly branched symmetrical structure and a high density of functional end groups. Dendrimers contain three regions core, branches and surface. The first and most widely studied dendrimers are poly (amidoamino) (PAMAM) dendrimer.

The advantage of dendrimers is that they are similar in size to many proteins and biomolecules like insulin, cytochrome C and haemoglobin. These are effective against bacterial and viral infection. Dendrimers hybridized with chitosan have useful antibacterial properties as well as potentially acting as drug delivery agents.

Carbon nanotubes: Carbon nanotubes are hexagonal networks of carbon atoms, 1nm in diameter and 1-100nm in length. Two types of nanotubes are present i.e., single-walled nanotubes, and multi-walled nanotubes. The advantages of nanotubes are ultra-light weight, high mechanical strength, and high surface area. Due to their size and shape, carbon nanotubes can enter living cells without causing cell death or obvious damage. Carbon nanotubes have the ability to transport drug molecules, protein and nucleotides. Therapeutic applications of carbon nanotubes including boron neutron capture therapy (BNCT), inducing immunoresponse, gene and Si RNA delivery.

Carbon nanohorns: Carbon nanohorns have a structure similar to carbon nanotubes except they are closed at one end, forming a cone shaped cap, or horn.

Nanodiamonds: Also called diamond nanoparticles, used to immobilize proteins and deliver drug molecules. Fluorescent nanodiamonds can enter cells, and may have applications in cell tracking and imagining.

Cyclodextrin Nanosponges: Cyclodextrin nanosponges are complex networks of cross-linked cyclodextrins and formed into a roughly spherical structure, about the size of a protein, with channels and pores inside.

Drug carrying Implantable Thin Films: These are nanoscale thin films that can be precisely controlled to release chemical agents by applying an electrostatic field. The advantages are ease of preparation, versatility, and capability of incorporating high loading of biomolecules into films. 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.

Quantum dots: Quantum dots (QDs) are semiconducting materials consisting of a semiconductor core (CdSe), coated by a shell (e.g., ZnS). These are used as diagnostic tools, detection and analysis of biomolecules, immunoassays, DNA hybridization, and development of non-viral vectors for gene therapy, transport vehicles for DNA, protein, drugs or cells.

TABLE 5: SOME OF THE SELECTED DRUGS AS NANO DRUG DELIVERY SYSTEMS NANOPARTICLES

NANOPARTICLES			
Sl. No.	**Name of the drug**	**Purpose**	**Reference**
1	Clonazepam	To determine the drug loading capacity & drug release	Jae-Woon N *et al.*,[17]
2	Morphine	To study antinociceptive activity and blood brain delivery (by nasal route)	Didier B *et al.*,[18]
3	Adriamycin	To enhance effective delivery of Adriamycin	Lee K.Y *et al* [19]
4	Dexamethasone	To increase the amount of drug release with respect to pure drug	Maria G.C *et al* [20]
5	Tamoxifen	To increase the local concentration of tamoxifen in estrogen receptor positive breast cancer cells	Jugminder S.C *et al* [21]
6	Cyclosporin A	To form stable suspension of submicron particles of Cyclosporin A	Timothy J.Y *et al* [22]
7	Amoxicillin	To evaluate the effectiveness of amoxicillin in eradiating Helicobacter pyroli	Umamaheshwari R.B *et al* [23]
8	Ketoprofen	To outline the effects of interactions between a model drug and various acrylic polymers	Hannele E *et al* [24]
9	Praziquantel	To study the effect of formulation variables on size distribution	Rubiana M.M *et al* [25]
10	Glycyrrhetic acid	Encapsulation efficiency of GLA is increased.	Yongli Z *et al* [26]
11	Aspirin	Capable of releasing the drug in a slow sustained manner.	Saikat D *et al* [27]
12	Indomethacin	To enhance sustained releasecof IMC and delay clearance of IMC without significant effect on metabolism of IMC itself	So Yeon K *et al*[28]
13	Docetaxel	For effective delivery of drug to solid tumors	Mohamed.N. K *et al* [29]
14	Estradiol	To increase oral bioavailability of Estradiol. (oral)	Hariharn S *et al.*,[30]
15	Cyproterone	To improve skin penetration of the poorly absorbed drug Cyproterone (topical)	Jana S T *et al* [31]
16	Curcumin	For coating curcumin onto a metal stent by electrophoretic deposition thereby avoiding problem with restenosis after percutaneous coronary intervention	So Hee.N *et al*[32]
17	Ropivacaine	To decrease the systemic toxicity of ropivacaine	Carolina M M *et al.*, [33]
18	salbutamol suyate	The achieved size and shape of spray dried nanosized particles is suitable for the respiratory deposition in lungs (pulmonary inhalation)	Bhavna *et al* [34]
19	Didanosine	For sustained release of Didanosine	Amandeep. K *et al* [35]
20	Lamivudine	Increased bioavailability of lamivudine is observed when tested in AIDS patients.	Tamizharsi S *et al* [36]
21	Simvastatin nanocarriers	To enhance effective delivery of poorly water soluble drug simvastatin. (oral)	Amber V *et al* [37]
22	Doxorubicin	To improve oral bioavailability of Doxorubicin	Kalaria D.R *et al* [38]
23	Amphotericin B	To improve oral bioavailability and to show reduced nephrotoxicity compared to intravenous fungizone. (oral)	Italia J L *et al* [39]
24	Rifampicin	To formulate Rifampicin for aerosol delivery in a dry powder, which is suited for shelf stability, effective dispersibility and extended release with local lung and systemic drug delivery (pulmonary).	Jean C.S *et al* [40]
25	Naringenin	To enhance hepatoprotective effect in-vivo on oral administration. (oral)	Feng-Lin Y *et al* [41]
26	Curcumin	To enhance the transport of curcumin to brain and to enhance the delivery system to cross the BBB. (intravenous)	Min S [42]

27	Methazolamide calcium phosphate	Local treatment of glaucoma. (ocular)	Rui C *et al* [43]
28	Withferin A	For better drug administration	Haripriya S *et al* [44]
SOLID LIPID NANOPARTICLES			
29	Ubidecarenone	Immobilization of the drug molecules by the triglyceride lattice allows sustained release	Heike B *et al*[45]
30	Vinpocetine	To improve oral bioavailability of poorly soluble drugs &in treatment of various types of cerebrovascular circulatory disorders. (oral)	Yifan L *et al.,* [46]
31	Etoposide	For effective treatment of ETP-sensitive peritoneal carcinoma and peritoneal metastasis. (intraperitoneal)	Harivardhan Reddy L *et al* [47]
32	Isotretinoin	Treatment of severe acne & other dermatological diseases. (topical delivery)	Jie L *et al* [48]
33	Lovastatin	To improbe bioavailability of Lovastatin. (duodenal)	Suresh G[10]
34	Oridonin	Antitumour effect,Anti-inflammatoryAnti-bacteria especially esophageal carcinoma & prostate carcinoma.(subcutaneous in rats)	Kui kui R *et al*[49]
35	Itraconazole	Used to improve the therapeutic efficiency and reduction of toxicity and improve antifungal activity	Swrupananda M *et al* [50]
36	Cryptotanshinone	Increased bioavailability compared with that of o Cryptotanshinone suspension	Lian D H *et al* [51]
37	Mitoxanthrone	To study the distribution of the anti-cancer drug and its capability to deliver the drug precisely to the desired site	Alok M *et al* [52]
NANOSUSPENSIONS			
38	Aphidicolin	To improve drug targeting effect against Leshmania infected macrophages	Kayser .O [53]
39	Cloricromene	To improve stability of the drug and its availability at the ocular level.	Rosario P *et al* [54]
40	Buparvaquone	To enhance effectiveness if the drug in the treatment of Pneumocystis pneumonia. (pulmonary)	Norma H-K *et al* [55]
41	Retinoic acid	To attain controlled release and high saturation solubility of the drug	Zhang.X *et al* [56]
42	1,3-dicyclohexyl urea	To maintain DCU free plasma levels above the soluble epoxide hydrolase inhibitor. (oral I.V bolus & I.V infusion dosing)	Jan L.W *et al* [57]
43	Risperidone	To treat Psychotic disorders. (parenteral)	Muthu M.S *et al* [58]
44	Acyclovir	For prolonged release of drug & to increase bioavailability. (ocular)	Panchaxari D *et al* [59]
45	Atorvastatin	To enhance solubility of the drug	Arunkumar N *et al* [60]
46	Hesperetin	To enhance the effect of drug through dermal delivery	Prabhat R.M *et al* [61]
47	Meloxicam	To enhance the dissolution of the drug. (oral)	Ambrus.R *et al* [62]
48	Itraconazole	To increase aqueous solubility & dissolution & hence to increase oral bioavailability. (aerosols)	Shivanandh P *et al* [63]
49	Forskolin	To enhance antiglaucoma efficacy. (ocular)	Saurabh G *et al* [64]
50	Silyben	Increase in bioavailability and sustained drug release drug profile is observed. (oral & I.V)	Yancci W *et al* [65]
51	Miconazole	To increase bioavailability	Ana M.C *et al* [66]
52	Diclofenac	To enhance solubility of the drug. (intramuscular)	Amit R P *et al* [67]
53	Simvastatin	To enhance dissolution of the drug compared to suspension	Vikram.M.P *et al* [68]
54	Famotidine	To improve dissolution rate of the drug. (mucoadhesive)	Dhaval J.P *et al* [69]
NANOEMULSIONS			
55	Glycyrrhetinic acid	Used in cosmetic field as lenitive & anti-reddening agent. (transdermal)	Puglia C, *et al*[70]
56	B-Carotene	To prepare protein-stabilized B-carotene nano dispersion by emlsification evaporation method	Boon-Seang C *et al*[71]
57	Aceclofenac	To increase the anti-inflammatory effect compared with Aceclofenac gel. (transdermal)	Faiyah S *et al*[72]
58	Celecoxib	Selective cyclo oxygenase-2 inhibitor, used in transdermal arthritis & Osteoarthritis. (transdermal)	Faiyah S *et al* [73]
GOLD NANOPARTICLES			
59	Insulin	To improve the surface properties for binding of biomolecules which improves pharmacodynamic activity (transmucosal)	Devika R.B *et al* [74]
60	Levodopa,6-Mercaptopurine	To prevent uptake by the mononuclear phagocyte system and to allow penetration through the smallest pores of membrane. (using natural cellular motors)	Harsimran K *et al* [75]

NANOSPONGES			
61	Itraconazole	To increse the solubility of the drug many folds compared to plain drug	Shankar S *et al* [76]
62	Paclitaxel	To enhance oral bioavailability of paclitaxel. (oral)	Torne S J *et al* [77]

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