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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 established a lot of devotion with never seen-before eagerness because of its upcoming potential. It has delivered fine lined diagnosis and attention treatment of disease at molecular level. This technology compromises the improvement of protecting drugs from degradation; reduce the number of doses required. In this review, a discussion was passed out on different techniques for the preparation of nanodrug delivery systems like nanoparticles, solid lipid nanoparticles, nanocrystals, nanosuspensions, nanoemulsions. The idea of nanotechnology is widely prolonged and applied to many drugs to the present. The vital application goal of nano drug delivery system is to develop clinically useful formulation for treating diseases in patients.

KEYWORDS:

I. INTRODUCTION

DEFINITION

Nanotechnology can basically be defined as the technology at the scale of one-billionth of a metre. It is the design, characterization, synthesis and application of materials, structures, devices and systems by controlling shape and size at nanometre scale[1,2.] It is the capability to work at the atomic, molecular and supramolecular levels to create and employ materials, structures, devices and systems with basically new properties[3.] Scientifically, nanotechnology is engaged to describe materials, devices and systems with structures and components exhibiting new and expressively improved physical, chemical and biological properties as well as the phenomena and processes enabled by the ability to control properties at nanoscale[4.]

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=10-9m). Nanomedicine deals with widespread monitoring, control, construction, repair, defense and improve human biological system at molecular level using engineered nanostructures and nanodevices.

Pharmaceutical nanotechnology grasps applications of nanoscience to pharmacy as nanomaterials, and as devices like drug delivery, diagnostic, imaging and biosensor materials. Pharmaceutical nanotechnology has providing more modified diagnosis and intensive treatment of disease at a molecular level. It supports in detecting the antigen accompanying 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.

BENEFITS OF NANOTECHNOLOGY:

Based on its wide-ranging sectors of applications, nanotechnology has numerous benefits worldwide both indeveloped and developing countries:

1. Manufacture of new products and improvement on current products.

2. Availability of stronger, harder and lighter materials for construction and engineering.

3. Cleaner drinking water due to the making of filters that can entrap organisms and toxins.

4. Cleaner environment through remediation to remove pollutants from the environment

5. Enhanced healthcare by fabrication of devices and drug delivery systems for better monitoring, diagnosis and treatment of chronic diseases.

6. Development on transport systems

7. Cheaper and clean energy

NANOTECHNOLOGY OFFERS NUMBER OF ADVANTAGES IN PHARMACY BY

1. Improved surface area

2. Increased solubility

3. Improved rate of dissolution

4. Improved 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. Reaching of drug targeting

9. Passive targeting of drugs to the macrophages present in the liver and spleen [1]

IMPACT OF NANOTECHNOLOGY:

1. Nanotechnology a wide technological platform for a varying range of potential applications.

2. The basic level of organization of atoms and molecules at which functions for man-made products and living things are defined can be manipulated by nanotechnology.

3. Nanotechnology is interdisciplinary and so it reverses the trend of specialization in specific disciplines. Thus it participates all disciplines especially biomedicine, engineering and technology.

4. It has extended and changed manufacturing capabilities, which were more of bulk manufacturing, to include self-assembling and top-down approach.

5. The speed and scope of research and development have been influenced by nanotechnology such that regulators cannot meet up in assessment and environmental impact.

6. Due to the massive areas of applications of nanotechnology, a number of governments such as U.S., Japan, China and Europe have deemed it fit to invest in nanotechnology.

7. Nanotechnology is presently one of the main propellant for technological, economical change and industrial competitions[51]

SOME VITAL 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 reveal new or greater size-dependent properties compared with larger particles of the same material. These enable the drug with; Improved bioavailability, Dose proportionality, Reduced toxicity ,Lesser dosage form and stable dosage forms of drugs which are either unstable or have unacceptably low bioavailability in non-nanoparticulate dosage forms [2]

PREPARATION OF NANOPARTICLES: Several methods are available for the developed 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 contain 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 methods are considered for the preparation of nanospheres.

i. Emulsification polymerization

ii. Dispersion polymerization.

I. EMULSIFICATION POLYMERIZATION: In case 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, prominent 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 accompanying 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 established for the production of very slowly biodegradable poly methyl methacrylate [PMMA] nanospheres.

In this technique, 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. Lastlynanospheres 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 method, the polymer is dissolved in chlorinated solvent e.g.; CH2Cl2, CHCl3 and emulsified in an aqueous phase containing a surfactants like polysorbates, poloxamers, sodium dodecyl sulfate. Emulsification can be

completed 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 emulsificationevaporation for parenteral drug delivery [3].

C) SALTING-OUT PROCEDURE: In this technique the use of possibly 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 technique 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 technique 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 happens resulting in formation of nanospheres. Cytostatic drug chlorambucil as an active compound have shown a good overall weight yield (91%) and relatively high drug loading (8.5%) [3].

E) PRECIPITATION PROCEDURE: In this technique, 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 technique for producing nanospheres that circumvents 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: 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. [4]

GOLD NANOPARTICLES: Gold nanoparticles can offer effective carriers for biomolecules such as DNA, RNA, proteins and drugs, protecting these materials from degradation and transporting them across the cellmembrane barrier without effective toxicity. [5]

MAGNETIC NANOPARTICLES (MNPS): These are a class of engineered particulate materials of < 100nm that can be employed 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. [6]

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

PROTEIN NANOPARTICLES: 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 (SLN_S): These are a new group 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.[7]

SOLID LIPID NANOPARTICLES PROVIDE THE FOLLOWING ADVANTAGES:

1) Control and target drug release

2) Increases the stability of pharmaceuticals

3) High and greater drug content when compared to other carriers

4) Achievability of carrying both lipophilic and hydrophilic drugs

5) Water based technology

6) Easy to scale-up and sterilize

7) Good biocompatibility

8) Lesser 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. [8, 9]

PREPARATION OF SOLID-LIPID NANOPARTICLES: 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 approaches used to prepare the SLNs are:

a. High shear homogenization

b. Hot homogenization

c. Cold homogenization

d. Ultrasonication/high speed homogenization

e. Solvent emulsification/evaporation f) Micro emulsion based SLNs preparations

f. SLNs preparation by using supercritical fluid

g. Spray drying method

h. Double emulsion method

i. Hot homogenization followed by ultrasonication.

A. HIGH SHEAR HOMOGENIZATION: This method was firstly 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. [9]

B. HOT HOMOGENIZATION: In this technique, 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 technique, drug is merged 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 importance 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 technique the SLNs are produced by high speed stirring or sonication. Bath and probe sonicators are used for production of SLNs. The main drawback of this method is physical instability like particle growth upon storage.

E. SOLVENT EMULSIFICATION/EVAPORATION METHOD: In this technique, 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 using thermostated syringe. The additional 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 method 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 ansubstitute 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. [8]

J. HOT HOMOGENIZATION FOLLOWED BY ULTRASONICATION: Drug, triglyceride and lipid are dissolved in an organic solvent. Organic solvents are completely removed using a rotoevaporator. The drug inserted lipid layer is melted by heating 5^{0}c 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 aultra homogenizer. Then SLNs are obtained by allowing the hot nanoemulsion to cool to room temperature. [10]

CHARACTERIZATION OF NANOPARTICLES AND SLNs[2, 12]: Nanoparticles and SLNs are characterized for various parameters by different methods as shown in table 1.

NANOCRYSTALS: Drug Nanocrystals are crystals with a size in the nanometer range, which means they are nanoparticles with a crystalline character. A additional 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: Fundamentally, 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 technique 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. [13]

CHARACTERIZATION OF NANOCRYSTALS: Nanocrystals are characterized for various parameters by different methods as shown in table 2.

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).

NANOSUSPENSIONSHOLD ADVANTAGES OF:

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 methods 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 approaches of these include as follows;

I. MICROPRECIPITATION: Similar to method discussed in Nanocrystals. [13]

II. EMULSION AND MICROEMULSION METHOD: 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 CO2 (SC CO2) 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 highpressure 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. [14]

CHARACTERIZATION OF NANOSUSPENSIONS[15]: Nanosuspensions are characterized for various parameters by different methods as shown in table 3.

NANO EMULSIONS: 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 oilin-water forms, where the core of particle is either water or oil, respectively.

NANOEMULSIONS PROVIDE NUMBER OF ADVANTAGES LIKE

1. Greater 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 multiplicity 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 method 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 technique 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. [16]

CHARACTERIZATION OF NANOEMULSION: Nanoemulsions are characterized for various parameters by different methods as shown in table 4.

Some other new delivery systems developed by nanotechnology are;

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 ultralight 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.[17]

NANOTECHNOLOGY AREAS AND APPLICATIONS

Nanotechnology, being an interdisciplinary field, has three

main extensively overlapping areas: 1.Nanoelectronics,

2. Nanomaterials and

3. Nanobiotechnology which find applications in

A. Materials
B. Electronics
C. Environment
D. Metrology
E. Energy
F. Security
G. Robotics
H. Healthcare
I. Information Technology
J. Biomimetics
K. Pharmaceuticals
L. Manufacturing
M. Agriculture
N. Construction
O. Transport
P. Food Processing and Storage[1, 2, 4, 44-50.]

Table 6 Indicates some examples of nanotechnological applications.

TABLE 1: PARAMETERS AND METHODS FOR CHARACTERIZATION OF NANOPARTICLES AND SLNS[2, 12]

PARAMETER	CHARACTERIZATION METHOD
PARTICLE SIZE/SIZE-DISTRIBUTION	PHOTONCORRELATIONSPECTROSCOPY(PCS), TRANSMISSIONELECTRONMICROSCOPY(TEM),SCANNINGELEC TRONMICROSCOPY (SEM), ATOMICFORCEMICROS COPY (AFM), SCANNING TUNNELING MICROSCOPY (STM), ORFREEZEFRACTUREELECTRON MICROSCOPY (FFEM).
SURFACE HYDROPHOBICITY	WATERCONTACTANGLEMEASUREMENTS, ROSEBENGAL (DYE) BINDING, HYDROPHOBIC INTERACTION CHROMATOGRAPHY, X-RAY PHOTO, ELECTRON SPECTROSCOPY.
CHARGE DETERMINATION	LASER DOPPLER ANEMOMETRY, ZETA POTENTIAL METER.
CHEMICAL ANALYSIS OF SURFACE	STATIC SECONDARY ION MASS SPECTROMETRY SORPTOMETER.
SLNS DISPERSION STABILITY	CRITICAL FLOCCULATION TEMPERATURE.

TABLE 2: PARAMETERS AND ITS METHODS FOR CHARACTERIZATION OF NANOCRYSTALS[13]

PARAMETER	CHARACTERIZATION METHOD
PARTICLE SIZE AND SHAPE	LASERDIFFRACTION(LD), SCANNINGELECTRON MICROSCOPY(SEM)
CRYSTALLINE STATE EVALUATION	DIFFERENTIAL SCANNING CALORIMETRY (DSC),PXRD

TABLE3: PARAMETERSANDMETHODSFORCHARACTERIZATION OFNANOSUSPENSIONS[13]

PARAMETER	CHARACTERIZATION METHOD
MEANPARTICLESIZEAND PARTICLE SIZEDISTRIBUTION	LASERDIFFRACTOMETRY(LD),PHOTONCORRELATION SPECTROSCOPY (PCS), MICROSCOPE AND COULTER- COUNTER
SATURATIONSOLUBILITY AND DISSOLUTIONRATE	PADDLEANDBASKETMETHODS(USP30)ANDFILM-DIALYSIS
SURFACECHARGE (ZETAPOTENTIAL)	ELECTRO-ACOUSTIC TECHNIQUE
CRYSTALLINE STATE AND MORPHOLOGY	X-RAYDIFFRACTIONANALYSISANDSUPPLEMENTED BYDIFFERENTIALSCANNINGCALORIMETRYSCANNING ELECTRON MICROSCOPY (SEM), ATOMIC FORCE MICROSCOPE OR TRANSMISSION ELECTRON MICROSCOPY(TEM)

TABLE 4: PARAMETERS AND METHODS FOR CHARACTERIZATION OF NANOEMULSIONS[17]

PARAMETER	CHARACTERIZATION METHOD
MORPHOLOGY	TRANSMISSION ELECTRON MICROSCOPY
THERMODYNAMIC STABILITY OF NANOEMULSIONS	HEATING COOLING CYCLES, CENTRIFUGATION, FREEZE THAW CYCLE
DROPLET SIZE AND SIZE DISTRIBUTION	PHOTON CORRELATION SPECTROSCOPY

VISCOSITY	BROOKFIELD VISCOMETER
REFRACTIVE INDEX	ABBES TYPE REFRACTOMETER

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

NANOPARTICLES			
SL. NO.	**NAME OF THE DRUG**	**PURPOSE**	**REFERENCE**
1	CURCUMIN	TO ENHANCE THE TRANSPORT OF CURCUMIN TO BRAIN AND TO ENHANCE THE DELIVERYSYSTEM TO CROSS THE BBB. (INTRAVENOUS)	MIN S [42]
2	NARINGENIN	TO ENHANCE HEPATOPROTECTIVE EFFECT IN-VIVO ON ORAL ADMINISTRATION. (ORAL)	FENG-LIN Y *et al* [41]
3	RIFAMPICIN	TOFORMULATERIFAMPICINFORAEROSOLDELIVERYINADRYPOWDER, WHICHISSUITEDFORSHELFSTABILITY, EFFECTIVE DISPERSIBILITY AND EXTENDED RELEASE WITH LOCALLUNG AND SYSTEMIC DRUG DELIVERY (PULMONARY).	JEAN C.S *et al* [40]
4	AMPHOTERICIN B	TO IMPROVE OR ALBIO AVAILABILITY AND TO SHOW REDUCED NEPHROTOXICITY COMPARED TO INTRAVENOUS FUNGIZONE. (ORAL)	ITALIA J L *et al* [39]
5	DOXORUBICIN	TO IMPROVE ORAL BIOAVAILABILITY OF DOXORUBICIN	KALARIA D.R *et al* [38]
6	SIMVASTATIN NANOCARRIERS	TO ENHANCE EFFECTIVE DELIVERY OF POORLY WATER SOLUBLE DRUG SIMVASTATIN.(ORAL)	AMBER V *et al* [37]
7	LAMIVUDINE	INCREASED BIOAVAILABILITY OF LAMIVUDINE IS OBSERVED WHEN TESTEIN AIDS PATIENTS.	TAMIZHARSI S *et al* [36]
8	DIDANOSINE	FOR SUSTAINED RELEASE OF DIDANOSINE	AMANDEEP. K *et al* [35]
9	SALBUTAMOL SUYATE	THE ACHIEVED SIZE AND SHAPE OF SPRAY DRIED NANOSIZEDP ARTICLES IS SUITABLE FOR THE RESPIRATORY DEPOSITION IN LUNGS (PULMONARY INHALATION)	BHAVNA*ET al* [34]
10	ROPIVACAINE	TO DECREASE THE SYSTEMIC TOXICITY OF ROPIVACAINE	CAROLINA MM *etal.,*[33]
11	CURCUMIN	FOR COATING CURCUMINONTOAMETALSTENT BY ELECTROPHORETIC DEPOSITION THEREBY AVOIDING PROBLEM WITH RESTENOS IS AFTER PERCUTANEOUS CORONARY INTERVENTION	SO HEE. N *et al*[32]
12	CYPROTERONE	TO IMPROVE SKIN PENETRATION OF THE POORLY ABSORBED DRUG CYPROTERONE (TOPICAL)	JANA S T *et al* [31]
13	CLONAZEPAM	TO DETERMINE THE DRUG LOADING CAPACITY & DRUG RELEASE	JAE-WOON N *et al.,*[17]
14	ESTRADIOL	TO INCREASE ORAL BIOAVAILABILITY OF ESTRADIOL. (ORAL)	HARIHARN S *et al.,*[30]
15	DOCETAXEL	FOR EFFECTIVE DELIVERY OF DRUG TO SOLID TUMORS	MOHAMED.N. K *et al* [29]
16	INDOMETHACIN	TO ENHANCE SUSTAINED RELEASECOF IMC AND DELAY CLEARANCE OF IMC WITHOUTSIGNIFICANT EFFECT ON METABOLISM OF IMC ITSELF	SO YEON K *et al*[28]
17	ASPIRIN	CAPABLE OF RELEASING THE DRUG IN A SLOW SUSTAINED MANNER.	SAIKAT D *et al* [27]
18	GLYCYRRHETIC ACID	ENCAPSULATION EFFICIENCY OF GLA IS INCREASED.	YONGLI Z *et al* [26]
19	PRAZIQUANTEL	TO STUDY THE EFFECT OF FORMULATION VARIABLES ON SIZE DISTRIBUTION	RUBIANA M.M *et al* [25]
20	KETOPROFEN	TOOUTLINETHEEFFECTSOFINTERACTIONSBETWEENAMODELDRUGAN DVARIOUSACRYLICPOLYMERS	HANNELE E *et al* [24]
21	AMOXICILLIN	TOEVALUATETHEEFFECTIVENESSOFAMOXICILLININERADIATINGHELIC OBACTERPYROLI	UMAMAHESHWARI R.B *et al* [23]
22	CYCLOSPORIN A	TO FORM STABLE SUSPENSION OF SUBMICRON PARTICLES OF CYCLOSPORIN A	TIMOTHY J.Y *et al* [22]
23	TAMOXIFEN	TO INCREASE THE LOCAL CONCENTRATION OF TAMOXIFEN IN ESTROGEN RECEPTOR POSITIVEBREAST CANCER CELLS	JUGMINDER S.C *et al* [21]

24	DEXAMETHASONE	TO INCREASE THE AMOUNT OF DRUG RELEASE WITH RESPECT TO PURE DRUG	MARIA G.C *et al* [20]
25	ADRIAMYCIN	TO ENHANCE EFFECTIVE DELIVERY OF ADRIAMYCIN	LEE K.Y *et al* [19]
26	MORPHINE	TOSTUDYANTINOCICEPTIVEACTIVITYANDBLOODBRAINDELIVERY(BYNASALROUTE)	DIDIER B *et al.,*[18]
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	ITRACONAZOLE	USED TO IMPROVE THE THERAPEUTIC EFFICIENCY AND REDUCTION OF TOXICITY ANDIMPROVE ANTIFUNGAL ACTIVITY	SWRUPANANDA M *et al* [50]
30	CRYPTOTANSHINONE	INCREASED BIOAVAILABILITY COMPARED WITH THAT OF O CRYPTOTANSHINONE SUSPENSION	LIAN D H *et al* [51]
31	MITOXANTHRONE	TOSTUDYTHEDISTRIBUTIONOFTHEANTI-CANCERDRUGANDITSCAPABILITYTODELIVERTHEDRUG PRECISELY TO THE DESIRED SITE	ALOK M *et al* [52]
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	ANTITUMOUREFFECT,ANTI-INFLAMMATORYANTI-BACTERIA ESPECIALLY ESOPHAGEALCARCINOMA & PROSTATE CARCINOMA.(SUBCUTANEOUS IN RATS)	KUIKUI R *et al*[49]
35	UBIDECARENONE	IMMOBILIZATIONOFTHEDRUGMOLECULESBYTHETRIGLYCERIDELATTICEALLOWSSUSTAINEDRELEASE	HEIKE B *et al*[45]
36	VINPOCETINE	TOIMPROVEORALBIOAVAILABILITYOFPOORLYSOLUBLEDRUGS&INTREATMENTOFVARIOUSTYPES OF CEREBROVASCULAR CIRCULATORY DISORDERS. (ORAL)	YIFAN L *et al.,*[46]
37	ETOPOSIDE	FOR EFFECTIVE TREATMENT OF ETP-SENSITIVE PERITONEAL CARCINOMA AND PERITONEALMETASTASIS. (INTRAPERITONEAL)	HARIVARDHAN REDDY L *et al* [47]
NANOSUSPENSIONS			
38	MICONAZOLE	TO INCREASE BIOAVAILABILITY	ANA M.C *et al* [66]
39	DICLOFENAC	TO ENHANCE SOLUBILITY OF THE DRUG. (INTRAMUSCULAR)	AMIT R P *et al* [67]
40	SIMVASTATIN	TO ENHANCE DISSOLUTION OF THE DRUG COMPARED TO SUSPENSION	VIKRAM.M.P *et al* [68]
41	FAMOTIDINE	TO IMPROVE DISSOLUTION RATE OF THE DRUG. (MUCOADHESIVE)	DHAVAL J.P *et al* [69]
42	APHIDICOLIN	TO IMPROVE DRUG TARGETING EFFECT AGAINST LESHMANIA INFECTED MACROPHAGES	KAYSER .O [53]
43	CLORICROMENE	TO IMPROVE STABILITY OF THE DRUG AND ITS AVAILABILITY AT THE OCULAR LEVEL.	ROSARIO P *et al* [54]
44	BUPARVAQUONE	TO ENHANCE EFFECTIVENESS IF THE DRUG IN THE TREATMENT OF PNEUMOCYSTISPNEUMONIA. (PULMONARY)	NORMA H-K *et al* [55]
45	RETINOIC ACID	TO ATTAIN CONTROLLED RELEASE AND HIGH SATURATION SOLUBILITY OF THE DRUG	ZHANG.X *et al* [56]
46	MELOXICAM	TO ENHANCE THE DISSOLUTION OF THE DRUG. (ORAL)	AMBRUS.R *et al* [62]
47	ITRACONAZOLE	TO INCREASE AQUEOUS SOLUBILITY & DISSOLUTION & HENCE TO INCREASE ORALBIOAVAILABILITY. (AEROSOLS)	SHIVANANDH P *et al* [63]

48	FORSKOLIN	TO ENHANCE ANTIGLAUCOMA EFFICACY. (OCULAR)	SAURABH G *et al* [64]
49	SILYBEN	INCREASE IN BIOAVAILABILITY AND SUSTAINED DRUG RELEASE DRUG PROFILE IS OBSERVED.(ORAL & I.V)	YANCCI W *et al* [65]
50	1,3-DICYCLOHEXYL UREA	TO MAINTAIN DCU FREE PLASMA LEVELS ABOVE THE SOLUBLE EPOXIDE HYDROLASEINHIBITOR. (ORAL I.V BOLUS & I.V INFUSION DOSING)	JAN L.W *et al* [57]
51	RISPERIDONE	TO TREAT PSYCHOTIC DISORDERS. (PARENTERAL)	MUTHU M.S *et al* [58]
52	ACYCLOVIR	FOR PROLONGED RELEASE OF DRUG & TO INCREASE BIOAVAILABILITY. (OCULAR)	PANCHAXARI D *et al* [59]
53	ATORVASTATIN	TO ENHANCE SOLUBILITY OF THE DRUG	ARUNKUMAR N *et al* [60]
54	HESPERETIN	TO ENHANCE THE EFFECT OF DRUG THROUGH DERMAL DELIVERY	PRABHAT R.M *et al* [61]
55	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]
NANOSPONGES			
56	ITRACONAZOLE	TO INCRESE THE SOLUBILITY OF THE DRUG MANY FOLDS COMPARED TO PLAIN DRUG	SHANKAR S *et al* [76]
57	PACLITAXEL	TO ENHANCE ORAL BIOAVAILABILITY OF PACLITAXEL. (ORAL)	TORNE S J *et al* [77]
GOLD NANOPARTICLES			
58	INSULIN	TOIMPROVETHESURFACEPROPERTIESFORBINDINGOFBIOMOLECULES WHICHIMPROVES PHARMACODYNAMIC ACTIVITY (TRANSMUCOSAL)	DEVIKA R.B *et al* [74]
59	LEVODOPA,6-MERCAPTO PURINE	TOPREVENTUPTAKEBYTHEMONONUCLEARPHAGOCYTESYSTEMAN DTOALLOW PENETRATION THROUGH THE SMALLEST PORESOFMEMBRANE.(USINGNATURALCELLULAR MOTORS)	HARSIMRAN K *et al* [75]
NANOEMULSIONS			
60	GLYCYRRHETINIC ACID	USED IN COSMETIC FIELD AS LENITIVE & ANTI-REDDENING AGENT. (TRANSDERMAL)	PUGLIA C, *et al*[70]
61	B-CAROTENE	TOPREPAREPROTEIN-STABILIZEDB-CAROTENENANODISPERSIONBYEMLSI FICATIONEVAPORATIONMETHOD	BOON-SEANG C *et al*[71]
62	ACECLOFENAC	TOINCREASETHEANTI-INFLAMMATORYEFFECTCOMPAREDWITHACECLOFE NACGEL. (TRANSDERMAL)	FAIYAH S *et al*[72]
63	CELECOXIB	SELECTIVECYCLOOXYGENASE-2INHIBITOR,USEDINTRANSDERMALARTHRIT IS&OSTEOARTHRITIS.(TRANSDERMAL)	FAIYAH S *et al* [73]

TABLE 6: APPLICATIONS OF NANOTECHNOLOGY[1, 2, 4, 44-50].

NANOTECHNOLOGY AREA	APPLICATION
NANOMATERIALS	
ONE-DIMENSIONAL MATERIALS	THIN FILMS AND LAYERS USED IN WATERPROOF FABRICS AND ELECTRONICS. SURFACES IN FUEL CELLS AND AS CATALYSTS
TWO-DIMENSIONAL MATERIALS	INORGANIC NANOTUBES SUCH AS MOLYBDENUM DISULPHIDE FOR CATALYSIS AND ENERGY STORAGE. NANOWIRES SUCH AS SILICON NANOWIRES FOR DATA STORAGE, ELECTRONIC AND OPTOELECTRONIC DEVICES. CARBON NANOTUBES FOR SENSORS, ELECTRIC CURRENT TRANSMISSION AND ANTISTATIC PACKAGING. NANOTUBES AS CONTAINMENT FOR HYDROGEN IN HYDROGEN FUEL CELLS BIOPOLYMERS SUCH AS DNA MOLECULES
THREE-DIMENSIONAL MATERIALS	NANOPARTICLES EMPLOYED IN COSMETICS, TEXTILES, PAINTS, CATALYSIS AND DRUG DELIVERY. FULLERENES ARE CARBON MATERIALS WHICH ARE EMPLOYED AS LUBRICANTS, DRUG DELIVERY VEHICLES AND IN ELECTRIC CIRCUITS. DENDRIMERS ARE POLYMERIC MOLECULES USED IN COATINGS AND INKS, FOR DRUG DELIVERY AND ENVIRONMENTAL REMEDIATION BY TRAPPING METALS SUCH AS COPPER (II) WHICH IS THEN REMOVED BY ULTRA-FILTRATION.
NANOBIOTECHNOLOGY	
BIONANO-SENSORS	COMBINATIONS OF ENZYMES AND SILICON CHIPS IMPLANTED IN HUMANS OR ANIMALS TO MONITOR HEALTH AND ADMINISTER CORRECTIVE DOSES OF DRUGS.
BIOMIMETIC STRUCTURES	DIAGNOSIS OF DISEASES, MOLECULAR IMAGING AND DRUG DELIVERY
DRUG DELIVERY	NEW FORMULATIONS FOR DRUG AND GENE THERAPIES
TISSUE ENGINEERING	REPRODUCTION AND REPAIR OF DAMAGED TISSUES USING NANOMATERIAL- BASED SCAFFOLDS
NANOELECTRONICS	
INFORMATION AND COMPUTING	QUANTUM DOTS AND NANOWIRES IN CAMERAS AND PERSONAL COMPUTERS. NANOTUBES INSTEAD OF CATHODE RAYS IN TELEVISIONS. SEMI CONDUCTOR – SILICON NANOWIRES CONTAINING FUNCTIONING ELECTRONIC AND OPTICAL DEVICES.
SENSORS	NANOMATERIALS USED TO ASSESS THE QUALITY OF THE SOIL AND WATER, AND DETERMINE THE STATE OF PLANTS, FOOD AND OTHER PRODUCTS.

CONCLUSION:

Nanotechnology has latent applications in many sectors containing drug delivery ,paints and coatings, textiles and clothing, cosmetics, food science, catalysis, etc. In adding, nanotechnology presents new opportunities to improve how we measure, monitor, manage. Nanotechnology has developed as a rising and quickly changing field. New generations of nanomaterial will advance, and with them new and possibly surprising issues. Nanotechnology is the future of advanced

development. It is everything today from clothes to foods there are every sector in its range we should promote it more for our future and for more developments in our current life.

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