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PHARMACEUTICAL NANOTECHNOLOGY AND APPLICATION

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ABSTRACT

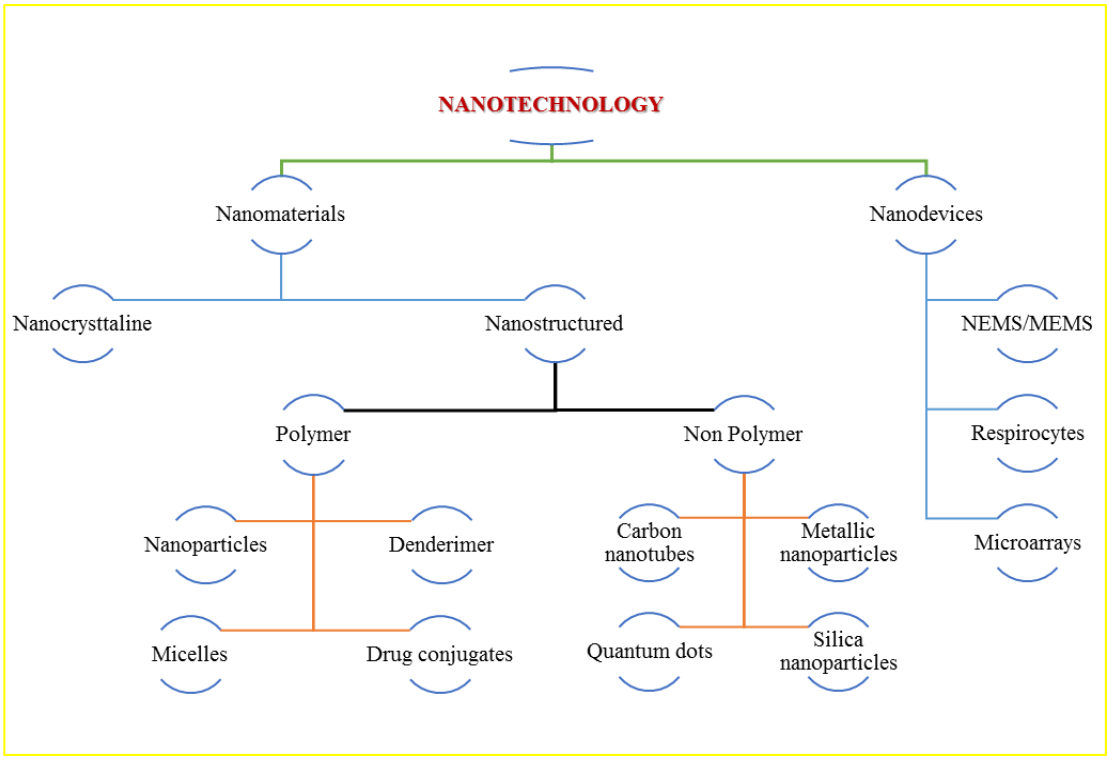
Size reduction is a fundamental unit operation having important applications in pharmacy. Nanotechnology is a field of applied science, focused on the design synthesis, characterization and application of materials and devices on the nanoscale. This branch of knowledge is a sub-classification of technology in colloidal science, biology, physics, chemistry and other scientific fields and involves the study of phenomena and manipulation of materials in the nanoscale. In this Review Article we Review about the Pharmaceutical Nanotechnology, by several angles, definition, techniques, we exhibiting some type of Nano-particles and Application.

Nano-Definitions

Nanoscience: can be defined as study of phenomenon and manipulation of materials at atomic and molecular scales. **Nanotechnology**: is related to design characterization, production and applications of structures, devices and systems by controlling shape and size at nanometer scale. **Pharmaceutical nanotechnology**: embraces applications of nanoscience to pharmacy as nanomaterials, and as devices like drug delivery, diagnostic, imaging and biosensor. **Nanomedicine**: is defined as submicron size (<1um) modules, used for treatment, diagnosis, monitoring, and control of biological system.[1]

General Introduction

Nanotechnology[16-17] is a field of applied science, focused on the design synthesis, characterization and application of materials and devices on the nanoscale. This branch of knowledge is a sub-classification of technology in colloidal science, biology, physics, chemistry and other scientific fields and involves the study of phenomena and manipulation of materials in the nanoscale. This results in materials and systems that often exhibit novel and significantly changing physical, chemical and biological properties due to their size and structure. In addition, a unique aspect of nanotechnology is the "vastly increased ratio of surface area to volume", present in many nanoscale materials, which opens new possibilities in surface-based sciences.[2]



Schematic diagram of various types of pharmaceutical nano-systems.

Nano-sized techniques

Size reduction is a fundamental unit operation having important applications in pharmacy. It helps in improving solubility and bioavailability, reducing toxicity, enhancing release and providing better formulation opportunities for drugs. In most of the cases, size reduction is limited to micron size range, for example, various pharmaceutical dosage forms like powder, emulsion, suspension etc. Drugs in the nanometer size range enhance performance in a variety of dosage forms. Major advantages of nano-sizing include (i) increased surface area,

(ii) enhanced solubility, (iii) increased rate of dissolution, (iv) increased oral bioavailability, (v) more rapid onset of therapeutic action, (vi) less amount of dose required, (vii) decreased fed/fasted variability, and (viii) decreased patient-to-patient variability.[1]

Bottom up Technologies

There are two basic approaches to produce drug nanosize, the bottom up[18] and the top down technologies.[3] In the bottom up processes, one starts from the molecule in solution, the molecules are aggregated to form particles, being crystalline or amorphous. There are various bottom up technologies.

Precipitation method

Sonocrystallization

Gas antisolvent recrystallization-GAS

Top Down Technologies

In the top down technologies, one starts from large crystals in the μm range and goes down to the nano dimension by diminuting the crystals. There are several top down technologies:

Media Milling

High Pressure Homogenization methods

Microfluidization (IDD-P™ technology)

Piston-gap homogenization

Nanopure® Technology

Combination Technologies

Nanoedge® Technology

Rapid expansion from a liquefied-gas solution (RESS)

Other Methods

1. ***Spray drying***[4]

Comparison of the advantages and disadvantages of different nano-formulations.[5]		
Nano-formulations	**Advantages**	**Disadvantages**
Nano-crystals	Established manufacturing techniques Good reproducibility with large-scale production Good compatibility with drugs having different solubility profiles Fast dissolution rates Excellent for oral formulations	High-energy input Require stabilizers Not suitable for cytotoxic drugs with small therapeutic indices Lack of controlled release Not ideal for intravenous administration
Nano-emulsions	High drug-loading content	Potential flocculation and

	Suitable for various administration routes Approved pharmaceutical ingredients Low-cost productions	coalescence Lack of controlled release Poor blood stability
Polymeric micelles	Excellent blood stability Passive and active targeting to tumors Controlled release functions Multifunctional design Suitable for intravenous administration	Limited number of polymers for clinical use Concerns over nano-toxicity Concerns over storage stability

Some Nanoparticles

Drug Nano-crystals

Drug nano-crystals are pure solid drug particles with a mean diameter below 1000 nm. A nano-suspension consists of drug nano-crystals, stabilizing agents such as surfactants and/or polymeric stabilizers, and a liquid dispersion medium. The dispersion media can be water, aqueous solutions, or non-aqueous media. The term. Drug nano-crystals. Implies a crystalline state of the discrete particles, but depending on the production method they can also be partially or completely amorphous. Drug nano-crystals have to be distinguished from polymeric nano particles, which consist of a polymeric matrix and an incorporated drug. Drug nano-crystals do not consist of any matrix material.[6]

Gold and Silver Nanoparticles

Silver nanoparticles synthesized through the reduction of $AgNO_3$ using $NaBH_4$. The borohydride anions adsorbed onto silver nanoparticles. The repelling forces of the borohydride anions prevented the aggregation of particles, but the addition of an electrolyte or agitation induced aggregation. The silver nanoparticle sol that, using a spectrophotometer, had Plasmon resonance at 386 nm gave off a yellow hue. The silver nanoparticles estimated to be 10 to 20 nm in diameter. Gold nanoparticles synthesized through the reduction of $HAuCl_4$ using $Na_3C_6H_5O_7$. The gold nanoparticle sol gave off a red hue that had Plasmon resonance at 515 nm. The gold nanoparticles estimated to be 10 to 25 nm in diameter.[7]

Nano-gels

Gelatin is obtained from the breakdown and hydrolysis of collagen, obtained from the connective tissues, bones and skins of animals. It is a known matrixing agent drug delivery. to describes a process for the controlled release of sulphamethoxazole used 2 different gelatin nano-particles {Type A (porcine skin) and type B gelatin(bovine skin)} and cross linked with gluteraldehyde; Nano-particles of varying gelatin concentrations were prepared by solvent

evaporation techniques and drug release kinetics evaluated using appropriate kinetic models. Findings from this system suggest that this system could be of use in targeted drug delivery such as colon drug delivery where pH is an important consideration. Drug release was found to increase following increased swelling of the nanoparticles.[8]

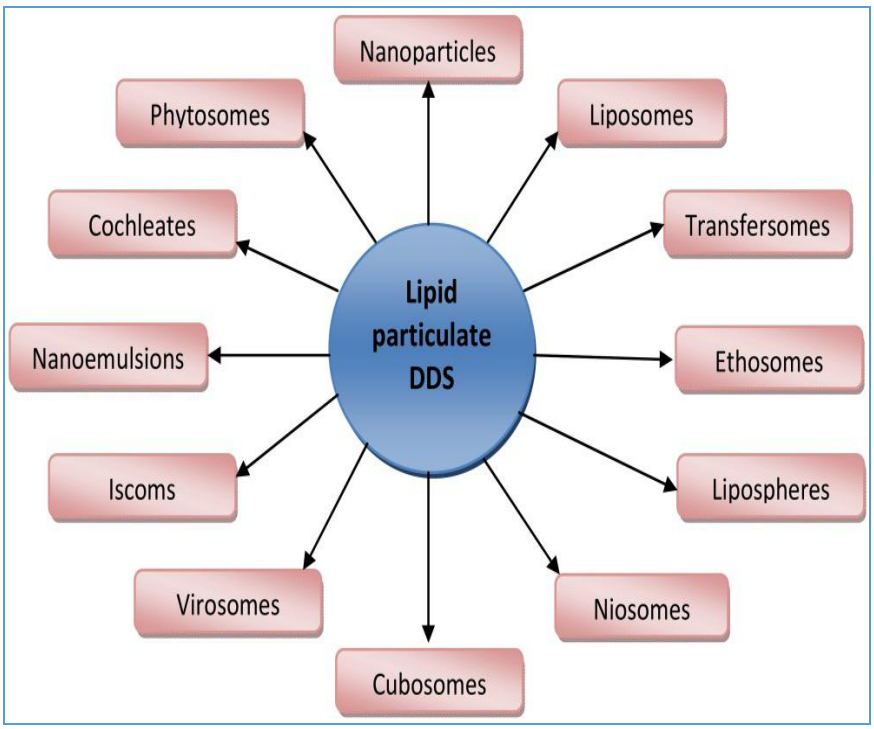
Vesicular phospholipid gels (VPGs) contain aqueous compartments both within the core of the vesicles as well as in-between the vesicles, can be loaded with hydrophilic, amphiphilic, and lipophilic drugs in different ways, retain a constant drug load within the core of the vesicles during long-term storage because there is no concentration gradient between the vesicles' core and surrounding water phase, release drugs in a controlled manner over extended periods of time, and can be transferred into ''conventional'' small-sized liposome (SUV) dispersions adding excess aqueous medium and gentle mechanical agitation shortly before use. Under appropriate conditions, the preformed vesicles remain intact during this dilution process and retain their drug load: 1. Thus, drugs can be entrapped into SUVs with an unusually high efficiency. 2. A high ratio of entrapped to un-entrapped drug may render removal of free drug unnecessary. In this case, diluted VPGs represent dual-drug formulations. They contain free and liposomally entrapped drug at a defined ratio.[9]

Drug-Delivery Systems

Nano-particulate drug-delivery systems (NPDDSs) can be defined as the Drug-Delivery Systems (DDSs) where nanotechnology is used to deliver the drug at nanoscale. Below 100 nm, materials exhibit different, more desirable physical, chemical, and biological properties. Given the enormity and immediacy of the unmet needs of therapeutic areas such as CNS disorders, this can lead to drugs that can extend life and save untimely deaths An ideal drug-delivery system possesses two elements: the ability to target and to control the drug release. Targeting will ensure high efficiency of the drug and reduce the side effects, especially when dealing with drugs that are presumed to kill cancer cells but can also kill healthy cells when delivered to them. The reduction or prevention of side effects can also be achieved by controlled release. Nano-particulate drug-delivery systems (NPDDS) provide a better penetration of the particles inside the body as their size allows delivery via intravenous injection or other routes. The nanoscale size of these particulate systems also minimizes the irritant reactions at the injection site. Early attempts to direct treatment to a specific set of cells involved attaching radioactive substances to antibodies specific to markers displayed on the surface of cancer cells. Antibodies are the body's means of detecting and flagging the

presence of foreign substances. Antibodies specific to certain proteins can be mass-produced in laboratories, ironically using the cancer cells. These approaches have yielded some good results, and Nano-particulate drug-delivery systems (NPDDSs) are demonstrating lot of potential in this area.[10]

The use of lipid particles as drug carrier systems has been favoured recently as result of the Generally Regarded as Safe (GRAS) status of the excipients and their traditional use in other food and pharmaceutical products. Lipids and lipid nanoparticles are promising delivery systems for oral administration of small molecule drugs, proteins and peptides. Lipid formulations of drugs are able to control the release of drugs and reduce absorption variability. The oral administration of lipid nanoparticles is possible as aqueous dispersion or alternatively transformed into a traditional dosage forms such as tablets, pellets, capsules, or powders in sachets. The ability to incorporate drugs into lipid nano-carriers offers a new prototype in drug delivery that could be used for passive and active drug targeting. Lipid nanoparticles for topical application could be formulated with high content of lipid matrix or dispersed in creams or gels to give it 'body'. With the development and interest in lipid particulate drug delivery systems shown by pharmaceutical formulation scientists, a future full of lipid nanoparticle products in the market is envisaged.[11]



Schematic diagram of Lipid particulate drug delivery systems.[11]

Applications of Nanotechnology

Cancer Nanotechnology

Cancer nanotechnology is emerging as a new field of interdisciplinary research, cutting across the disciplines of biology, chemistry, engineering, and medicine, and expected to lead to major advances in cancer detection, diagnosis, and treatment. The basic rationale is that metal, semiconductor; polymeric particles have novel optical, electronic, magnetic, and structural properties that are often not available from individual molecules or bulk solids. Recent research has developed functional nanoparticles that are covalently linked to biological molecules such as peptides, proteins, nucleic acids, or small-molecule ligands. Medical applications have also appeared, such as the use of super-paramagnetic iron oxide nanoparticles as a contrast agent for lymph node prostate cancer detection and the use of polymeric nanoparticles for targeted gene delivery to tumor vasculatures. New technologies using metal and semiconductor nanoparticles are also under intense development for molecular profiling studies and multiplexed biological assays.[13]

Applications of Nanotechnology[12]	
Nanotechnology area	**Application**
Nano-electronics	
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.
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.

Nanotechnology for water purification

Nanotechnology holds great promise for improving the efficacy and efficiency of water treatment. Most scientific reviews of nanomaterials have concluded that the risks associated with these substances can be managed, but due to the paucity of information regarding toxicity, more health and environmental effects, research is needed. Some studies show that smaller particles are not necessarily more toxic, but the ability of these smaller particles to disperse and become mobile in both the environment and the human body must be evaluated. If nanomaterials are used in the water market for filtration, disinfection, and other treatment, product-specific implications should be considered, particularly for products that are designed to stay or otherwise degrade in situ.[14] ***Nanoparticles as antimicrobial agents,*** for water disinfection, used for killing of disease causing bacteria, viruses and protozoa. ***Nanomaterials as catalysts***, used for removal of pesticides and other organic matter including toxins. ***Nanomaterials as sorbents***, used for the removal of heavy metals and inorganic contaminants. ***Nanomaterials as filtering agents,*** used for removal of contamination by filtration.[15]

CONCLUSION

Pharmaceutical nanotechnology offers new tools, opportunities and scope, which are expected to have a great impact on many areas in disease diagnostics and therapeutics. Few nanotechnology based products and delivery systems are already in market. Pharmaceutical nanotechnology provides opportunities to improve materials, medical devices and help to develop new technologies where existing and more conventional technologies may be reaching their limits. Pharmaceutical nanotechnology raises new hope to pharmaceutical industries by providing new cutting age patentable technologies in view of revenue loss caused due to off-patent drugs. Scientific societies, industries and governments all over world are looking with great anticipation and contributing their best to clutch the potential of this technology. This technology has the potential to make significant contributions to disease detection, diagnosis, therapy, and prevention. Pharmaceutical nanotechnology could have a profound influence on disease prevention efforts because it offers innovative tools for understanding the cell as well as the differences between normal and abnormal cells. It could provide insights into the molecular basis of disease. However going towards bottom size increases the unknown health risk. We still lack sufficient data and guidelines regarding safe use of these nanotechnology based devices and materials. There are several confounding unresolved issues, which warrant the application in its full bloom. Pharmaceutical

nanotechnology is still in infancy. Some concerning issues like safety, toxicity hazards, bioethical issues, physiological and pharmaceutical challenges get to be resolved by the scientists.

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