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A Review on Role of Nanotechnology in the Development of Therapeutics

Shubham Sharma[1], Yadvendra Singh Thenuan[2], Prottay Dutta[3], Abhishek Pandey[4], Bhupen Subba [5]
[1,2]Assistant Professor, School of Pharmacy, Mangalayatan University, Aligarh, UP, India
[3]Assistant Professor, Faculty of Pharmacy, Usha Martin University, Ranchi, Jharkhand
[4]Assistant Professor, Faculty of Pharmacy, Himalayan University, Itanagar, Arunachal Pradesh
[5]Assistant Professor, College of Pharmacy, Sikkim Professional University, Gangtok, Sikkim

Abstract

Nanoscience or Nanotechnology is the study of the unique properties of materials that have range between 1 100 nm, and nanotechnology is the application of such research to create or modify novel objects.
The ability of nanotechnology to manipulate structures at the small scale allows for the creation of nanomaterials (1 3). Nanomaterials can be used in the healthcare fields. Nanomaterials are unique as they provide a large surface area to volume ratio.

Key Words: Nanotechnology in medicine and healthcare

Introduction

Nanoscience or Nanotechnology is the study of the unique properties of materials that have range between 1-100 nm, and nanotechnology is the application of such research to create or modify novel objects.
The ability of nanotechnology to manipulate structures at the small scale allows for the creation of nanomaterials (1-3). Nanomaterials can be used in the healthcare fields. Nanomaterials are unique as they provide a large surface area to volume ratio.

Nanoscience is the study of phenomenon and manipulation of materials at molecular and macro-molecule scales, where properties differ significantly from those at large scale.

Nanotechnologies have had a significant impact in almost all industries and areas of society as it offers
Better built,
Safer and cleaner,
Longer-lasting and
Smarter products for medicine, everyday life, agriculture and other industries. (4)

The use of nanomaterials in everyday products can be generally divided into two types. First, nanomaterials can be merged or added to a pre-existing product and improve the composite objects.

Secondly, nanomaterials such as nanoparticles can be used directly to create products. The benefits of nanomaterials could potentially affect the future of nearly all industrial sectors. (5)

Nanotechnologies have **changed advances in medicine**, specifically in **diagnostic methods, and drug delivery**. Given below table illustrates the areas where nanotechnologies have had a significant role.

S. No.	Area	Applications
1	Healthcare	Development of personalised medicine Precise and accurate drug delivery systems Nanotechnology plays an important role in improving the therapeutic efficacy of drugs. Nanoparticles can be used as contrast agents in imaging techniques like MRI, CT, and ultrasound Nanotechnology can improve the solubility of poorly water-soluble drugs, making them more easily absorbed in the body and enhancing their therapeutic effectiveness
2	Cosmetics	Nanotechnology is used in cosmetics and personal care products for better delivery of active ingredients and improved skin penetration. Nanoscale particles can enhance the texture and appearance of cosmetic products.
3	Environment	Reduce pollution by acting as molecular sieves for capture of pollutants Detect pollutants in the air and water through new disposable sensors

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4	Agriculture	Nanotechnology is used in agriculture to develop nano-pesticides and nano-fertilizers

Nanotechnology allow mass-creation of products with enhanced functionality, significantly lower costs, and greener and cleaner manufacturing processes, to improve healthcare. (6)

Nanotechnology in medicine and healthcare-
Nanotechnology is the term used to refer to the use of Nanomedicine in healthcare. Specifically, nanomedicine uses technologies at the nanoscale to prevent, diagnose, monitor and treat diseases. (7)
Nanotechnologies show significant potential in the field of medicine, including in imaging techniques and diagnostic tools, drug delivery systems and has advanced treatments of several diseases, including cardiovascular diseases, cancer, bacterial, viral infections and diabetes. (8)

Benefits of Nano technology-

- Nanotechnology delivers the drug to the target site more efficiently
- As Nanoscale contrast agents enhance medical imaging for more accurate and detailed diagnostics.
- Unsolved medical problems such as cancer, benefiting from the Nano medical approach.
- Advanced therapies
- Nano sensors detect pathogens and toxins in body fluids with high sensitivity, aiding rapid and accurate diagnosis. (9)

Types of nanoparticles-
Several nanoparticles and nanomaterials have been investigated and approved for clinical use. Some common types of nanoparticles are discussed below.

S. No.	Organic nanoparticles	Inorganic nanoparticles
1	Polymeric Nanoparticles	Carbon Nanotubes
2	Micelles	Gold nanoparticles
3	Liposomes	Silica Nanoparticles
4	Niosomes	

Polymeric Nanoparticles-

- Polymer is a large molecule or macromolecule consisting of repeated sub units.
- Polymer nanoparticles (PNPS) are defined as dispersions or solid particles with size in the range 10-100nm and used as a nanocarrier for both hydrophobic and hydrophilic drug substances.
- Drug may be dissolved, entrapped, encapsulated or attached to a nanoparticle matrix.
- Because these systems have very large surface areas, drugs may be absorbed into their surface and effectively carry drugs, proteins and DNA to target cells.
- Depending upon the method of preparation two types of polymeric nanoparticles are formed. (10)

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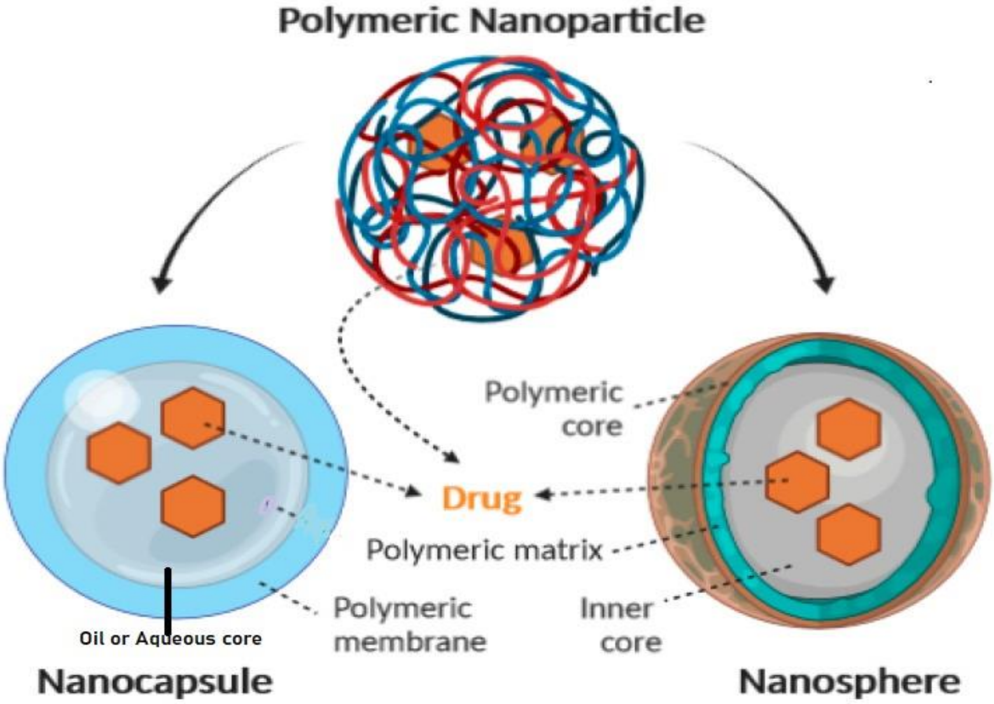

1. Nano capsule-

Nano-capsule is a nanoscale shell made from a non-toxic polymer. Nano-capsules are the systems in which drug is kept to a cavity consisting of an inner liquid core (oil or aqueous) surrounded by a unique polymer membrane.

Nanospheres-

Nanospheres are the spherical particles which have size in between 10 to 200 nm in diameter. The nanospheres are matrix systems in which drug is physically and uniformly dispersed. They are self-assembling and have potential as drug carriers and imaging agents. (11)

Role of Polymeric Nanoparticles-

Healthcare-

- Drug delivery involves nanoparticles to deliver drugs to cancer cells
- These particles are directly attracted to cancer cells and reduces damage to healthy cells. Targeted drug delivery system (TDDS) is applied to treat cancer.
- Polymeric nanoparticles are used as the carrier of anticancer agents in TDDS.
- In diagnostic techniques antibodies attached to carbon nanotubes are used to detect cancer cells.
- In medical robotics nano robots are programmed to repair specific diseased cells which functions as antibodies as in healing process. (12)
- In anti-microbial techniques polymer coated iron oxide nanoparticles to treat chronic bacterial infections.
- In cosmetic industry polymeric nanoparticles are used in drug delivery are useful in makeups, perfumes, sunscreen lotions, creams.
- This encapsulated polymer nanoparticles penetrate into the top layer of the skin due to small size of the particles. (13)

Industry-

- Polymeric nanoparticles are employed in food packaging to enhance the shelf life of products. They can act as barriers against oxygen, moisture, and contaminants, thus preserving the quality and safety of food items. Additionally, these nanoparticles can be used to encapsulate flavours, colours, and nutrients, Improved, active and intelligent food packing.
- In textile industry Polymeric nanoparticles are utilized to impart specific properties to textiles. They can be used to create nanofibers OR fabrics.
- In electronic industry the polymer nanoparticles are used to prepare solar cells of high flexibility and cheaper.

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- They can be used to remove pollutants and contaminants from water and soil through processes such as adsorption and filtration.
- Polymer nanoparticles are used in batteries and memory devices.
- In military coated polymer threads woven into the soldier's uniform is used for communication purposes. (14)

2. Micelles-

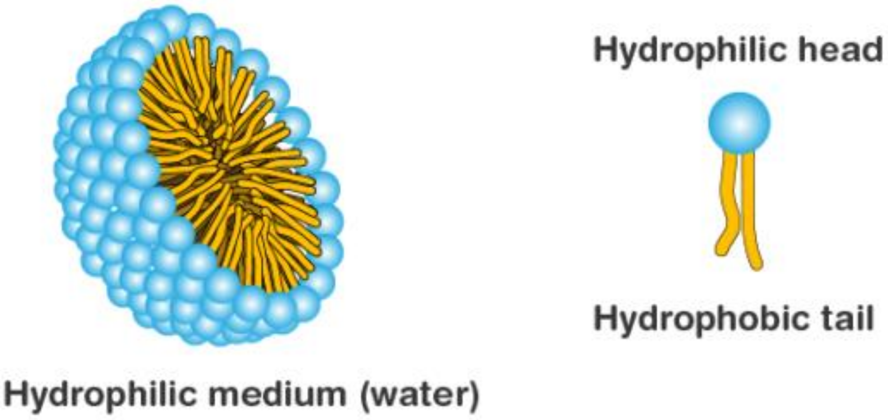
Micelles are amphiphilic surfactant molecules that consist **of lipids and amphiphilic molecules**.

Micelles **self-aggregate and self-assemble** into spherical vesicles under aqueous conditions with a **hydrophilic outer monolayer (Head) and a hydrophobic core (Tail)**, and thus can be used to incorporate **hydrophobic** therapeutic agents.

The unique properties of micelles allow for the enhancement of the **solubility of hydrophobic drugs**, or water insoluble drugs thus improving bioavailability.

The diameter of micelles ranges from **10-100 nm**. Micelles have various applications, such as drug delivery agents, imaging agents, contrast agents and therapeutic agents. (15)

Role of Micelles-



- They are termed as efficient favourable nano-carries in various applications namely drug delivery.
- Micelles are widely used as drug delivery vehicles, hydrophobic drugs that have poor solubility in aqueous solutions can be encapsulated within the hydrophobic core of micelles, thus improving their solubility, stability, and circulation time in the body.
- Micelles can be designed to carry imaging agents, such as contrast agents for imaging techniques like in magnetic resonance imaging.
- The micellar solution is required in the digestive system of the human body that plays an important role in the removal of complex lipids and fat-soluble vitamins which are indigestible in the human body.
- Delivering medicines to patients, or to the specific locations within the patients. (16)

3. Liposomes-

- Liposomes are simple microscopic bilayer vesicles in which an **aqueous core is entirely enclosed or encapsulated** by a membrane composed of lipid molecules.
- Liposomes are spherical bilayer vesicles with particle sizes ranging from 30 nm to 3 microns, that consist of lipid bilayers.
- Structurally, Liposomes are **bilayer vesicles** in which an aqueous volume is entirely enclosed by a **membranous lipid bilayer mainly composed of phospholipids.**
- A **hydrophilic head and a hydrophobic core tail**, and thus can be used to incorporate **hydrophilic and hydrophobic (lipophilic)** therapeutic agents inside the aqueous phase.
- Polyethylene glycol liposomal doxorubicin (Doxil®) is the first FDA-approved nanomedicine, which has been used for treatment of breast cancer. (17)

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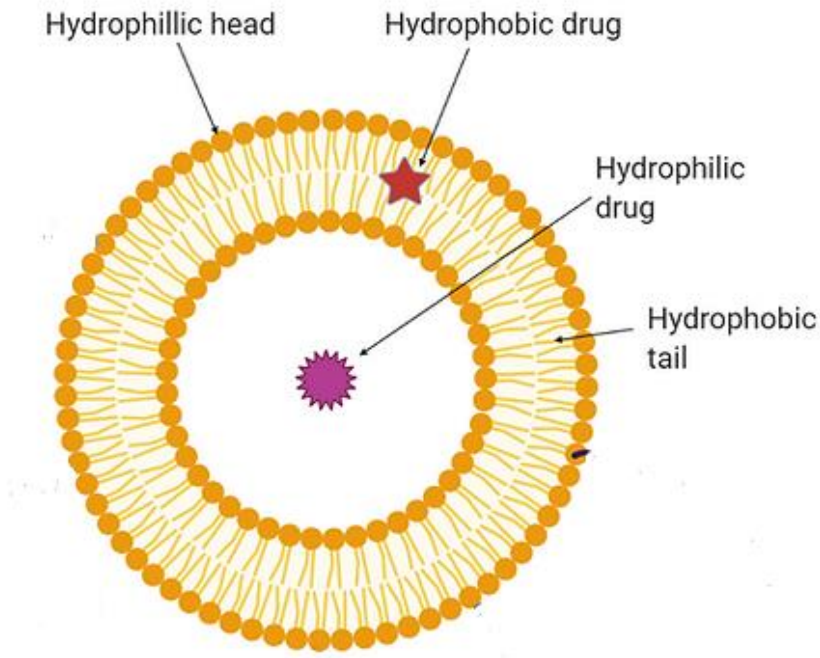

Role of Liposomes-

- Liposomes have been a promising tool to deliver drugs through cell membranes, and they assist drugs to target specific disease sites.
- Food ingredients can be encapsulated in liposomes to improve their stability against degradation. Liposomes are much smaller than other kinds of encapsulation systems.
- Liposome is biologically compatible with human skin and has been applied as a powerful tool in various cosmetic technologies.
- Liposomes can capture and deliver active cosmetic ingredients through layers of the skin. Liposomal cosmetics contain various entrapments such as moisturizers, extracts and antibiotics.
- Besides the common applications in medicine and pharmacy, liposomes have also been applied as a valuable tool in various non-food agricultural systems such as pesticide, toxin attack, and veterinary applications.
- Liposomes with essential oils provide an effective nourishing treatment that penetrates deeply in to the skin. (18)

4. Niosomes-

- Niosomes are non-ionic surfactant based Unilamellar or multilamellar bilayer vesicles.
- The Niosomes are very small, and microscopic in which the medication is encapsulated in a vesicle with particle sizes ranging from 30 nm to 100 nm.
- Both hydrophilic & lipophilic drugs, entrap either in the aqueous layer or in lipid layer specially cholesterol.
- These vesicles systems are similar to liposomes that can be used as carriers of amphiphilic and lipophilic drugs.
- They are less toxic and improve the therapeutic index. (19)

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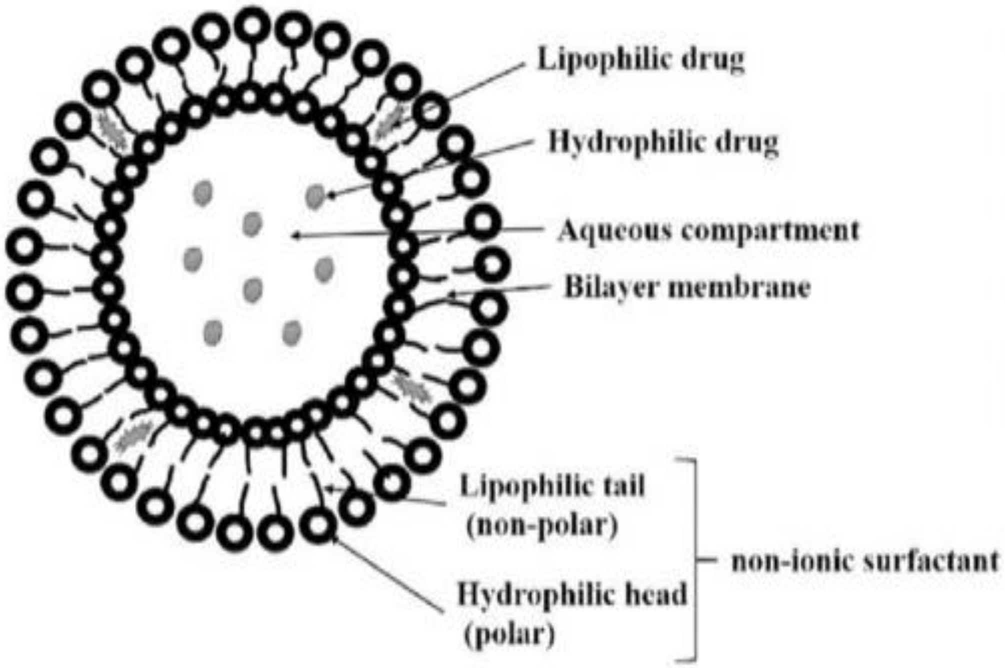
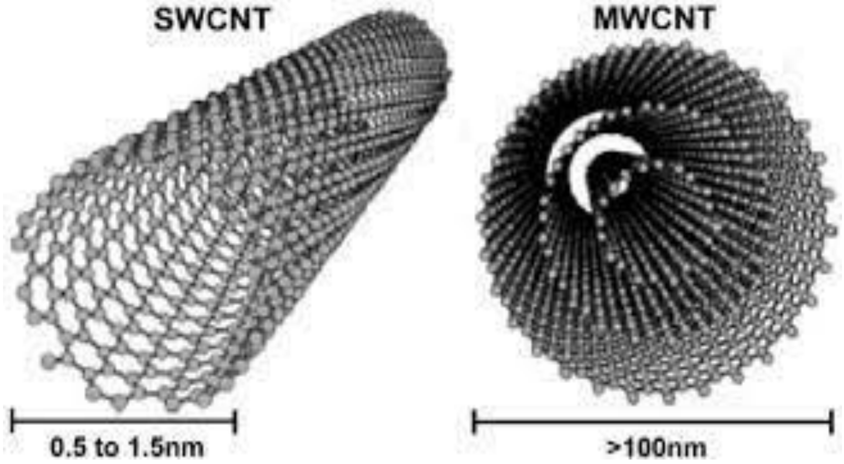


Role of Niosomes-

- Niosomes are used as carriers to encapsulate and deliver drugs, both hydrophilic and hydrophobic, to specific target sites within the body. They can improve the solubility and bioavailability of poorly water-soluble drugs, leading to enhanced therapeutic effects and reduced side effects.
- Niosomes can be designed to release the encapsulated drug in a controlled and sustained manner, leading to prolonged therapeutic effects and reduced dosing frequency. This can improve patient compliance and overall treatment outcomes.
- Sustained release action of Niosomes can be applied to drugs with low therapeutic index and low water solubility.
- Niosomes can encapsulate cosmetic ingredients and skin care actives, enabling controlled release and improved penetration into the skin. They are used in various cosmetic and dermatological products for skin like anti-aging, and other applications.
- To improve the stability and physical properties of drugs.
- It is used in ophthalmic drug delivery.
- It is used as carrier system for the treatment Cancer Disease. (20)

Carbon nanotubes-

- Carbon nanotubes are cylindrical molecules that consist of rolled-up sheets of a single-layer of carbon atoms (graphene).
- Graphene is a single layer of carbon atoms arranged in a hexagonal lattice structure.
- They can be **single-walled (SWCNT) with a diameter of less than 1 nanometre (nm) or multi-walled, consisting of several concentrically interlinked nanotubes**, with diameters reaching more than 100 nm. Their length can reach several micrometers or even millimeters.
- Nanotubes are formed by folding or rolling **two-dimensional graphene** into a cylindrical shape structure.
- Nanotubes are hollow from inside. The diameter of the nanotube is around 1-3 nanometers.
- In short, we can say that carbon nanotubes (CNT) is a folded form of the two-dimensional graphene sheet.
- Due to their high external surface area, carbon nanotubes can achieve considerably high loading capacities as drug carriers. (21)

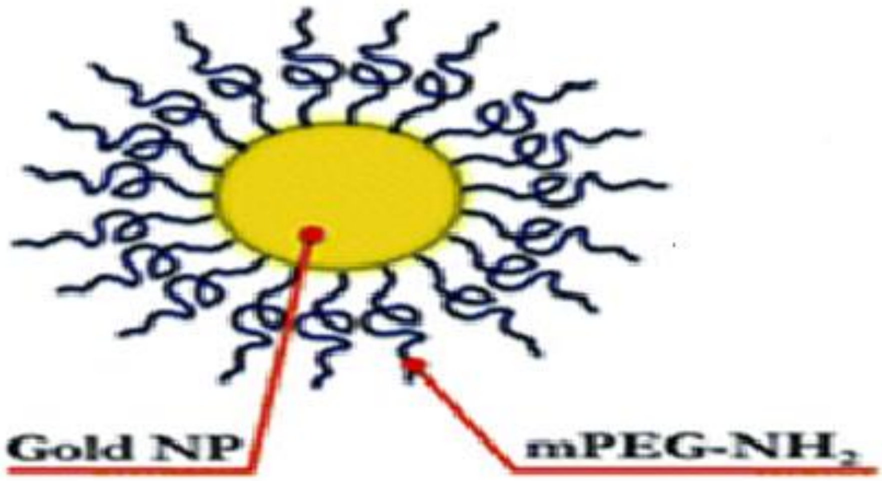


Role of carbon Nanotubes-

- The main applications of CNTs in pharmacy and medicine include drug, biomolecule delivery to cells or organs.
- Because of their large surface area, CNTs have been successfully used in pharmacy and medicine to adsorb or conjugate a wide range of medicinal and diagnostic substances. (22)
- Carbon nanotubes can be used as contrast agents in various imaging techniques, such as magnetic resonance imaging (MRI).
- CNTs can be considered as antitumor agents and when in combination with conventional drugs, can significantly enhance their chemotherapeutic effect with the help of the advanced drug delivery system.
- Carbon nanotubes can be integrated into biosensors for the detection of biomolecules, pathogens, and disease markers. (23)

Gold nanoparticles-

- Gold nanoparticles are small gold particles with a diameter of 1 to 100 nm. Once dispersed in water, gold nanoparticles are also known as colloidal gold.
- In a study published in the July 2007 scientists used gold nanoparticles to detect cancer cells and breast cancer.
- Gold nanoparticles are composed of a gold atom core surrounded by negative reactive groups (mPEG-NH_2, methoxy polyethylene glycol Amine) on the surface, that can rapidly react with activated carboxyl acid to form stable amide bonds. (24)
- Gold nanoparticle are the most Stable metal nanoparticle.
- Gold nanoparticle shows a combination of physical and chemical property.
- Because of these unique physical–chemical properties, the gold nanoparticles are widely used as carriers of drugs delivery and molecules to improve the diagnosis and treatment of diseases. (25)

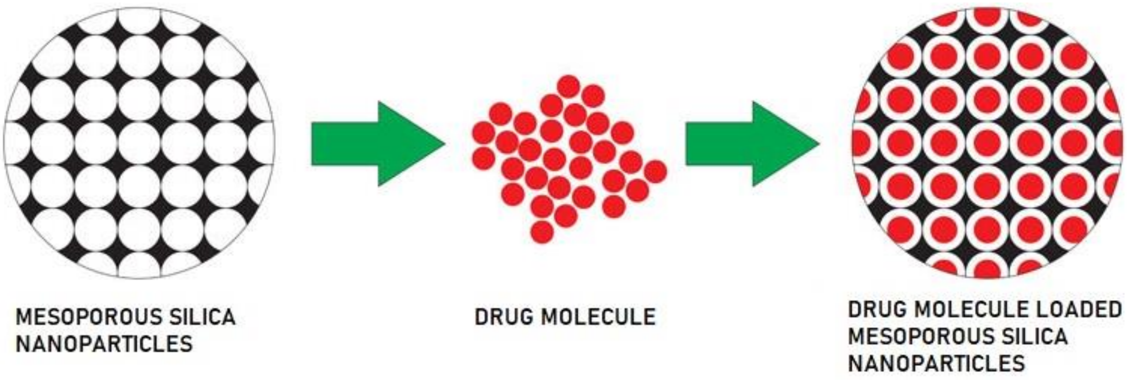


Role of Gold nanoparticles-

- Gold nanoparticles conjugated with therapeutic agents improve the pharmacokinetics of the drug and provides controlled or sustained release properties.
- Gold nanoparticles are used as contrast agents in the diagnosis of heart diseases, cancers, and infectious agents.
- Gold nanoparticles can be encapsulated drugs and deliver them to specific targets in the body. Their size, surface chemistry, and make them ideal for controlled drug release, reducing side effects and improving therapeutic efficacy.
- Gold nanoparticles have shown antibacterial properties and can be used to bacterial infections. They can be coated onto surfaces, such as medical devices or wound dressings, to inhibit bacterial growth and prevent infections. (26)

Silica nanoparticles-

Silica nanoparticles (SiNPs) or silicon dioxide are amorphous substances that have a spherical form.
They can be produced in a variety of shapes and sizes, and the properties of their surfaces can be easily changed to suit several purposes.
Silica nanoparticles with hexagonal mesoporous structures have great importance in nanomedicine and drug applications. (27)



Role of silica Nanoparticles-

- silica nanomaterials present unique properties that qualify them as ideal nano-carriers for transporting of drugs to the target site.
- Silica nanoparticles play an important role in medical imaging, and they are utilized to encapsulate contrast agent's particles.
- The pores in the nanoparticles provide sites to keep drug molecules, and addition agents like gold nanoparticles, are required as caps to close the pores. (28)
- Silica nanoparticles carry and deliver therapeutic agents such as drugs, and proteins to specific target sites in the body. Their surface can be modified to control release rates and improve the bioavailability of drugs. This targeted drug delivery minimizes side effects and enhances treatment efficacy.
- Silica nanoparticles can be designed to selectively accumulate in tumour tissues due to their enhanced permeability. They can be loaded with anticancer drugs, or even used in combination with other therapies to enhance cancer treatment outcomes. (29)
- Silica nanoparticles can be used to create biosensors that detect specific biomolecules or pathogens. By functionalizing the nanoparticles with recognition elements like antibodies, these sensors can offer rapid, sensitive, and specific detection of diseases and infections.
- Silica nanoparticles can combine therapeutic and diagnostic functions in a single entity, known as **theranostic** nanoparticles.
- These nanoparticles can simultaneously deliver therapies and monitor treatment response, providing a personalized approach to medicine. (30)

Regulation and products now in the market-

- In the current medical nanotechnology scenario, there are 51 products based on this technology. (31)
- Notably, such nanomedicines are primarily developed for drugs, which have low aqueous solubility and high toxicity, and these nano formulations are often capable of reducing the toxicity while increasing the pharmacokinetic properties of the drug.

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- ❖ According to a recent review by Caster et al. [2016], although few nanomedicines have been regulated by the FDA there are many initiatives that are currently in progress in terms of clinical trials suggesting many nanotechnology-based new drugs will soon be able to reach the market.
- ❖ As a strategy for the lack of regulation of nanomedicines and nano drug delivery system; the safety assessment and the toxicity and compatibility of these are performed based on the regulations used by the FDA for conventional drugs.
- ❖ After gaining the status of a new research drug by the FDA, nanomedicines, nano-drug delivery systems start the clinical trials phase to investigate their safety and efficacy in humans.
- ❖ These clinical trials are divided into three phases:

Onivyde® (Merrimack)	Liposomal irinotecan	Pancreatic cancer	2015
Abelcet® (Sigma-tau)	Liposomal amphotericin B	Fungal infections	1995
Tricor® (Lupin Atlantis)	Fenofibrate	Hyperlipidaemia	2004
Feridex®/Endorem® (AMAG phamaceu- ticals)	SPION coated with dextran	Imaging agent	1996
GastroMARK™; umirem® (AMAG pharma- ceuticals)	SPION coated with silicone	Imaging agent	2001
Abelcet® (Sigma-tau)	Liposomes Amphotericin B lipid complex	Fungal infection	1995
Krystexxa® (Horizon)	PEG-loticase	Chronic gout	2010
ADYNOVATE (Baxalta)	Factor VIII PEGylated factor VIII	Haemophilia	2015
Emend® (Merck)	Aprepitant Nanocrystals	Antiemetic drug	2003
Tricor® (Lupin Atlantis)	Fenofibrate Nanocrystals	Hyperlipidaemia	2004
NanOss® (Rti Surgical)	Hydroxypatite Nanocrystals	Bone substitute	2005
EquivaBone® (Zimmer Biomet)	Hydroxypatite Nanocrystals	Bone substitute	2009
Vitoss® (Stryker)	Calcium phosphate	Bone substitute	2003
Ostim® (Heraseus Kulzer)	Hydroxyapatite	Bone substitute	2004
OsSatura® (IsoTis Orthobiologics)	Hydroxyapatite	Bone substitute	2003
NanOss® (Rti surgical)	Hydroxyapatite	Bone substitute	2005
GastroMARK™; umirem® (AMAG pharmaceuticals)	Superparamagnetic iron oxide nanoparticles (SPION)	Imaging material	2001

Phase 1 (Mainly assess safety)
Phase 2 (Mainly evaluates efficacy) and
Phase 3 (Safety, efficacy and dosage are evaluated).
After approval in these three phases the IND can be filed to the FDA.

The list of nano-medicine approved by FDA classified by type of carrier material used in preparation of the formulation is shown in below table. (32)

Future of nanomedicine-

- ❖ The science of nanomedicine is currently among the most attractive areas of research.
- ❖ A lot of research in this field in the last two decades has already led to the filling of 1500 patents & completion of several dozens of clinical trials.

- As given above, cancer appears to be the best example of diseases where both its diagnosis and therapy have benefited from nonmedical technologies.
- By using various types of nanoparticles for the delivery of the accurate amount of drug to the affected cells such as the cancer cells, without disturbing the physiology of the normal cells. (33)
- Nanoscale sensors and devices could be designed to detect biomarkers at very early stages of diseases, allowing for rapid and accurate diagnosis. This could lead to earlier intervention and better treatment outcomes
- Nanoparticles deliver drugs directly to specific cells or tissues, minimizing side effects and maximizing therapeutic efficacy, this could lead to more personalized and efficient treatments for various diseases.
- Nanoparticles can enhance medical imaging techniques. They could improve contrast and resolution, allowing for earlier and more accurate diagnosis of diseases.
- Nanotechnology could accelerate the drug development process by facilitating high-throughput screening (HTS) of potential drug compounds and improving the understanding of drug interactions within the body.
- Portable nanodevices could be developed for diagnostics, making medical testing more accessible, affordable, and rapid in various ways. (34)
- Nano sensors integrated into wearable devices could continuously monitor a patient's health and transmit real-time data to healthcare providers, enabling remote monitoring and telemedicine for more accurate and timely interventions.
- Nano sensors could be used for detecting environmental toxins, pollutants, and pathogens, contributing to public health by providing real-time data on air and water quality. (35)

Challenges and Safety Concerns-

- **Toxicity:** The potential toxicity of nanomaterials must be evaluated to ensure their safe use in therapeutic applications.
- **Manufacturing and Scale-up:** The scalability and reproducibility of nanotechnology-based drug delivery systems present challenges in large-scale production and commercialization. (36)
- The scalable production of nanoparticles with consistent quality is a challenge. Variability in manufacturing processes can lead to variations in nanoparticle properties, which could impact safety and performance. (37)
- Limited information is available on the long-term health effects of chronic exposure to nanoparticles. Comprehensive studies are needed to understand effects, including carcinogenicity and chronic diseases.
- Regulatory Considerations: Nanomedicines require unique regulatory pathways, and guidelines must be followed to ensure patient safety and efficacy. (38)

Conclusion

- There is no doubt that nanotechnologies have helped to improve the quality of life of patients by providing a platform for advances in biotechnological, medicinal and pharmaceutical industries.
- They have also simplified healthcare procedures, from diagnosis to therapeutic interventions and follow-up monitoring.
- The hope of nanotechnology lies within using the right nanomaterials and reducing any possible harmful effects.
- It is important to note that, risk evaluations are required before any new nano-based products are approved for clinical and commercial use, as with any other product, to minimise hazards to human health and the environment.
- A full life cycle evaluation is required to more accurately determine the safety of their use for a long period of time.
- There is a constant push to create and develop novel nanomaterials to improve diagnosis and cures for diseases in a targeted, accurate, potent and long-lasting manner, with the ultimate aim of making medical practices more personalised, cheaper and safer.

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