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A Review of the Benefits, Evaluation, and Requirement for Design of Nanoparticles

Miss. Anushka Pingle*, Mr. G. D. Basarkar
Department of Pharmaceutics, SNJB's Shriman Sureshdada Jain College of Pharmacy, Chandwad, Nashik.
**Corresponding Author: Miss. Anushka Pingle,*
Department of Pharmaceutics, SNJB's Shriman Sureshdada Jain College of Pharmacy, Chandwad, Nashik.

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Abstract:-
The most recent field of pharmaceutical sciences, known as" Pharmaceutical nanotechnology," introduces new tools, prospects, and scope that are projected to have substantial applications in disease diagnostics and therapies. Recently, nano-pharamceuticals have shown tremendous promise in drug delivery as a carrier for the spatial and temporal distribution of bioactive and diagnostic agents. Furthermore, it offers smart materials for tissue engineering. Through its nano-engineered instruments, this discipline is now well-established for medication delivery, diagnosis, prognosis, and treatment of disorders. Some nanotechnology-based goods and delivery systems are already available for purchase. Pharmaceutical nanotechnology is made up of nano-sized goods that can be altered in a variety of ways to improve their properties. Drugs that have been changed into the nano range have several distinct characteristics that can contribute to longer circulation and increased medicinal efficacy.
Keywords: Nanotechnology ,Nanoparticles , Types, Methods, Characteristics

I. Introduction:-

The prefix "Nano" is derived from the ancient Greek vavoc, via the Latin nanus, which means dwarf or exceedingly little. It typically ranges from 1nm to 100nm. Nanotechnology is defined as the study of microscopic science. Nanotechnologies that promote therapeutic effect have increased bioavailability and patient compliance. The drug has been dissolved, entrapped, encapsulated, or linked to the drug carrier.

The key goal is to manage particle size, surface characteristics, and active material release to ensure medication site-specific actin to optimise rate and dose schedule. Nanotechnology has the potential to revolutionise the pharmaceutical sector through illness treatment and quick detection. It aids in overcoming biological barriers in order to direct the medicine through the use of unique drug delivery system design.

Need of Nanoparticle:-

Nanotechnology has recently demonstrated that nanoparticles have a high potential as drug carriers. Size reduction methods and technologies provide a variety of nanostructures with distinct physicochemical and biological features. Nanotechnology uses drugs with nanometre dimensions to increase performance in various dosage forms.

Advantage of nanoparticles:-

1. Reduced fasting variability.
2. Greater drug solubility.
3. Less variation between patients.
4. Better bioavailability.
5. More surface area.
6. Faster dissolving rate.
7. Quick action.
8. Dose reduction regimen.
9. System of targeted drug administration.
10. Drug builds up at target areas in the body that is effective.
11. Particle size and size distribution control.
12. Encapsulated medication safeguard.
13. Drug retention at active site.
14. Increased clearance time.
15. Enhance therapeutic efficacy.
16. There is less toxicity.

Disadvantage of nanoparticle:-

1. Limited targeting capabilities.
2. Cytotoxicity.
3. Carcinogenicity
4. Therapy is unable to be discontinued.

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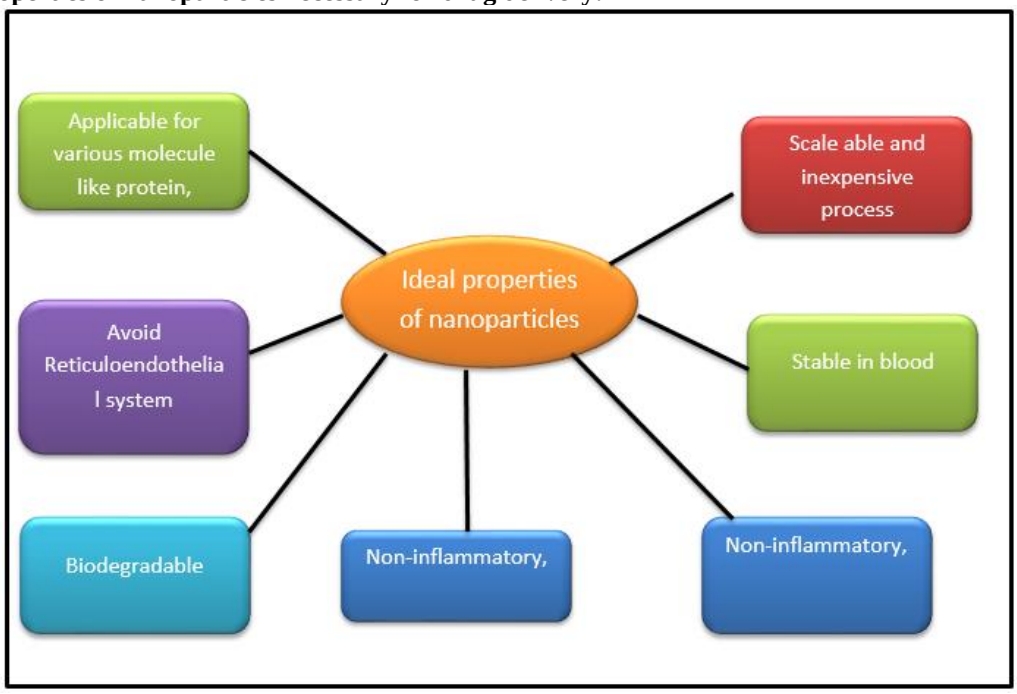
Limitation:-

1. Physiochemical processes that cause particle aggregation, dry develops as a result of higher particle area and reduced particle size.
2. Drug loading is restricted.
3. Reactive to its surroundings in the cellular environment.
4. Issues before clinical use or commercial availability.

Toxicity:-

Tiny particles easily enter the body through the skin, lungs, and digestive system, deposit in organs, and may induce toxicity by modifying the physicochemical properties of the drug. It may result in lung and cardiovascular problems.

Ideal properties of nanoparticles necessary for drug delivery:-



Types of Nanoparticles:-

1. Based on method of Preparation:-

a) Nano-sphere:-

Nano-sphere are matrix system in which physically and uniformly dispersed**.**

b) Nano-capsules:-

Nano-capsules are system in which the drug is confined to a cavity surrounded by a unique polymeric membrane

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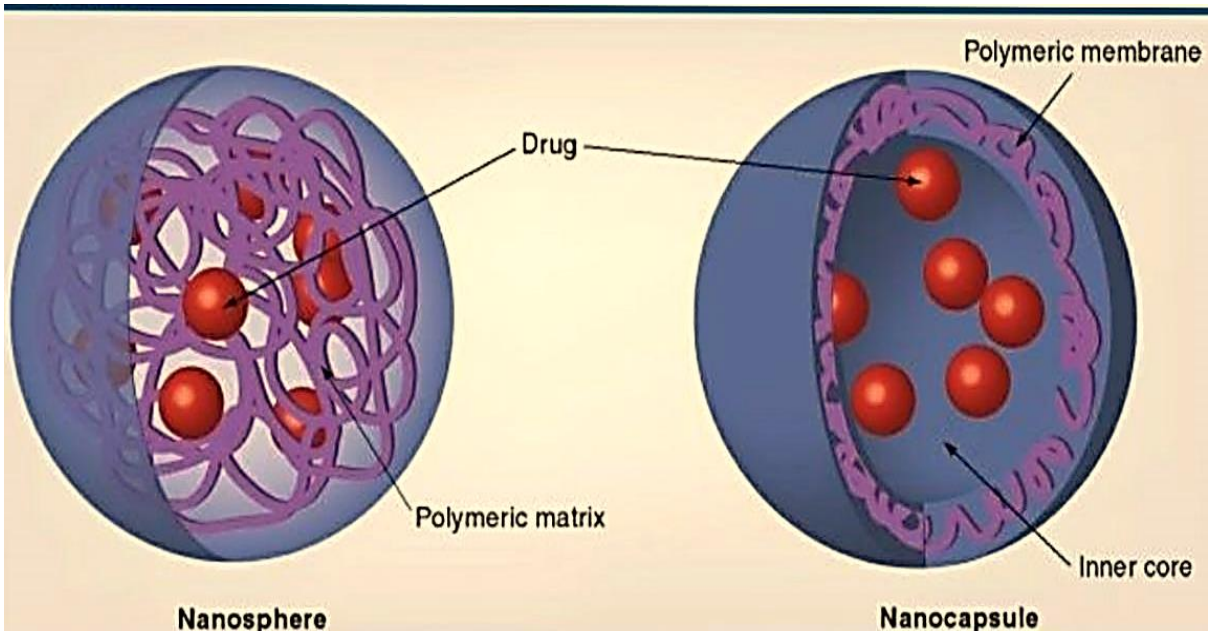

2. Based on Dimensions:

a) Nanoparticles with zero dimensions:

Materials with all dimensions smaller than the nanoscale (1-100nm). Nanoparticles, nanospheres, and quantum dots, for example.

Nanoparticles can take the following forms:

a) Amorphous and crystalline materials
b) Polycrystalline or single crystalline
c) Display diverse shapes and forms.
d) Exist on their own or as part of a matrix.

b) One-dimensional Nanoparticles:

Materials with one dimension outside the range of the nanoscale. Nanowires, nanotubes, and nanorods are a few examples.

One dimension can be:

a) Amorphous and crystalline
b) Chemically pure or impure
c) Stand alone or embedded within another matrix.

c) Two-dimensional nanoparticles:

Materials have two dimensions that are outside the nanoscale range.For example, nanofilm and nanolayer.

Two-dimensional nanoparticles can be:

a) Made consisting of numerous chemical compositions
b) Used as a single layer or multiple layer structure
c) deposited on a substrate Integrated into a matrix material.

d) Three-dimensional nanoparticles:

Materials that are not restricted to the nanoscale range in any dimension. All dimensions beyond the nanoscale.

As an example, consider bulk material.

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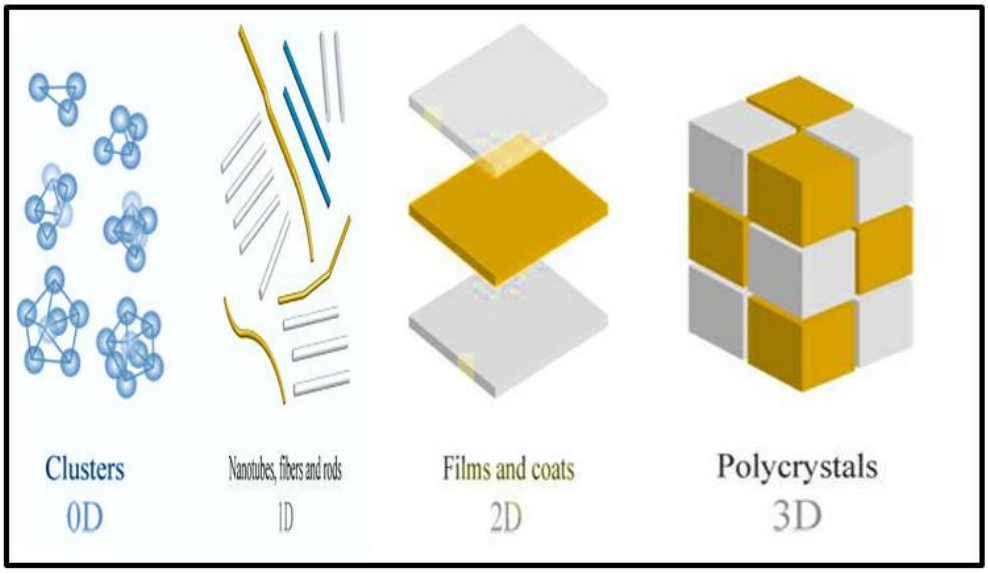
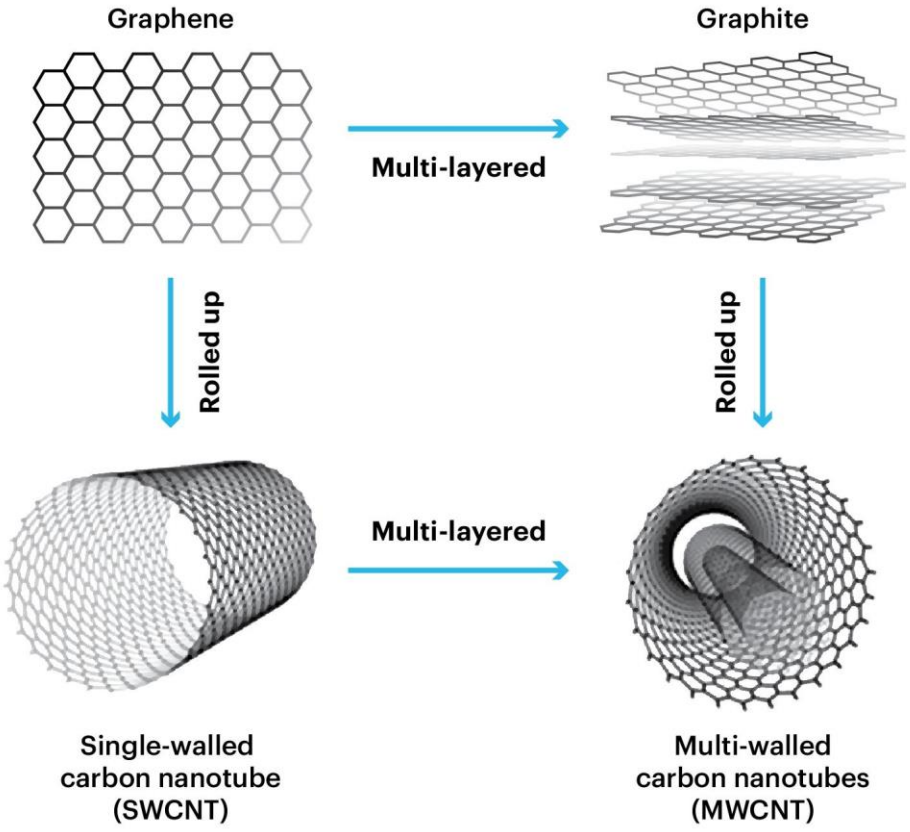


3. Carbon-Based Nanoparticles:

Carbon-based nanoparticles are made up of two major materials: carbon nanotubes (CNTs) and fullerenes. CNTs are just graphene sheets folded into a tube. These materials are mostly utilised for structural reinforcement because they are 100 times stronger than steel.CNTs are classed as single-walled carbon nanotubes (SWCNTs) or multi-walled carbon nanotubes (MWCNTs).



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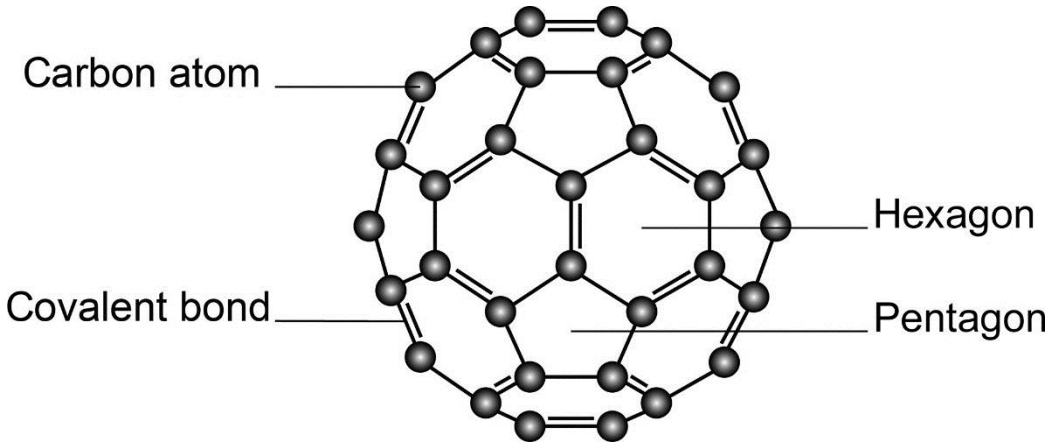
Fullerenes are the allotropes of carbon having a structure of hollow cage of sixty or more carbon atoms, and looks like a hollow football. The carbon units in these structures have a pentagonal and hexagonal arrangement. Fullerenes have been used as carrier for gene and drug delivery systems.



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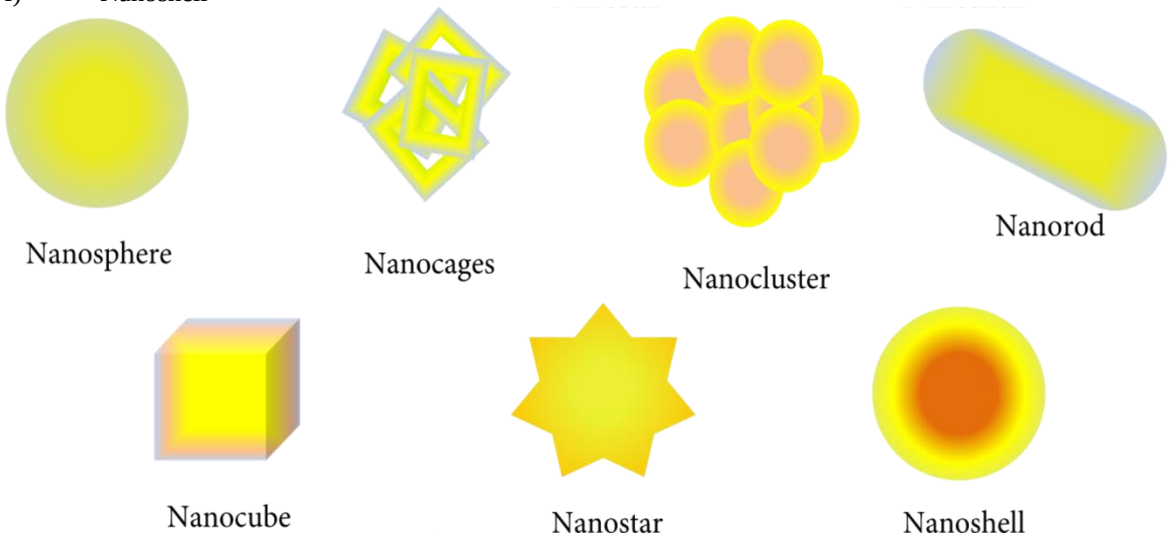
4. Based on shapes:

a) Nanosphere
b) Nanorods
c) Nanocages
d) Nanocube
e) Nanostars
f) Nanoshell



Nanoshell:

A nanoshell is a spherical nanoparticle made up of a dielectric core and a thin metallic shell, typically made of gold. These nanoshell-related quasiparticles, also known as plasmons, oscillate synchronously with regard to all ions and are collective excitation phenomena or quantum plasma oscillations.

5. Based on composition:-

a) Organic Nanoparticle:
i. Silver oxide(Ag)
ii. Iron oxide (Fe_3O_4)
iii. Titanium oxide(TiO_2)
iv. Copper oxide(CuO)
v. Zinc oxide(ZnO)
b) Inorganic Nanoparticle:-
i. Poly-ε-lysine
ii. Quaternary ammonium compounds
iii. Cationic quaternary polyelectrolytes

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iv. N- halamine compounds
v. Chitosan

6. Based on chemical structure and nature:

a) Polymeric nanoparticles
b) Nanoshell
c) Solid Lipid Nanoparticle
d) Hydrogel Nanoparticle
e) Ceramic Nanoparticles
f) Co-polymeric peptide Nanoparticles
g) Nanocrystal and Nanosuspension

Nanocrystals and nanosuspension:

Nanocrystals are nanometer-sized crystals, which means they are nanoparticles having crystalline properties. Drug powder is dissolved in a surfactant solution to form nanocrystals.

The term "nanosuspension" refers to a very tiny colloidal biphasic, dispersed and solid drug particle in an aqueous vehicle, size less than 1 micrometre without any matrix material, stabilised by surfactant and polymer, and prepared by proper drug delivery application by multiple routes of administration.

Nanobubble:

Nanoscale bubble-like formations called nanobubbles (NBs) are produced at the interface of hydrophobic surfaces in liquids. When heated to physiological temperature inside the body, these nanobubbles combine to produce microbubbles and are stable at normal temperature. The mechanism of NB creation is based on the nucleation of gas from a supersaturated solution at the hydrophobic surface, trapping ambient gases. Although the generation of NBs is thermodynamically prohibited, they do have a life span that can approach orders of hours. There are four different kinds of nanobubbles: oscillating, interfacial, bulk, and plasmonic. These bubble-like nanoscale structures can contain cancer treatment medicines. Potential benefits of nanobubbles include their ability to target tumour tissue and deliver drugs under the influence of ultrasonic exposure, might demonstrate advantages in targeting the tumour tissue and administering the medicine selectively. This could improve the tumour cells' ability to absorb the medication intracellularly. Furthermore, these nanobubbles can be clearly seen in tumours using a variety of ultrasound techniques [91, 92].

Dendrimers

A special type of polymers known as dendrimers has compartmentalised chemical polymers, hyperbranched, tree-like structures, and controllable size and shape. Either convergent step growth polymerization or divergent step growth polymerization is used to create dendrimers from monomers. The number of branching that can be adjusted determines the size of these regular branching polymeric nanostructures. Through polymerization, numerous branches of these nanostructures emerge from the core in the form of a spherical structure, creating cavities.

Ceramic Nanoparticles:

These are the Nanoparticles made up of inorganic compound silica, titania and alumina. Exist in size less than 50nm, which help them in evading deeper part of body.

Hydrogel Nanoparticle:

Hydrogel Nanoparticle are formed in water by self-assemblage and self-aggregation of nature polymer amphiphiles.
Ex-Cholesteroyl dextran
Cholesteroyl pullan

Copolymeric peptide Nanoparticles:

It is drug polymer conjugate which form its own Nanoparticultae drug delivery systems.
Ex- n-butylcynoacrylat

Solid Lipid Nanoparticles (SLN):

Solid Lipid Nanoparticles are nano-size colloidal carrier(50-1000nm),which are composed of lipid, surfactants and drugs in appropriate ratios. SLN are generation of submicron sized lipid emulsion where liquid-liquid has been substituted by solid-liquid.

Methods of Nanoparticles:-

1. Nanoprecipitation
2. High pressure homogenization(HPH)

A. Hot HPH
B. Cold HPH

3. Ultrasonic homogenization
4. Micro-emulsion based method
5. Spray drying technique
6. SCF method
7. Solvent emulsification-evaporation technique
8. Solvent emulsification-diffusion technique
9. Melting dispersion method
10. Solvent injection
11. Double emulsion technique

Nanoprecipitation:-

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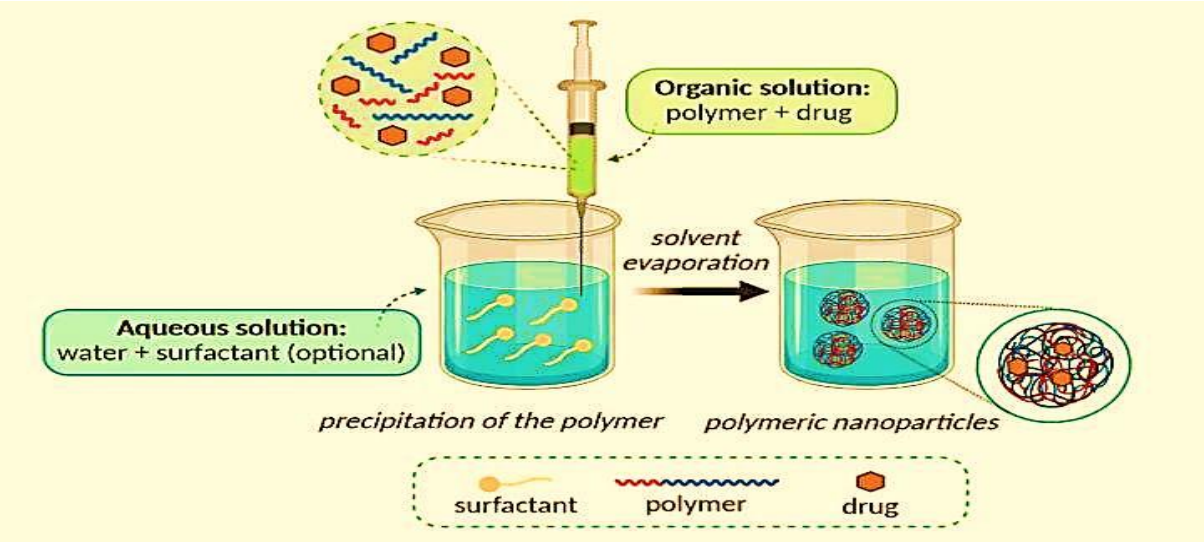
Precipitation has been used to create submicron particles over the past ten years, particularly for medications that aren't easily soluble. The medicine is first dissolved in an organic solvent before being diffused into water with or without the assistance of surfactants. Rapid drug solution addition to the antisolvent causes drug supersaturation to occur suddenly and the development of ultrafine crystalline or amorphous drug solids.

Advantages: Simple procedure, simple scaling, and cost-effective production**.** Disadvantages: Growing of crystals needs to be limit by surfactant addition. Drug must be soluble at least in one solvent



High Pressure Homogenizer:

This method primarily entails three steps: first, a stabiliser solution is used to disperse the powder drug to create a presuspension; next, the presuspension is homogenised using a high-pressure homogenizer at a low pressure; and finally, the homogenised mixture is homogenised at a high pressure for 10 to 25 cycles until the nanosuspensions with the desired drug size are formed.

This method of creating nanosuspension is straightforward and has broad drug acceptance. The technique can be used to make nanosuspensions that are both heavily diluted and intensely concentrated.

Cold homogenization and hot homogenization are additional divisions of the HPH process. The process of cold homogenization, which prevents drug breakdown by controlling temperature, is frequently used to create nanosuspensions. For the creation of microemulsions, hot homogenization is frequently used.

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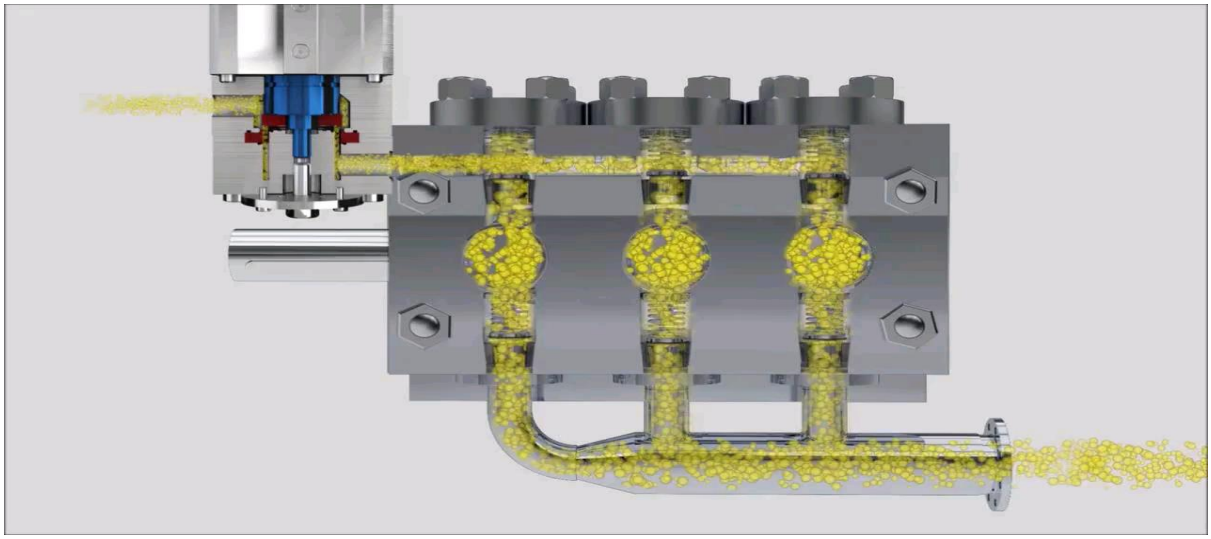

When continuously operated shell rotate and lifts the ball up and drops them from near the top of these shell that cause grinding of particles inside.

MICROEMULSION TECHNIQUE:

In this method, the lipids are melted and the medicine is added to the molten lipid. The co-surfactant(s), the surfactant, and water are heated to the same temperature as the lipids and added to the melted lipids while being gently stirred.The compounds are mixed in the proper ratios for the creation of microemulsions, resulting in a transparent, thermodynamically stable system. As a result, the microemulsion serves as the starting point for the development of nanoparticles with the necessary size.

The hot microemulsion is then mechanically gently mixed with water in the ratio of 1:25 to 1:50 to disperse it in a cold aqueous media. This dispersion in a cold aqueous media causes the oil droplets to quickly recrystallize. Among the surfactants and co-surfactants are lecithin, biliary salts, and alcohols like butanol. Butanol is an excipient that is less frequently utilised because of its regulatory implications. In order to precipitate the microemulsion, it is first prepared in a sizable, temperature-controlled tank and then pumped from there into a cold water tank.

SOLVENT EMULSIFICATION-EVAPORATION TECHNIQUE:-

The hydrophobic drug and lipophilic substance are dissolved in a water-immiscible organic solvent and then emulsified in an aqueous phase using a high-speed homogenizer in the solvent emulsification-evaporation process. By putting the coarse emulsion through the microfluidizer right away, the efficiency of fine emulsification is increased.

By further mechanically stirring the organic solvent at room temperature and low pressure (using a rotary evaporator, for example), lipid nanoparticle precipitates are left behind.

Spray drying:

Here, high pressure homoginization of a water soluble matrix material in aqueous solution can result in the production of nanosuspension. If the conditions are right, the aqueous drug nanosuspension can then be spray dried, producing a dry powder that is made up of drug nanocrystals embedded in a water-soluble matrix of spray-dried substance.

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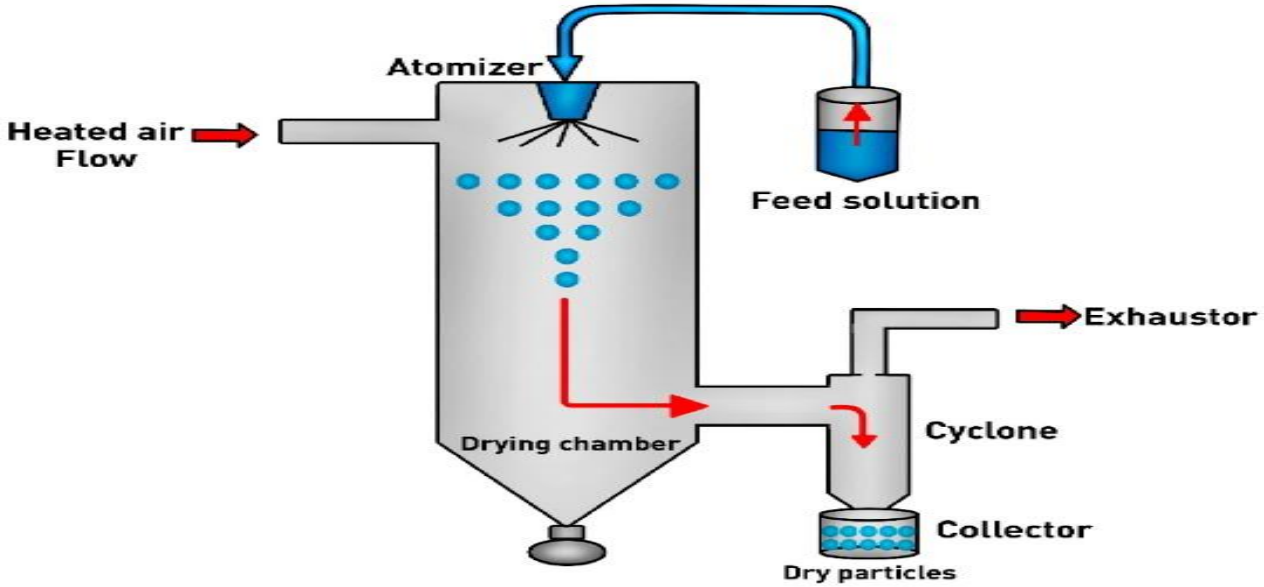
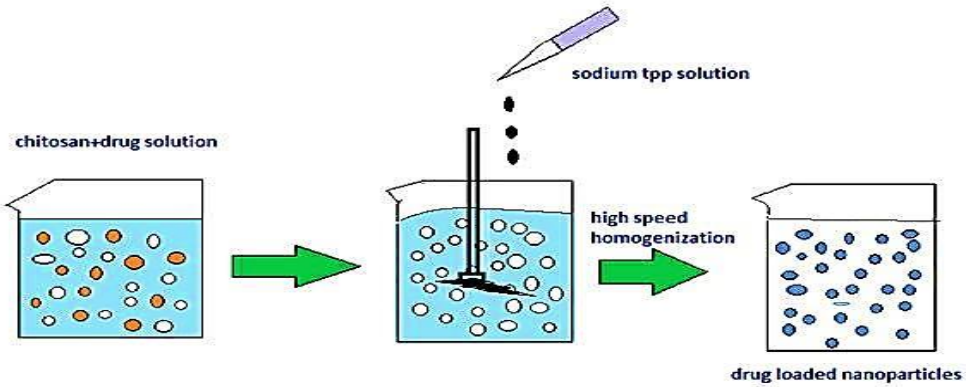


Ionic gelation technique:

The use of natural polymers like chitosan and alginates in oral administration systems rather than harmful chemical polymers improves the penetration effect, enzyme inhibitory ability, and mucoadhesive property of the medication.

According to the drug's and polymer's solubility, they are dissolved in water or a weak acidic medium, and the resulting solution is then added dropwise while being constantly stirred to the solution containing the counterions and stabiliser. The complexation of oppositely charged species causes gelation and precipitation, resulting in the formation of spherical particles.



Solvent evaporation technique:

Polymeric nanoparticles are frequently prepared using the solvent evaporation approach. In an organic solvent, which also contains the medication, the polymer is dissolved. The end product is then mixed well to create an emulsion by adding it to an aqueous phase that already contains a surfactant or emulsifying agent, such as polyvinyl alcohol, polysorbate 80, poloxamer 188, etc. Following the creation of a stable emulsion, the organic solvent is either evaporated or eliminated by raising the temperature while decreasing the pressure or by constant stirring.

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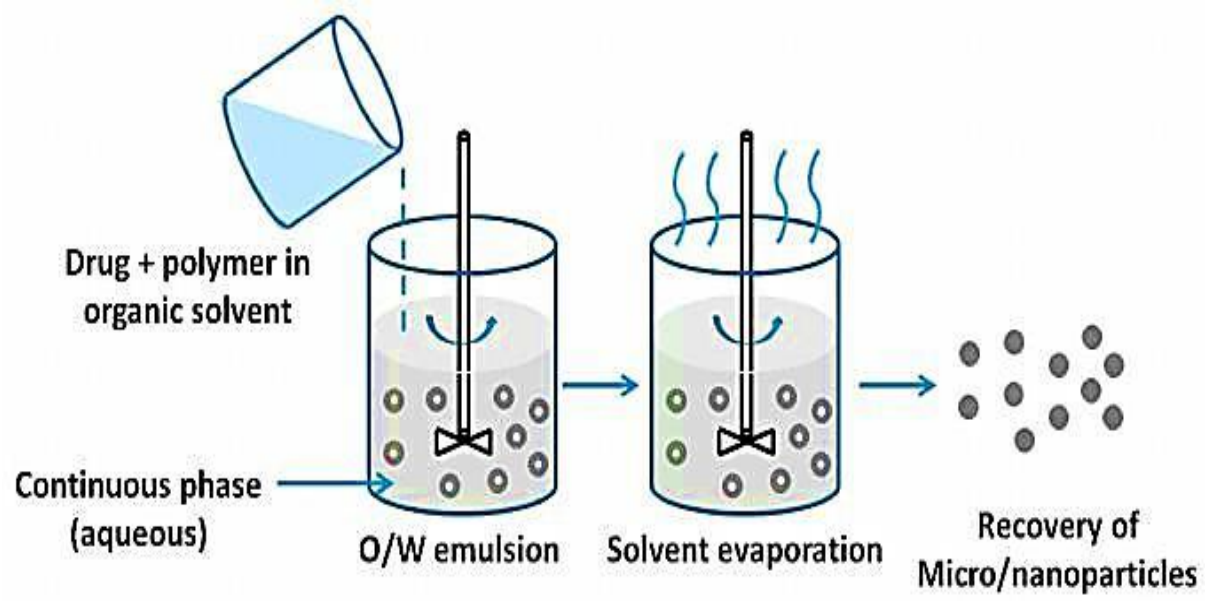

SUPERCRITICAL FLUID TECHNIQUE:

By avoiding the use of organic solvent, supercritical fluid technology provides an intriguing and successful method of producing polymeric nanoparticles. However, environmentally benign solvents that have the ability to create highly pure polymeric nanoparticles free of even a speck of organic solvent are employed. A supercritical fluid is used to dissolve drugs and polymers to create a solution, which is then quickly expanded over an aperture or a capillary nozzle into the surrounding air.

High levels of supersaturation combined with a quick pressure drop after expansion lead to homogeneous nucleation and evenly disseminated nanoparticles of all sizes.

Characterization of Nanoparticles:-

The size, shape, and surface charge of nanoparticles are characterised using cutting-edge microscopic methods as atomic force microscopy (AFM), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). The distribution of nanoparticles in vivo and their physical stability are influenced by factors like size distribution, average particle diameter, and charge. Electron microscopy techniques are used to analyse characteristics such as surface morphology, size, and overall shape. The physical stability, redispersibility, and in vivo performance of a polymer dispersion, as well as its surface charge, are all influenced by the nanoparticles' charges on the outside. In order to properly characterise nanoparticles, it is crucial to consider the surface charge.

1. Particle size:-

Particle size distribution and shape are the primary criteria used to assess nanoparticle characteristics. The morphology and size of nanoparticles can now be determined with the help of electron microscopy. It is simple to assess how nanoparticles are used in drug delivery and targeting by using a variety of methods. The impact of nanoparticle particle size on medication release has already been well-documented.

2. Photon-Correlation Spectroscopy (PCS) or Dynamic Light Scattering (DLS):-

The quickest and most widely used method of assessing particle size is required by current research. Brownian nanoparticle sizes in colloidal solutions are often determined using the quickest and most popular techniques, such as photon-correlation spectroscopy (PCS) or dynamic light scattering (DLS). In this method, when subjected to bright monochromatic light (laser), spherical particles in Brownian motion generate a Doppler shift.

3. Scanning Electron Microscopy (SEM):-

This method, which is based on electron microscopy, directly observes the nanoparticles to identify their size, shape, and surface morphology. Scanning electron microscopy, then, has a number of benefits for morphological and size study.

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However, they only offer a scant amount of data on the size distribution and actual population numbers. The initial transformation of the nanoparticle solution into a dry powder is required for SEM characterization. This dry powder is then deposited on a sample holder and coated using a sputter coater with a conducting metal (such as gold). The entire sample is then scanned using a laser-focused electron beam for analysis [20]. The surface properties of the sample are determined by secondary electrons that are emitted from the sample surface. The nanoparticles' polymer might frequently be harmed by this electron beam.

4. Transmission Electron Microscope:-

Because of their small size, which restricts the use of conventional methods for assessing their physical properties, nanostructures provide experimental challenges. With an atomic or sub-nanometer spatial resolution, transmission electron microscopy techniques can give imaging, diffraction, and spectroscopy data of the specimen concurrently or in a serial fashion. Although TEM and SEM operate on separate principles, they frequently produce the same kinds of data. Because samples must be super thin for electron transmission, sample preparation for TEM is difficult and time-consuming. The fundamental research essential to nanoscience and nanotechnology depends on high-resolution TEM imaging in combination with nanodiffraction, atomic resolution electron energy-loss spectroscopy, and nanometer resolution X-ray energy dispersive spectroscopy techniques.

5. Atomic Force Microscopy:-

This technique is also known as scanning force microscopy (technique that forms images of surfaces using a prob that scans the specimen), very high resolution type of scanning probe microscopy, with reported resolution on the order of fractions of a nanomerter, more than 100 times better than the optical diffraction limit. The atomic force microscopy is based on a physical scanning of samples at sub-micron level using a probe tip of atomic scale and offers ultra-high resolution in particle size measurement.

6. Drug Release:-

It's very essential to determine extent of the drug release and in order to obtain such information most release methods require that the drug and its delivery vehicle be separated. drug loading capacity of the nanoparticles is defined as the amount of drug bound per mass of polymer or in another term it is the moles of drug per mg polymer or mg drug per mg polymer or it could also be given as percentage relative to the polymer. Various techniques such as UV spectroscopy or high performance liquid chromatography (HPLC) after ultracentrifugation, ultra filtration, gel filtration, or centrifugal ultrafiltration are used to determine this parameter. Methods that are employed for drug release analysis are also similar to drug loading assay which is more often assessed for a period of time to evaluate the drug release mechanism

The best criteria for designing therapeutic nanoparticles are:

The fast clearance upon systemic distribution is one of the most important criteria to be considered while creating therapeutic nanoparticles. Nanoparticle surfaces may undergo asopsonization, a type of non-specific protein adsorption, after entering the bloodstream. By doing this, they become more apparent to phagocytic cells. By being phagocytosed by the mononuclear phagocyte system (MPS) in the liver and by spleen filtering, these opsonized nanoparticles may be easily removed from the bloodstream. Before creating therapeutic nanoparticles, it is important to take into account factors that control the clearance and biodistribution of nanoparticles. The circulation and biodistribution of nanoparticles as they pass through physiological processes such hepatic filtration, tissue extravasation/diffusion, and kidney excretion are significantly influenced by nanoparticle size. Since particle size influences its protein absorption rate, naoparticles (size range: 200 nm) demonstrated various rates.

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