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RECENT PROGRESS IN NANOTECHNOLOGY

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ABSTRACT

Nanotechnology is the branch of science in which involves manipulating small sized atoms and molecules at the nanoscale. Nanotechnology is the technique. The rapid development of Nanotechnology research in the recent year is closely related to advances made in metrology. Nanotechnology is the opened way for creating and verifying the various types of nanostructures. Nanotechnology is the technique and it having the full scope of contribution in the field of human health care. The nanotechnology is impact on the disease prevention, treatment, care and diagnosis. In the Nanotechnology the drug has rapid absorption, distribution, and controlled dose release and less side effect or adverse effect. Progress in nanotechnology has resulted in the development of nanomaterials with physico-chemical characteristics. Nanotechnology can be helpful for the treatment of cancer or targeting the cells. In nanotecnology the dose of drug is less and therapeutic effect is high. The concentration of drug is minimum but their helpful effect are maximum and they are treat the patient. Our aim is to review on the progress in nanotechnology.

Keywords: Nanotechnology, Metrology, Concentration, Healthcare, Neosomes.

I. INTRODUCTION

Nanotechnology can be defined as the science and engineering it involves in the synthesis, design characterization and applications of materials and devices whose smallest functional organization in atleast one dimension is one of the nanometer scale. Nanotechnology represents a broad field with an exponential growth holding of the immense potential in the cancer cells treatment. In recent searching procedure mainly focusing on the targeted cancer cell using nano-sized particles. The nanoparticles are small colloidal particles which are made up of non-biodegradable and biodegradable polymers. The biodegradable polymers can be dissolve itself. In nanotechnology the nanoparticles can be used its size between 1-100 nanometer with interracial layer and diameter is 200 nm. In the Nanotechnology technique the nanoscale device can be use. The nanodevices are serve as customized targeted drug delivery vehicles to carry large doses of chemotherapeutic drugs and genes into the malignant cells while it is sparing healthy cells. In the Nanotechnology the engineering concepts focuses on the diffusion, erosion, degradation, shear, swelling passive cell uptake, active cell uptake of the drugs. And the science are focuses on the absorption, Distribution, Metabolism, Excreation of drugs. In Nanotechnology drugs has capability to regulate release of drug and improve the effectiveness of drug. A number of obstacles may be overcome with various novel applications of nano drug delivery.

Carriers In Nanotechnology

1) Liposomes
2) Neosomes
3) Ethosomes
4) Microparticles
5) Dendrimers

(1) LIPOSOMES

The liposomes are the spherical, closed colloidal structure composed of lipid bilateral.

The liposomes were discovered in the early 1960s by Bingham and Co-workers it became the most extensively explored drug delivery system.

The liposomes are phospholipid based colloidal vesicular arrangement in which hydrophilic core is entirely enclosed by lipid bilayer.

The liposomes are manufactured using various procedures in which the hydrophilic materials entrapped by using aqueous solution of these materials as hydrating fluid or by the addition of drug at some stages during manufacturing.

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The liposomes due to their biphasic environment can act as carriers for hydrophilic and lipophilic.

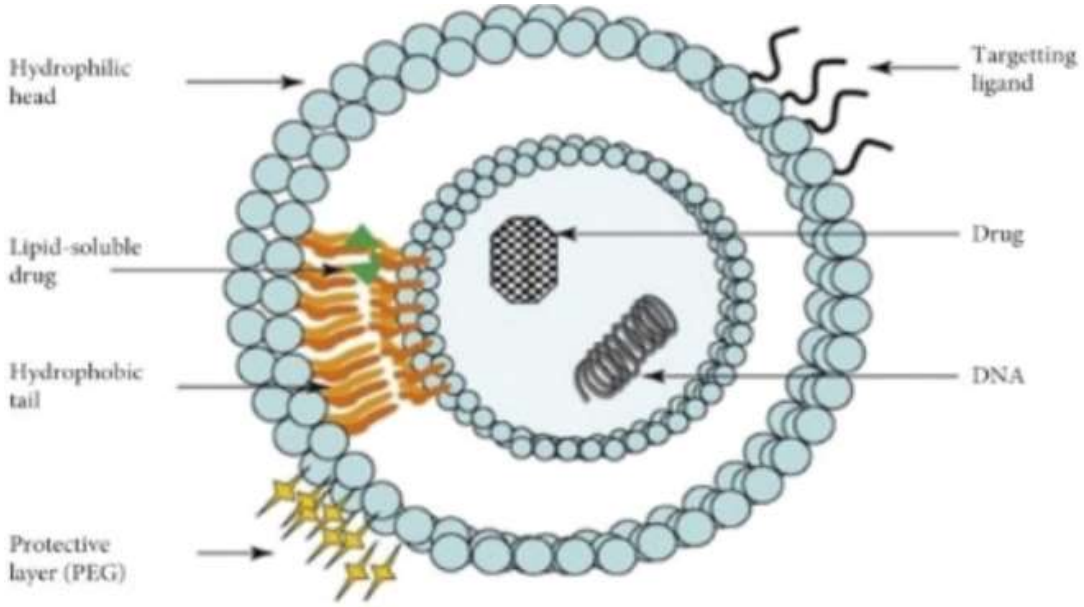

Fig 1: Structure of liposomes

Highly hydrophilic drugs are located in aqueous domains.

And highly lipophilic drugs are entrapped within bilayer of liposomes.

Drugs with poor biphasic insolubility mostly anticancer drugs like 6-mercaptopurine and allopurinol are experienced to be problematic due to their immiscibility with both aqueous and lipidic domains

In liposomal formulations the drug phospholipid ratio is kept maximum that favors homing /loading of the drug.

The drug is hydrophilic, lipophilic, amphiphilic or biphasic the degree of entrapment may range from nil to 100%.

Liposomes have also been successfully used for several other practices in drug delivery such as solubilization of water insoluble drugs,protection of sensitive drug molecules,alteration of pharmacokinetics and biodistribution and enhancing intracellular uptake.

The delivery aspect of liposomes could also be exploited for drugs that must penetrate the plasma membrane in order to be therapeutically beneficial.

The use of liposomal delivery system is the formulation of better tolerated preclinical and clinical formulations where these carriers serve as a formulation adjuvant or excipients.

AmBisome (liposomal formulation) is the hallmark in the field of liposomal research as the product is now available in the market for clinical uses.

Methods Of Liposome Preparation

(1)Physical dispersion technique –

A) Lipid film hydration by hand shaking,non hand shaking

B) High shear homogenization/Sonication

C) Membrane extrusion

D) Microfluidizer technique for micro emulsification

E) French pressure cell

F) Dried-reconstituted vehicles

G) Fusion method

(2) Solvent dispersion technique-

A) Ethanol injection

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B) Eher injection

C) Reverse phase evaporation vehicles

D) Emulsion and double Emulsion vehicles

(3) Detergent solubilization technique

(2) NIOSOMES

Niosomes are non-ionic surfactant vesicles with a similar structure of liposomes.

Non-ionic surfactant vesicle results from the self-assembly of hydrated surfactant monomers.

Non-ionic surfactant of a wide variety of structural types have been found to be useful alternatives to phospholipid.

Non-ionic surfactant vesicles are prepared by the incorporation of components containing Non ionic surfactants.

They may also be prepared with various ionic amphiphiles such as dicetylphosphate ,Stearylamine etc in order to achieve a stable vesicular suspension.

The ultimate identity of any niosomal system and hence its properties are determined by the its factors.

Although pharmaceutical niosome formulations have yet to be commercially exploited a number of studies have demonstrate the potential of niosomes in drug delivery.

Niosomes have been proven to be useful in the delivery of anti-infective agent,anticancer agent and fairly recently as vaccine adjuvants.

Examination of the literature reveals that on I.V.administration of niosomes the highest drug levels are found in liver.

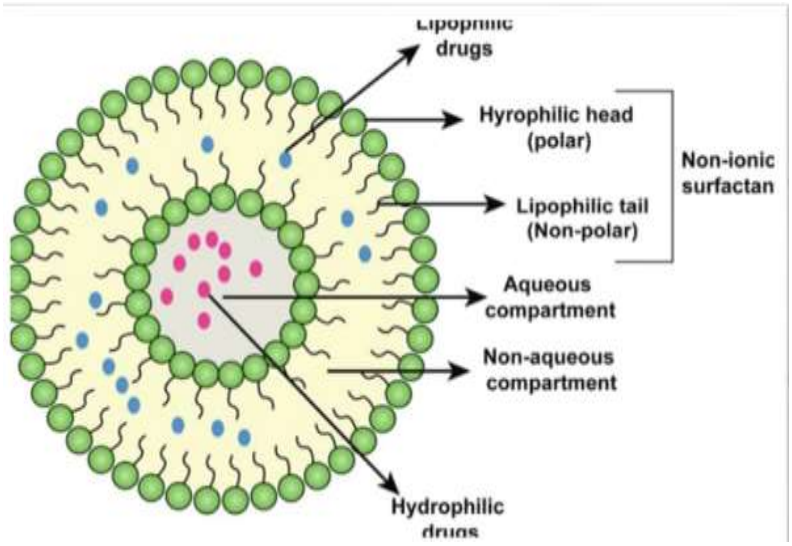

Fig 2: Structure of Niosomes

Preparation Methods of Niosomes-

1) Hand shaking method

2) Reverse phase evaporation technique

3) Ether injection method

4) Multiple membrane extrusion method

5) Bubble Method

6) Sonication

(3) Ethosomes

Ethosomes are lipid vesicles with high content of Ethanol.

They can penetrate the skin and enhance compound delivery both to deep skin strata and systemically because Ethanol flui dizes both lipid bilayer of the stratum corneum and intercellular lipid.

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Ethosomal system are easy to prepare non irritant and it compose mainly of phospholipid and Ethanol compound commonly found in the pharmaceutical preparation.

The liposomes, Ethosomes are shown to exhibit high encapsulation efficiency for a wide range of molecules including lipophilic drugs and are effective at delivering molecules and through the skin.

The liposomes prepared in the absence of Ethanol the phospholipid in Ethosomes are loosely packed and the membrane tends to be permeable for cations.

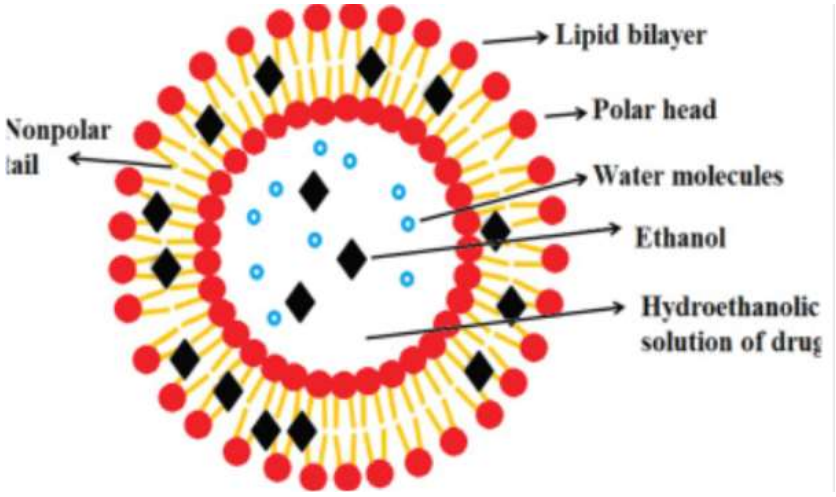

Fig 3: Structure of Ethosomes

Permeation enhancement is greater in case of ethosomes than Ethanol alone.

And this indicates that there may be some kind of synergistic mechanism between Ethanol vesicles and skin lipids.

The exact mechanism of drug delivery by Ethosomes remains a matter of speculation most like a combination of processes which contribute to the enhanced permeation effect.

Ethanol in the Ethosomes seems to disrupt the organization of the stratum corneum lipid bilayer and hence enhances its lipid fluidity.

It was found that the fluorescent probe D-289 penetrate the skin to a much greater depth from Ethosomes than from classic liposomes the latter as expected remained in the upper layers of the skin.

Preparation Methods of Ethosomes –

1) Hot method

2) Cold method

(4) Microparticles

There are defined as a spherical particing core 2mm containing a core substance. Microspheres am sense, spherical empty particles.

However, the terms microcapsules and In addition, some related terms are used as microspheres are often used interchangeably. Well. For example, “microbeads” and “beads” particles are also used for particles of large are used alternatively.

Spheres and spherical size and rigid morphology.

The dried micro spheres form a free-flowing powders.

They which biodegrade and ideally have a size consist of proteins or synthetic polymers, degradable microspheres bearing a drug range less than 200 μm.

The solid bio- dispersed or dissolved throughout particle matrix have a potential in controlled-release attention not only as prolonged-release of drugs.

These carriers received much formulations but also for their carrier potential in drug targeting particularly anti-cancer drugs to the tumor.

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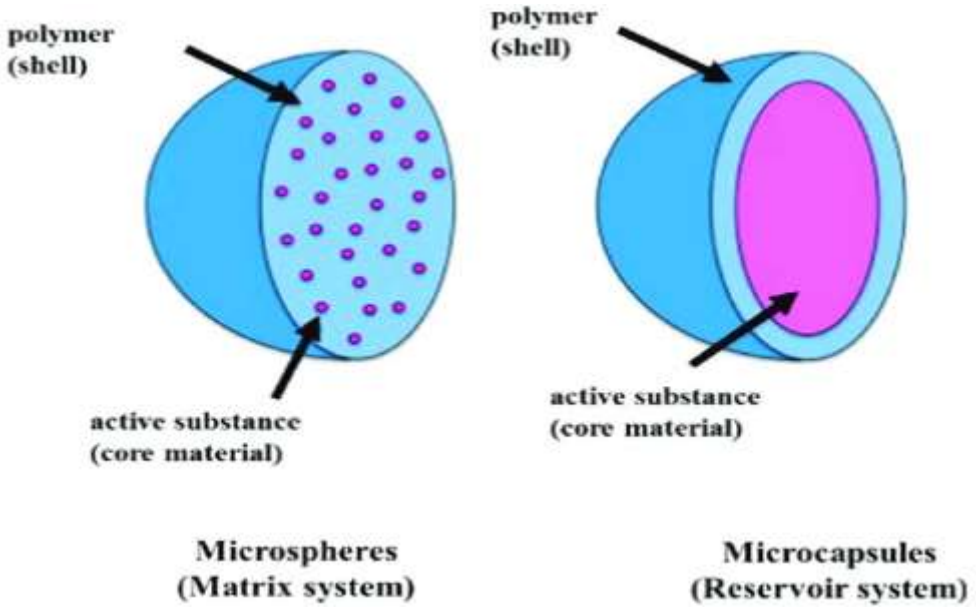

Fig 4: Structure of Microparticles

A number of different substances both biodegradable as well as non-biodegradable have been investigated for the preparation of microspheres.

These materials include the polymers of natural and synthetic origin and also modified natural substances.

Synthetic polymers employed as carrier materials are methyl methacrylate, acrolein, lactide, glycolide and their copolymers, ethylene vinyl acetate copolymer, polyanhydrides, etc.

The natural polymers used for the purpose include ase albumin, gelatin, starch, collagen and carrageenan.

Preparation Methods of Microparticles

(A) Chemical Method-

1) Emulsion method

2) Inter facial polymerization

3) Insitu Polymerization

(B) Physical Method-

1) Suspension cross linking

2) Solvent evaporation

3) Hot melt microencapsulation

4) Phase separation

5) Spray drying

6) Fluidized bed coating

7) Controlled coating

8) Rapid expansion

(5) Dendrimers –

Dendrimer construction is fundamentally based on two basic methods.

The divergent method, where one branching unit after another is successively attached to the core molecules.

The multiplication of the number of peripheral groups is dependent on the branching multiplicity. -Secondly, the method that involves the opposite course is the convergent method.

The skeleton is built stepwise starting from the end group towards molecule to produce the dendrimers.

Either of the synthetic strategies possesses relative advantages and disadvantages of their choice depends mainly on the kind of monomer employed and the ultimate target polymer structure

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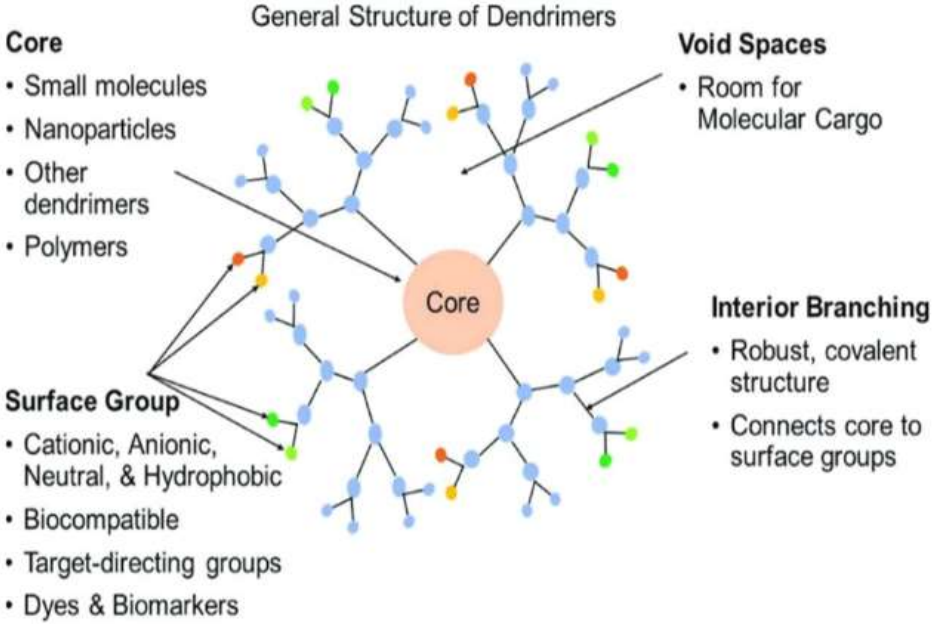

Fig 5: Structure of Dendrimers

The application of dendrimers in pharma- ceutical and medical chemistry is becoming one of the most attractive areas. -Being well- defined structure, compact globular shape, size, monodispersity and controllable surface functionalities, dendrimers offer excellent candidature for drug delivery.

Dendimers can be utilized as potential drug carriers in two ways: firstly, drug molecules can be physically entrapped inside the dendritic structure, and secondly, drug molecules can be covalently linked onto the dendrimer surface or other functionalities to produce dendrimer-drug conjugates.

A variety of applications have been explored especially in gene transfection and medical imaging vis-a-vis as drug delivery systems. -Dendrimers provide new platform for the transfection and mani- pulations of cells.

They are structurally- defined and provide very high transfection efficiency in vitro with a wide variety of cell types.

These polymeric moieties also furnish a soluble nanometric matrix for drug mole- cule(s) attachment/incorporation or other materials useful in enhancing transfection.

Preparation Methods of Dendrimers-

1) Divergent method

2) Convergent method

Recent Formulations in Nanotechnology

1) Nanosuspension
2) Nanoneedles
3) Carbon nanotubes
4) Micro emulsion
5) Nanogel

(1) Nanosuspension

Nanosuspension is defined as the dispersion of sub-micron colloidal drug particles in water and stabilized by using surfactant. The particle size-distribution of the solid particles in nanosuspensions is usually less than 1 micrometer with an average particle size range of 200-600 nm. The need for nanosus- pensions as a dosage form is recognized as a means to administer therapeutic quantities of water-insoluble dosage forms. The reduction of drug particles into the sub-micron range leads to a significant increase in the disso- lution rate and therefore, enhances bioavaila- bility. Various mechanisms have been explained which account for the improved bioavaila- bility of these systems. These include adhesion of drug nanoparticles to the mucosa, increased saturation solubility which leads to increased concentration gradient across GI tract lumen and blood, and

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increased dissolution rate of the drug. Preparation of nanosuspensions has been reported to be a more cost-effective and technically-simpler alternative, particularly for poorly soluble drugs. It yields a physicallymore stable product than liposomes, the conventional colloidal drug carriers. The stability of the particles obtained in the nano- suspension is attributed to their uniform particle size which is created by various manufacturing processes. The absence of particles with large differences in their size in nanosuspensions prevents the existence of different saturation solubilities and con- centration gradients, consequently preventing the Ostwald ripening effect. Nanosuspension engineering processes currently used are preparation by precipitation, high-pressure homogenization, emulsion and milling techniques. The inherent high loading of this dosage form distinguishes it from liposomes, emulsions, cyclodextrins, and polymeric nanoparticles. These delivery systems can be administered through different routes including parenteral, ocular, pulmonary, oral, etc. Many drugs such as paclitaxel, clofa- zimine and itraconazole have been administered through parenteral route and resulted into an enhanced efficacy. The safety profile of drug has been reportedly observed to be improved in many drugs when compared to their respective conventional solution forms. This occurs due to deletion of noxious excipients, change in the pharma co kinetic profile, or regional delivery, thus minimizing systemic toxicity. Nanosuspensions have numerous applications such as the delivery of regional anaesthetics, treatment of malignant hyper- thermia, fungal treatment, cancer chemo- therapy and intrathecal pulmonary/nasal delivery of drugs. Nanosuspensions can also be used for targeted delivery by altering the surface properties of dispersed phase.

Preparation Methods of Nanosuspension

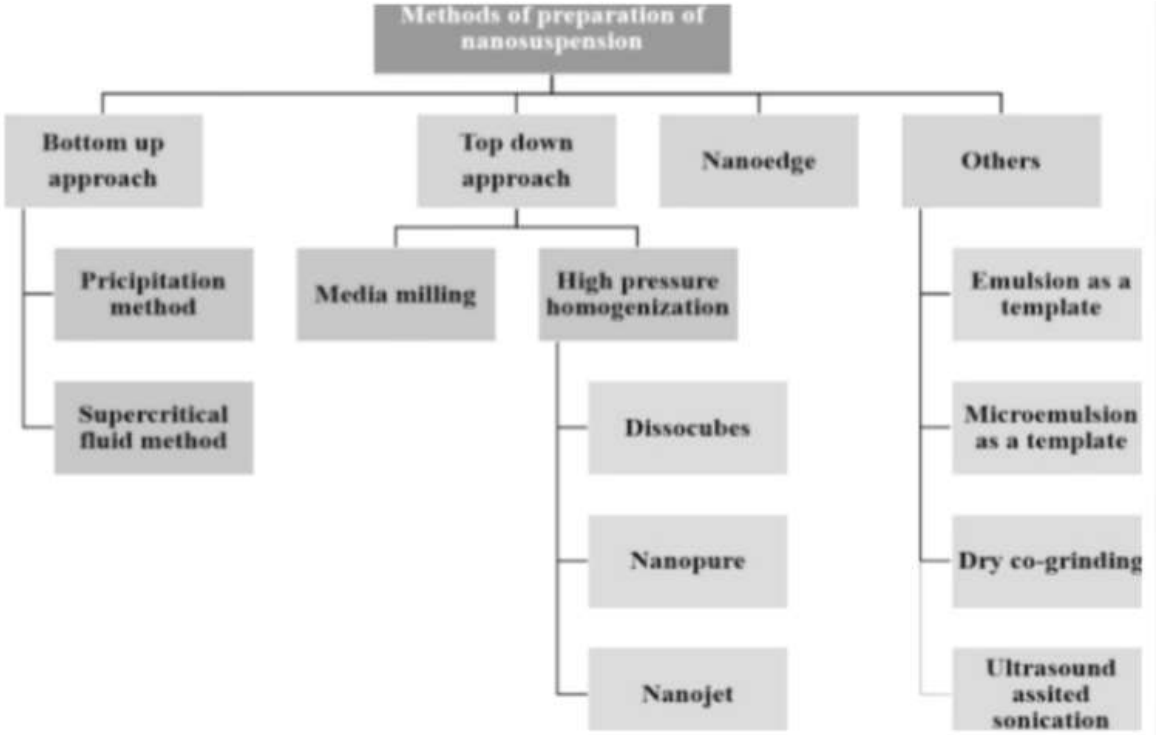

Fig 6:

Evaluation methods of Nanosuspension

A) In vitro evaluation

1) Particle size and size distribution

2) Particle charge

3) Crystalline state and morphology

4) Saturation solubility and dissolution viscosity

B) In vivo evaluation

1) Surface hydrophobicity

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2) Interaction with body protein

Stability Enhancement of Nanosuspension-

1. Select the appropriate stabilizer – The type of stabilizer used can be affect on the solubility of drug. Stabilizer can be emulsifier,Texture modifiers,weighing agents and ripening retarded.
2. Use Ultrasound- Ultrasound assisted sonocrystallization can be reduce the Particle size and control the size distribution of the active ingredient. It can be minimize crystallization process.
3. Use mechanical and chemical techniques.
4. Use Electron microscopy- This technique can be use to observe the distribution and aggregation of Nanoparticles
5. Use differential scanning colorimetry – Used to inspect the melting point and recrystallization behaviour of Crystalline materials.

(2) Nanoneedles

The most popular nanomaterial for genetic delivery in cell engineering is nanoparticles, however introducing nucleic cargoes or medications into cells directly and selectively is typically challenging.An alluring substitute method for directly delivering several genetic payloads into a single cell over a predetermined time span is the use of nanoneedles. Because of their nanoscale dimension, nanoneedles can be directly introduced into the cytoplasm or nucleus without inflicting major cellular damage, unlike microinjection, which is typically difficult to accomplish without harming cells (Han et al., 2008). Using an atomic force microscope (AFM) tip measuring 200 nm in diameter and 6 μm in length, for instance, it was possible to successfully introduce a plasmid expressing the green fluorescent protein (GFP) gene into human embryonic kidney and primary cultured MSCs.

Fig 7: Nano needle

By employing electrostatic contact, the GFP plasmid was adsorbed onto the AFM tip and introduced into cells with a high degree of effectiveness (over 70%) and minimal cellular damage. Solid and hollow nanoneedles can be distinguished from one another based on their 1D nanostructures. The manufacture of nanoneedles can be categorised into two approaches based on basic fabrication principles: top down and bottom up. This section will provide a quick overview of the common methods used to fabricate nanoneedles and discuss their uses in drug delivery and cell sensing.

Advantages of nanoneedles-

1) Increasing hydration of skin

2) Reducing swelling of skin

3) Improving the appearance of acne scarring

4) Improve skin texture

5) Reducing the appearance of enlarged pore

(3) Carbon nanotubes

Preparation Methods of Carbon Nanotubes –

Carbon nanotubes (CNTs) are a one-dimensional (1 D) carbon allotrope composed of a cylindershaped sp2 hybridised carbon lattice. The most basic type of CNT is called a singlewall CNT (SWCNT), and it is made up of a single, cylindrical graphene tube. Doublewall and multiwall carbon nanotubes (CNTs) consist of two or more

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tubes that are coiled in a scroll-like pattern or nested concentrically. SWCNTs typically have a diameter of 0.4-2 nm, whereas MWCNTs can have much larger diameterstens of nanometersand are typically capped on both ends by domes that resemble fullerenes.First of all Because of their form and graphitelike arrangement of carbon atoms, carbon nanotubes (CNTs) have extraordinary and unique features that make them comparable to fullerenes and graphene, which are the related 0- and 2-D allotropes of carbonin the extensive application of carbon nanotubes (CNTs) in a variety of scientific and technological domains, including as electronics, energy storage, structural composites, biomaterials, and others. CNTs are perfect for usage in metal, ceramic, and polymer matrix composites due to their highly anisotropic mechanical, electrical, and thermal properties resulting from their 1D structure. They are also used in battery and supercapacitor components due to their electrical characteristics extremely high surface to volume ratio and possibility for chemical functionalisation. Similarly, functionalized with polyethylene glycol (PEG) (known as PEGylated CNTs) ene also been extensively used to improve has solubility of CNT-conjugates, as well as to impart biocompatibility to the carrier. Wu et al., reported the possible use of functionalized CNTs in targeted delivery of Amphotericin B (Amp B) to the Jurkat cells in vitro. In this study they demonstrated that the solubility- related toxicity of Amp B can be decreased on covalent attachments of Amp B to the f-CNT. FCNT have also been studied for the delivery of macromolecules such as proteins, peptides and vaccine.

1) Arc discharge method

2) Laser Ablation Method

3) CVD (Chemical Vapour Deposition)

Stability Enhancement of Carbon nanotubes –

Adding boron and phosphorus compound it improve thermal stability.

Surfactant mediation and novel matrix integration can improve dispersion stability

Advantages of Carbon nanotubes-

1) Chemical Stability

2) Enhanced flexibility

3) Biocompatible

4) Multifunctional

5) Temperature resistant

(4) Microemulsion

Microemulsion is a dispersion of two immiscible liquids that is thermodynamically stable and isotropically transparent. It is composed of microdomains of one or both liquids that are stabilised by interfacial films of molecules that are surface active. The transparent, fluid systems created by desiccating a regular milky emulsion (macroemulsion) to the point of clarity and adding a mediumchain alcohol, such as pentanol or hexanol, are referred to as microemulsions by Schulman and colleagues. Thus, throughout the course of the year, the same systems that Schulman referred to as micro-emulsions have been precisely described as thermodynamically-stable emulsions, transparent emulsions, micellar emulsions, swelling micelles, and reverse micelles in the literature. Three forms of microemulsions can be distinguished bicontinuous, oil-in-water (oil/water), and water-in-oil (water/oil).It is thus demonstrated that droplet phases and bicontinuous phases are related to microemulsions. Microemulsion is made up of tiny oil droplets scattered throughout water at higher water concentrations, or o/w microemulsion. At lower water concentrations, on the other hand, the situation is inverted and the system is made up of water droplets scattered throughout oil, or w/o microemulsion. A surfactant-rich film separates the water and oil in each phase. The electrical double layers that envelop the oil droplets in o/w microemulsions can reach a significant distance (up to 100 nm) into the external phase, contingent upon the concentration of electrolyte.In contrast, w/o systems are stabilized primarily by steric interactions between the absorbed films in such a way that the hard sphere volume of the droplets tends only slightly greater than that of the water pools. The droplet interaction can take place at relatively short distances of separation, where the tail of the hydrocarbon chains can interpenetrate each other.

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Preparation Methods of Microemulsion

1. Phase titration method
2. Phase inversion method

Evaluation methods of microemulsions

1. Thermodynamic stability test
2. Visual inspection
3. Photon correlation Spectroscopy
4. Digital PH meter

Advantages of Microemulsion-

1) Increase rate of absorption
2) Helps solubilize lipophilic drug
3) Increase bioavailability
4) Helful in taste masking

Stability Enhancement of Microemulsion

1. Adding emulsifiers -These reduce surface tension and prevent droplet flocculation.
2. Selecting suitable cosurfactants -These are soluble in both water and oil, and can reduce interfacial tension, increase fluidity, and adjust the hydrophilic–lipophilic balance of surfactants.
3. Adding stabilizers - These increase the viscosity of the aqueous phase and increase the repulsive force between oil droplets.

(5) Nanogels

Physically and chemically crosslinking polymers to hydrogel at the nanoscale yields nanogel. The normal size of a nanogel is 20200 nm. Nanogels are distinguished by their size, increased surface area, and hygroscopicity, in addition to their bulging and degrading features. Nanogels enable the regulated and extended release of pharmaceuticals. They are easily able to ensnare medications, polymers, and liquid phases in suspension employing nanogels due to their three dimensional framework. The holes in nanogel can accommodate even very large molecules. Because of their ability to swiftly establish biomolecular connections with physiologically active substances like salt bonds and hydrophobic or hydrogen bonds, they are useful as drug carriers. A special kind of composite material known as nanogel combines the properties of liquids and solids.The length of time that nanoparticles remain in touch with the skin following their entrapment inside a nanogel matrix is positively connected with the success of the therapy, as per the theoretical framework.4.5

Preparation Methods of Nanogels

1. Emulsions Solvent diffusion method
2. Nano precipitated method
3. Evaporation of the Solvent method
4. Reverse micellar method
5. Modified diffusion emulsification method

Stability Enhancement of Nanogels –

1. Use Physical self-assembly – Instead use thermal denaturation gelation to form nanogels through physical self-assembly.
2. Add surface modifiers
3. Add Co Solvent- Add water or dimethyl sulfoxide to improve the monomers solubility and Stability of droplets .
4. Use Temperature responsive polymers.

Evaluation methods of Nanogels

1. PH measurement
2. Viscosity measurement

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3. Infrared spectroscopy

4. Atomic force microscopy

Advantages of Nanogels

1. Highly biocompatible

2. Biodegradable

3. Release of therapeutic can be regulated by cross linking densities

4. Good transport characteristics

II. CONCLUSION

Nanothechnology has emerged as a ground breaking scientific disciplines with profound implications for various fields. To sum up our discussion, I would like to state that nanotechnology is a relatively new technology that has just recently emerged. It is a scientific revolution that will completely alter our previous understanding of the world. In not too distant a future, the science fiction future we have been witnessing will come true. Because technology will transform energy more effectively, it will provide us with abundant energy. Since nanotechnology is so vast and will continue to expand in the near future, it will enable many of the inventions that scientists are now working on, such as teleportation, to become a reality. In ground transportation, ships, aeroplanes, and space vehicles, nanotechnology may enable the production of lighter, stronger, and programmable materials that promise better fuel efficiency and need less energy to generate than conventional materials. The application of nanorobotics may play a significant role in the future of nanotechnology. These nanorobots may perform jobs that humans could never accomplish as well as things that humans could never perform. A whole field of nanosurgery would be developed to treat conditions including diabetes, bone spurs, and natural ageing.

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