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SOLID LIPID NANOPARTICLE IN DRUG DELIVERY SYSTEM- A REVIEW

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ABSTRACT

Strong lipid nanoparticles (SLN) are at the bleeding edge of nanotechnology, with various possibilities utilizes in drug conveyance and exploration. Lipid nanoparticles give the chance of growing new treatments because of their size-subordinate attributes. The capacity to integrate drugs into Nano carriers makes a clever medication conveyance idea that may be utilized for drug focusing on. Accordingly, strong lipid nanoparticles certainly stand out from specialists as a promising method for accomplishing the target of controlled and site-explicit medication conveyance. This audit covers the objectives, creation methods, lead, limitations, and potential answers for strong lipid nanoparticles. Photon connection spectroscopy, filtering electron microscopy, and disparate examining calorimetric are among the fitting insightful methods for the portrayal of SLN. Angles

Key words- Lipid, Nano particle, Drug, nanotechnology

Presentation

1.1 NANOPARTICLES IN DRUG DELIVERY SYSTEM

Nanoparticles are characterized as particulate scatterings or strong particles with a size in the scope of 10-1000nm. The medication is broken up, ensnared, epitomized or connected to a nanoparticle lattice. Contingent on the strategy for readiness, nanoparticles s, Nano spheres or Nano cases can be gotten. Nanoparticles are materials with generally aspects in the Nano scale, i.e., under 100 nm. Lately, these materials have arisen as significant players in current medication, with utilize going from contrast specialists in clinical imaging to transporters for quality conveyance into individual cells. Nanoparticles have various properties that separate them from mass materials essentially by ethicalness of their size, like compound reactivity, energy ingestion, and organic versatility.

Strong lipid nanoparticles (SLN) presented in 1991 address an elective transporter framework to custom colloidal transporters, for example, - emulsions, liposomes and polymeric miniature - and nanoparticles1. Nanoparticles produced using strong lipids are drawing in significant consideration as original colloidal medication transporter for intravenous applications as they have been proposed as another particulate transporter framework. SLN are sub-micron colloidal transporters going from 50 to 1000 nm, which are made out of physiological lipid, scattered in water or in watery surfactant arrangement. SLN offer extraordinary properties, for example, little size, huge surface region, high medication stacking.

Grouping of Nanoparticles

The nanoparticles are by and large characterized into the natural, inorganic and carbon based.

2.1 Natural nanoparticles

Dendrimers, micelles, liposomes and ferritin, and so forth are generally knows the natural nanoparticles or polymers. Deeply, otherwise called nano cases and are touchy to warm and electromagnetic radiation like intensity and light. These remarkable qualities settles on them an optimal decision for drug conveyance. The medication conveying limit, its soundness and conveyance frameworks, either captured drug or adsorbed drug framework decides their field of uses and their effectiveness separated from their ordinary attributes like the size, structure, surface morphology, and so forth. The natural nanoparticles are most generally utilized in the biomedical field for instance drug conveyance framework as they are effective and furthermore can be infused on unambiguous pieces of the body that is otherwise called designated drug conveyance.

Natural nanoparticles:

a – Dendrimers

b - Liposomes and

c - micelles.

2.2. Inorganic nanoparticles

Inorganic nanoparticles are particles that are not comprised of carbon. Metal and metal oxide-based nanoparticles are by and large classified as inorganic nanoparticles

2.2.1. Metal based.

Nanoparticles that are integrated from metals to nanometric estimates either by horrendous or valuable techniques are metal based nanoparticles. Practically every one of the metals can be blended into their nanoparticles. The usually involved metals for nanoparticle combination are aluminum (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc (Zn). The nanoparticles have unmistakable properties such sizes as low as 10 to 100nm, surface attributes like high surface region to volume proportion, pore size, surface charge and surface charge thickness, glasslike and nebulous designs, shapes like circular and round and hollow and variety, reactivity and aversion to natural factors, for example, air, dampness, intensity and daylight and so on.

2.2.2. Metal oxides based.

The metal oxide-based nanoparticles are incorporated to change the properties of their particular metal-based nanoparticles, for instance nanoparticles of iron (Fe) in a flash oxidizes to press oxide (Fe_2O_3) within the sight of oxygen at room temperature that expands its reactivity contrasted with iron nanoparticles. Metal oxide nanoparticles are integrated basically because of their expanded reactivity and effectiveness. The ordinarily incorporated are Aluminum oxide (Al_2O_3), Cerium oxide (CeO_2), Iron oxide (Fe_2O_3), Magnetite (Fe_3O_4), Silicon dioxide (SiO_2), Titanium oxide (TiO_2), Zinc oxide (ZnO). These nanoparticles have had an uncommon property when contrasted with their metal partners.

2.3. Carbon based

The nanoparticles made totally of carbon are knows as carbon based [8]. They can be characterized into fullerenes, graphene, carbon nano tubes (CNT), carbon nanofibers and carbon dark and in some cases enacted carbon in nano size.

Carbon based nanoparticles:

a - fullerenes

b - graphene

c - carbon nanotubes

d - carbon nanofibers and

e - carbon dark

association of stages at the point of interaction and are appealing for their capability to further develop execution of drugs (Ref 5,7,8). To beat the impediments related with the fluid condition of the oil drops, the fluid lipid was supplanted by a strong lipid, which in the long run changed into strong lipid nanoparticles. The purposes behind the rising interest in lipid-based framework are many - overlap and incorporate.

1. Lipids improve oral bioavailability and diminish plasma profile changeability.

2.Better portrayal of lipoid excipients.

3. A better capacity to resolve the main points of contention of innovation move and assembling increase.

Union of Nanoparticles

The nanoparticles are integrated by different techniques that are classified into base up or hierarchical strategy. A worked on portrayal of the interaction is introduced in Figure3.

The benefits of utilizing nanoparticles as a medication conveyance framework incorporate the accompanying:

1. Molecule size and surface qualities of nanoparticles can be effectively controlled to accomplish both detached and dynamic medication focusing after parenteral organization.

2. They control and support arrival of the medication during the transportation and at the site of restriction, adjusting organ dispersion of the medication and resulting leeway of the medication in order to accomplish expansion in drug restorative adequacy and decrease in incidental effects.

3. Controlled delivery and molecule debasement attributes can be promptly balanced by the decision of framework constituents. Drug stacking is somewhat high and medications can be integrated into the frameworks with next to no compound response; this is a significant element for safeguarding the medication action.

4. Site-explicit focusing on can be accomplished by connecting focusing on ligands to surface of particles or utilization of attractive direction.

5. The framework can be utilized for different courses of organization including oral, nasal, parenteral, intra-visual and so forth.

Utilizations of Nanoparticles

A rundown of a portion of the utilizations of nanomaterials to science or medication is given underneath:

• Fluorescent organic names

• Medication and quality conveyance

• Bio identification of microbes

• Identification of proteins

• Testing of DNA structure

• Tissue designing

• Cancer annihilation through warming

• Division and cleansing of organic particles and cells

• X-ray contrast improvement

• Phagokinetic studies

As referenced over, the way that nanoparticles exist in similar size space as proteins makes nanomaterials appropriate for bio labelling or marking. Nonetheless, size is only one of numerous qualities of nanoparticles that itself is seldom adequate assuming one is to utilize nanoparticles as natural labels. To communicate with natural objective, an organic or sub-atomic covering or layer going about as a bioinorganic point of interaction ought to be appended to the nanoparticle. Instances of natural coatings might incorporate antibodies, biopolymers like collagen, or monolayers of little particles that make the nanoparticles biocompatible. Moreover, as optical discovery methods are

Classification of Nanoparticles

The nanoparticles are generally classified into the organic, inorganic and carbon based.

2.1. Organic nanoparticles

Dendrimers, micelles, liposomes and ferritin, etc. are commonly knows the organic nanoparticles or polymers. These nanoparticles are biodegradable, non-toxic, and some particles such as micelles and liposomes have a hollow core, also known as nano capsules and are sensitive to thermal and electromagnetic radiation such as heat and light. These unique characteristics makes them an ideal choice for drug delivery. The drug carrying capacity, its stability and delivery systems, either entrapped drug or adsorbed drug system determines their field of applications and their efficiency apart from their normal characteristics such as the size, composition, surface morphology, etc. The organic nanoparticles are most widely used in the biomedical field for example drug delivery system as they are efficient and also can be injected on specific parts of the body that is also known as targeted drug delivery.

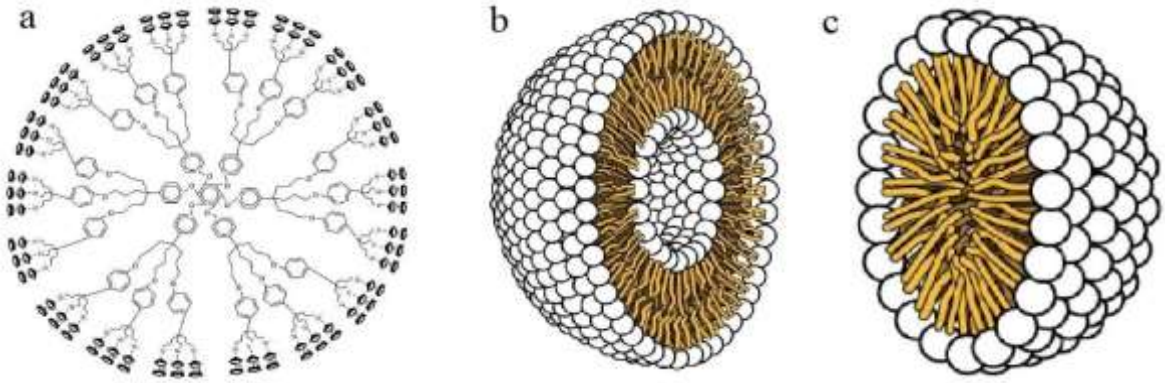

Figure 1. Organic nanoparticles: a – Dendrimers, b – Liposomes and c – micelles.

2.2. Inorganic nanoparticles

Inorganic nanoparticles are particles that are not made up of carbon. Metal and metal oxide-based nanoparticles are generally categorised as inorganic nanoparticles

2.2.1. Metal based.

Nanoparticles that are synthesised from metals to nanometric sizes either by destructive or constructive methods are metal based nanoparticles. Almost all the metals can be synthesised into their nanoparticles. The commonly used metals for nanoparticle synthesis are aluminium (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc (Zn). The nanoparticles have distinctive properties such sizes as low as 10 to 100nm, surface characteristics like high surface area to volume ratio, pore size, surface charge and surface charge density, crystalline and amorphous structures, shapes like spherical and cylindrical and colour, reactivity and sensitivity to environmental factors such as air, moisture, heat and sunlight etc.

2.2.2. Metal oxides based.

The metal oxide-based nanoparticles are synthesised to modify the properties of their respective metal-based nanoparticles, for example nanoparticles of iron (Fe) instantly oxidises to iron oxide (Fe_2O_3) in the presence of oxygen at room temperature that increases its reactivity compared to iron nanoparticles. Metal oxide nanoparticles are synthesised mainly due to their increased reactivity and efficiency. The commonly synthesised are Aluminium oxide (Al_2O_3), Cerium oxide (CeO_2), Iron oxide (Fe_2O_3), Magnetite (Fe_3O_4), Silicon dioxide (SiO_2), Titanium oxide (TiO_2), Zinc oxide (ZnO). These nanoparticles have possessed an exceptional property when compared to their metal counterparts.

2.3. Carbon based

The nanoparticles made completely of carbon are knows as carbon based [8]. They can be classified into fullerenes, graphene, carbon nano tubes (CNT), carbon nanofibers and carbon black and sometimes activated carbon in nano size and are presented in Figure2.

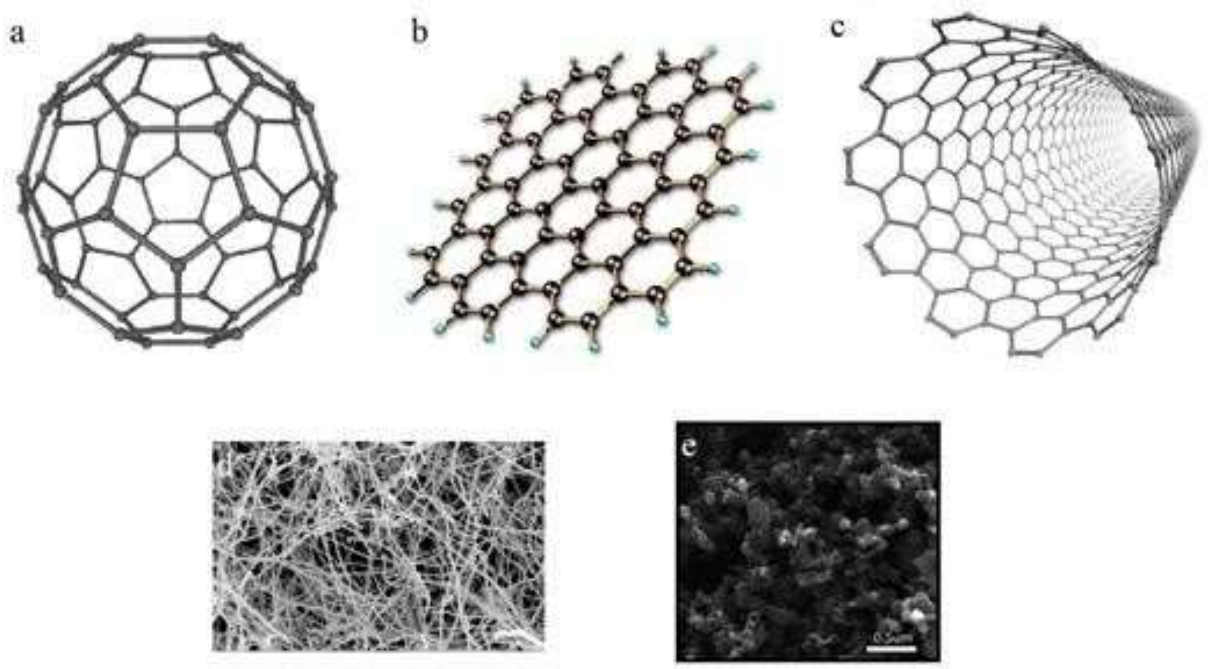

Figure 2. Carbon based nanoparticles: a – fullerenes, b – graphene, c – carbon nanotubes, d – carbon nanofibers and e – carbon black

interaction of phases at the interface and are attractive for their potential to improve performance of pharmaceuticals (Ref 5,7,8). In order to overcome the disadvantages associated with the liquid state of the oil droplets, the liquid lipid was replaced by a solid lipid, which eventually transformed into solid lipid nanoparticles. The reasons for the increasing interest in lipid-based system are many – fold and include.

1. Lipids enhance oral bioavailability and reduce plasma profile variability.

2.Better characterization of lipoid excipients.

3. An improved ability to address the key issues of technology transfer and manufacture scale-up.

Synthesis of Nanoparticles

The nanoparticles are synthesised by various methods that are categorised into bottom-up or top-down method. A simplified representation of the process is presented in Figure3.

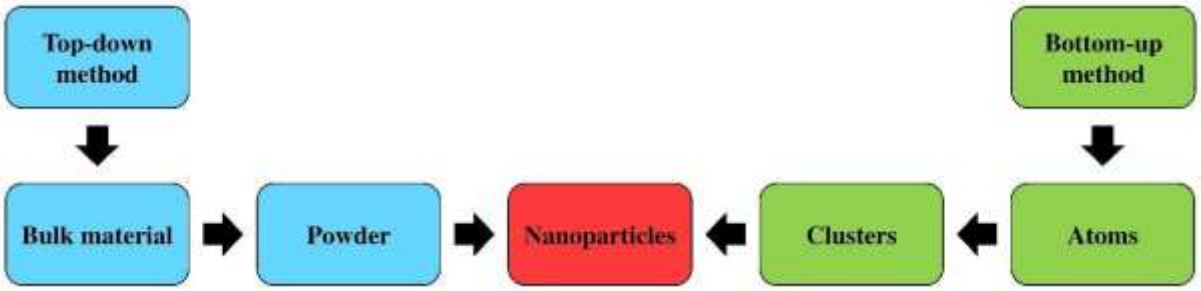

Figure 3. Synthesis process

The advantages of using nanoparticles as a drug delivery system include the following:

1. Particle size and surface characteristics of nanoparticles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.

2. They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.

3. Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents. Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction; this is an important factor for preserving the drug activity.

4. Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.

5. The system can be used for various routes of administration including oral, nasal, parenteral, intra-ocular etc.

Applications of Nanoparticles

A list of some of the applications of nanomaterials to biology or medicine is given below:

- Fluorescent biological labels
- Drug and gene delivery
- Bio detection of pathogens
- Detection of proteins
- Probing of DNA structure
- Tissue engineering
- Tumor destruction via heating
- Separation and purification of biological molecules and cells
- MRI contrast enhancement
- Phagokinetic studies

As mentioned above, the fact that nanoparticles exist in the same size domain as proteins makes nanomaterials suitable for bio tagging or labelling. However, size is just one of many characteristics of nanoparticles that itself is rarely sufficient if one is to use nanoparticles as biological tags. In order to interact with biological target, a biological or molecular coating or layer acting as a bioinorganic interface should be attached to the nanoparticle. Examples of biological coatings may include antibodies, biopolymers like collagen, or monolayers of small molecules that make the nanoparticles biocompatible. In addition, as optical detection techniques are wide spread in biological research, nanoparticles should either fluoresce or change their optical properties. The approaches used in constructing nano-biomaterials are schematically presented below.

Advantages of SLN

- Control and / or target drug release.
- Excellent biocompatibility.
- Improve stability of pharmaceuticals.
- High and enhanced drug content.
- Easy to scale up and sterilize.
- Better control over release kinetics of encapsulated compounds.
- Enhanced bioavailability of entrapped bioactive compounds.
- Chemical protection of labile incorporated compounds.
- Much easier to manufacture than biopolymeric nanoparticles.
- No special solvent required.
- Conventional emulsion manufacturing methods applicable.
- Raw materials essential the same as in emulsions.
- Very high long-term stability.
- Application versatility.

Disadvantages of SLN

- Particle growth.
- Unpredictable gelation tendency.
- Unexpected dynamics of polymeric transitions.

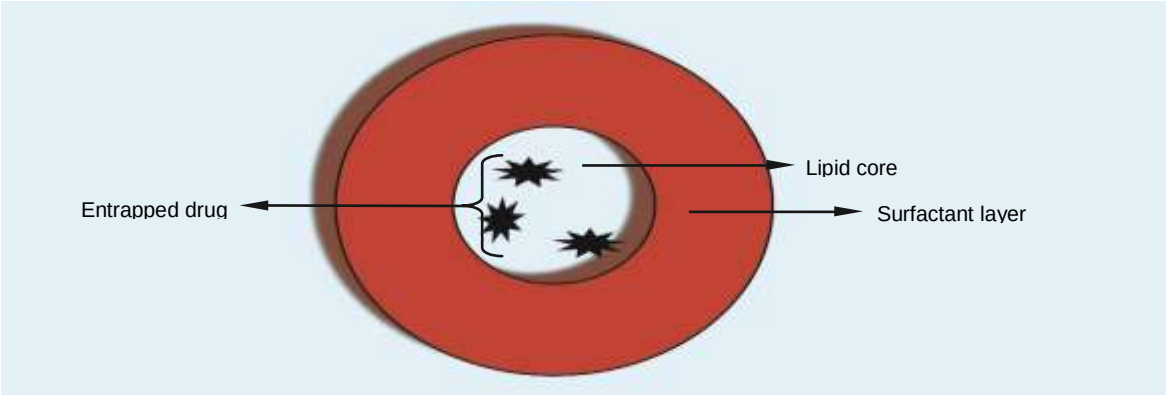

Figure 4. Simple diagram of a solid lipid nanoparticle showing the lipid core, entrapped drug and surfactant layer.

Routes of administration of SLN

Oral administration

SLN can be orally administered in form of dispersion, SLN-based tablets, pellets or capsules or as lyophilized unit dose powders for reconstitution for oral use. Dried SLN powders can be encapsulated, compressed into tablets or incorporated into pellets. Aqueous SLN dispersion can be used for granulation instead of a granulation fluid for the production of tablets. The possible effect of enzymatic actions on the SLN following administration via the oral route has to be taken into account to ensure the stability of the nanoparticles unto delivery to the target

site. The routes of particle uptake after oral application are transcellular (via the M cells in the Peyer's patches or enterocytes) or paracellular (diffusion between the cells). However, the uptake via M cells is the major

of drugs due to its sustained release effect, improve patient compliance and provide an effective treatment. When injected intravenously, SLN are sufficiently small to circulate in the microvascular system and prevent macrophage uptake, especially when coated with hydrophilic materials such as polyethylene glycol (PEG). Therefore, SLN have been suggested for protein and gene delivery.

Rectal administration

Delivery of SLN through the rectal route is still a virgin area of research as very few reported investigations exist. Rectal administration of drugs ensures rapid response and pharmacological effect. This route of drug administration is of vital importance and often used for paediatric patients in some clinical conditions such as seizures. It has been shown that plasma levels and therapeutic efficacy of drug-loaded SLN administered via the rectal route were higher.

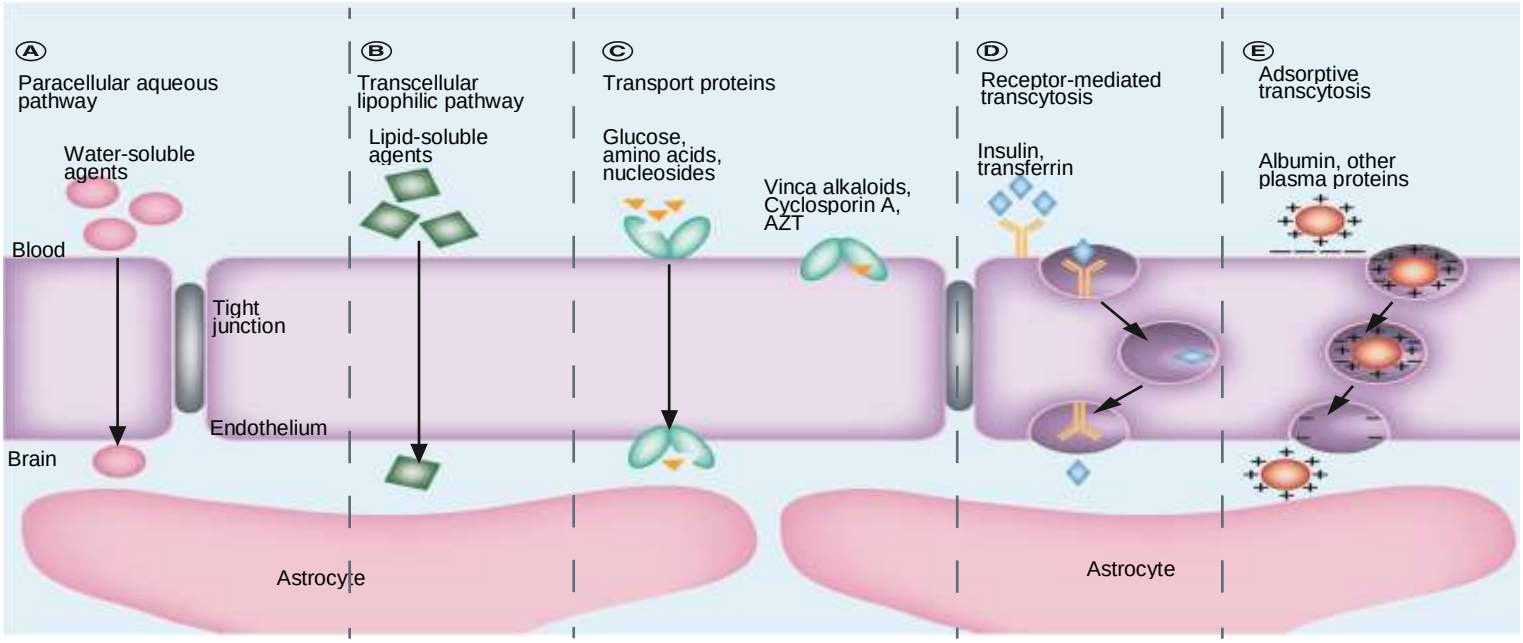

Figure 5. Schematic diagram of pathways across the blood–brain barrier

Aims of solid lipid nanoparticles

- Possibility of controlled drug release.
- Increased drug stability.
- High drug pay load.
- No bio-toxicity of the carrier.
- Avoidance of organic solvents.
- Incorporation of lipophilic and hydrophilic drugs. (Ref.8)

Methods of preparation of solid lipid nanoparticles

1. High pressure homogenization

A. Hot homogenization

B. Cold homogenization

2. Ultrasonication/high speed homogenization

A. Probe ultrasonication

B. Bath ultrasonication

3. Solvent evaporation method

4. Solvent emulsification-diffusion method

5. Supercritical fluid method

6. Microemulsion based method

7. Spray drying method

8. Double emulsion method

9. Precipitation technique

10. Film-ultrasound dispersion

Mechanisms of drug release from solid lipid nanoparticles.

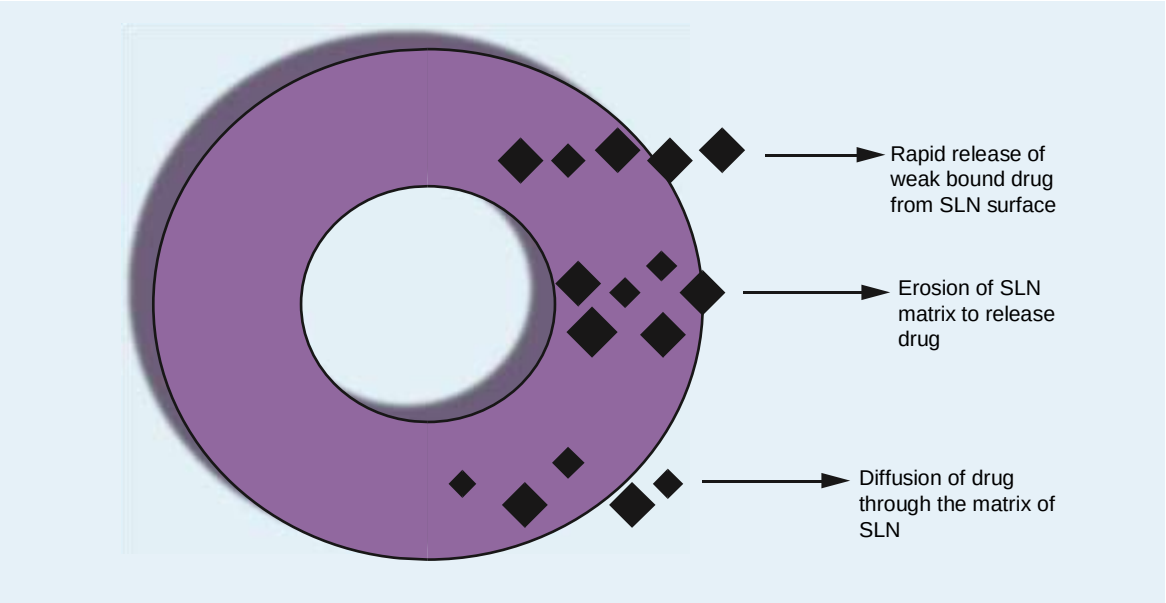

Figure 6. Mechanisms of drug release from solid lipid nanoparticles.

Classification of Nanoparticles The nanoparticles are generally classified into the organic, inorganic and carbon based.

2.1. Organic nanoparticles Dendrimers, micelles, liposomes and ferritin, etc. are commonly knows the organic nanoparticles or polymers. These nanoparticles are biodegradable, non-toxic, and some particles such as micelles and liposomes have a hollow core also known as nano capsules and are sensitive to thermal and electromagnetic radiation such as heat and light. These unique characteristics makes them an ideal choice for drug delivery. The drug carrying capacity, its stability and delivery systems, either entrapped drug or adsorbed drug system determines their field of applications and their efficiency apart from their normal characteristics such as the size, composition, surface morphology, etc. The organic nanoparticles are most widely used in the biomedical field for example drug delivery system as they are efficient and also can be injected on specific parts of the body that is also known as targeted drug delivery.

ROLE OF DRUG DELIVERY SYSTEM

A drug delivery system is a formulation or a device that enables the introduction of a therapeutic substance in the body and improves its efficacy and safety by controlling the rate, time and place of release of drugs in the body.

Drug delivery systems used in current medical practice

Clinicians historically have attempted to direct their interventions to areas of the body at risk or affected by a disease. Depending on the medication, the way it is delivered, and how our bodies respond, side effects sometimes occur. These side effects can vary greatly from person to person in type and severity. For example, an oral drug for seasonal allergies may cause unwanted drowsiness or an upset stomach.

Administering drugs locally rather than systemically (affecting the whole body) is a common sway to decrease side effects and drug toxicity while maximizing a treatment's impact. A topical (used on the skin) antibacterial ointment for a localized infection or a cortisone injection of a painful joint can avoid some of the systemic side effects of these medications. There are other ways to achieve targeted drug delivery, but some medications can only be given systemically.

CONCLUSION

Solid lipid nanoparticles do not, as proposed, ''combine the advantages of other colloidal drug carriers and avoid the disadvantages of them''. The results cannot simply be regarded as nano emulsions with a solid core. Clear advantages of SLN include the composition (physiological compounds), the rapid and effective production process including the possibility of large-scale production, the avoidance of organic solvents and the possibility to produce carriers with higher encapsulation efficiency. Disadvantages include low drug-loading capacities, the presence of alternative colloidal structures (micelles, liposomes, mixed micelles, drug nanocrystals), the complexity of the physical state of the lipid (transformation between different modifications) and the possibility of super cooled melts which cause stability problems during storage or administration (gelation, particle size increase, drug expulsion). Sample dilution or water removal might significantly change the equilibria between the different colloidal species and the physical state of the lipid. The appropriate characterization of the complex surfactant/lipid dispersions requires several analytical methods in addition to the determination of the particle size. Kinetic aspects to be taken into account. NMR, ESR and synchrotron irradiation will help the drug Nano suspensions coexist in the sample. Unfortunately, these aspects have not always been considered and the terminus 'drug incorporation' in the SLN literature is often misleading. In summary, SLN are very complex systems with clear advantages and disadvantages to other colloidal carriers. Further work needs to be done to understand the structure and dynamics of SLN on molecular level in vitro and in vivo studies.

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