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A COMPREHENSIVE RESEARCH ON SOLID LIPID NANOPARTICLES

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ABSTRACT:

Noble drug administration and traditional drug distribution have both failed to enhance medication bioavailability and mitigate drug toxicity. In recent years, tailored drug delivery systems have become significant for administering medications with less toxicity and enhanced bioavailability. Nanotechnology has revolutionized medicinal delivery. Solid lipid nanoparticles (SLNs) have demonstrated efficacy as superior medication carriers. SLNs possess several uses in the prevention of cancer and tuberculosis, and they serve as adjuvants in different vaccinations. The preparation procedures for solid lipid nanoparticles (SLNs) encompass homogenization under pressure, ultrasonication, and solvent evaporation, and are contingent upon the characteristics of the medication. The biodistribution of pharmaceuticals is a difficulty, effectively addressed by selecting the optimal route of administration. The characterization of drugs is crucial for solid lipid nanoparticles (SLNs) to enhance drug bioavailability, encompassing several techniques such as electron microscopy, particle size analysis, and zeta potential measurement.

Keywords: Solid lipid nanoparticles, colloidal drug carriers, hydrophilic, lipophilic, homogenization

INTRODUCTION:

Traditional drug distribution has encountered numerous limitations over the years concerning patient treatment. To conceal the shortcomings of traditional medication distribution, tailored drug delivery systems (TDDs) were devised. Unlike traditional drug delivery systems, TDDs specifically target organs, tissues, and cells. This method enhances medication release at the targeted place within the body. Nanotechnology has advanced targeted medication delivery systems by addressing the limitations of traditional drug administration methods. Nanotechnology typically involves the targeted delivery of drugs utilizing nanoparticles as carriers. Nanoparticles denote little particles

that measure between 10 and 1000 nanometers in size. The utilization of nanoparticles in TDDs has becoming increasingly significant.[1] The medicine will be encapsulated within the nanoparticles and transferred to the targeted location. Typically, nanoparticles are encapsulated with various polymers depending on the drug's characteristics.

These polymers safeguard the medications from degradation and facilitate their traversal over various physiological barriers. This technique ensures the medicine remains untouched by bodily circumstances while delivering the desired dosage to the target site. The primary benefit of nanotechnology is its reduced toxicity and enhanced cellular penetration capability. The sustained release of a medicine at the targeted site can be accomplished by the utilization of biodegradable nanoparticles. Various categories of nanoparticles exist, distinguished by their size, shape, and physical and chemical properties. Several of them are enumerated below.[2]

1. Carbon-based nanoparticles
2. Ceramic nanoparticles
3. Metal nanoparticles
4. Semiconductor nanoparticles
5. Polymeric nanoparticles
6. Lipid-based nanoparticles.[3]

SOLID LIPID NANO PARTICLES:

Solid lipid nanoparticles (SLNs) are characterized by a size range of 100 to 150 nm. They have a solid lipid coating. The lipid coating of nanoparticles enhances their stability and protects the medication from degradation compared to conventional drug delivery methods. Solid lipid nanoparticles comprise polymeric and lipid components. The lipid utilized is contingent upon the method of medication delivery. The parenteral and oral routes are the most often utilized for solid lipid nanoparticles (SLNs).[4]

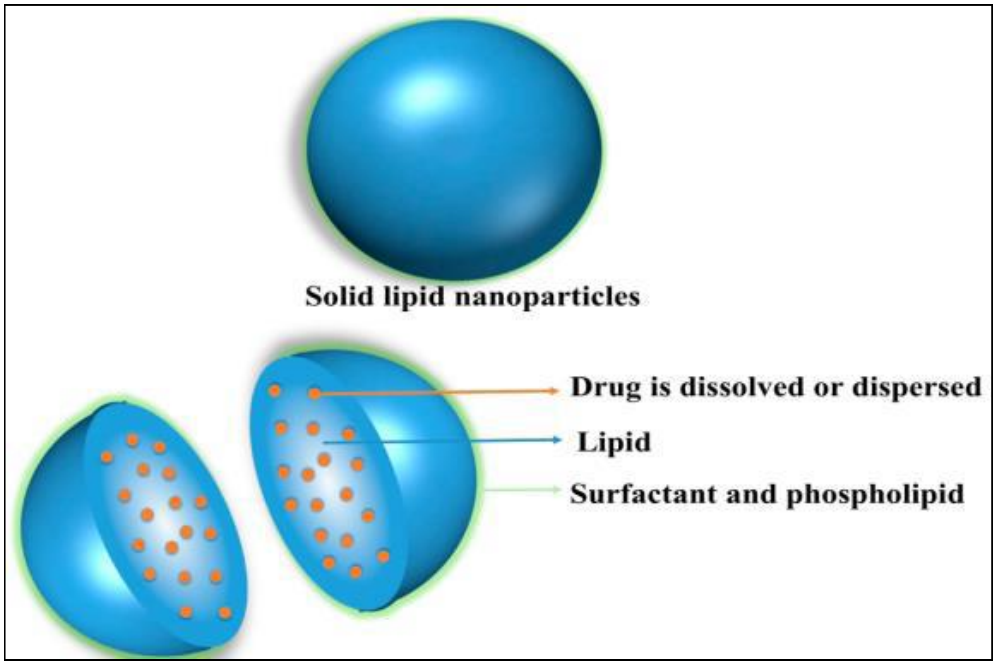


Figure: 1: Solid Lipid Nanoparticles

ADVANTAGE:

• Good biocompatibility
• Long term stability

• Controlled drug release
• Easy to manufacture
• Special solvents are not required
• Toxic metabolites are not produced
• Raw materials essential as same as in emulsion
• Large scale production is possible

DISADVANTAGE:

• Medication stacking limit is poor
• Particle growth
• Relatively higher H2O content of the dispersion (70-99.9%)want to remove too much H2O in tablets/ pellets production.
• Unpredictable gelatin tendency [4]

METHODS OF PREPARATION OF SLNs[5, 6]:

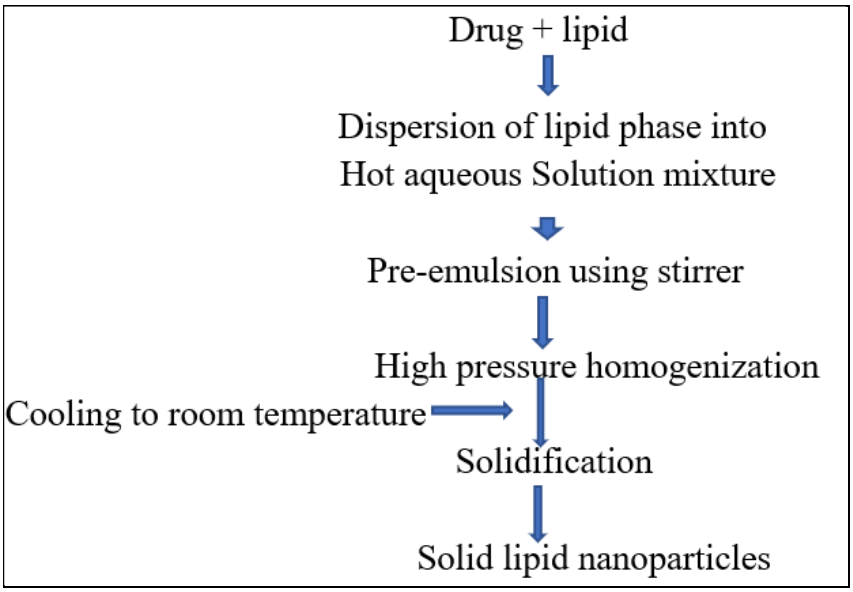
A. High pressure homogenization
• Hot homogenization
• Cold homogenization
B. Ultrasonication/High speed homogenization
• Probe Ultrasonication
• Bath Ultrasonication
C. Solvent evaporation method
D. Solvent emulsification-diffusion method
E. Supercritical fluid method
F. Micro emulsion-based method
G. Spray drying method
H. Double emulsion method
I. Precipitation technique
J. Film-ultrasound dispersion

A. High pressure homogenization:

This method is a dependable and potent technology employed in the creation of solid lipid nanoparticles. High pressure homogenizers propel a liquid at elevated pressures (exceeding 200 bar) via a tiny aperture of a few microns. The fluid accelerates over a minimal distance to a significantly high velocity. Excessive shear stress and pressures reduce particles to the submicron range. Typically, a lipid percentage of 5-0% is employed, while a lipid content of 40% has also been examined.
Hot homogenization and cold homogenization are the two general approaches of HPH to work on the same concept. [7]

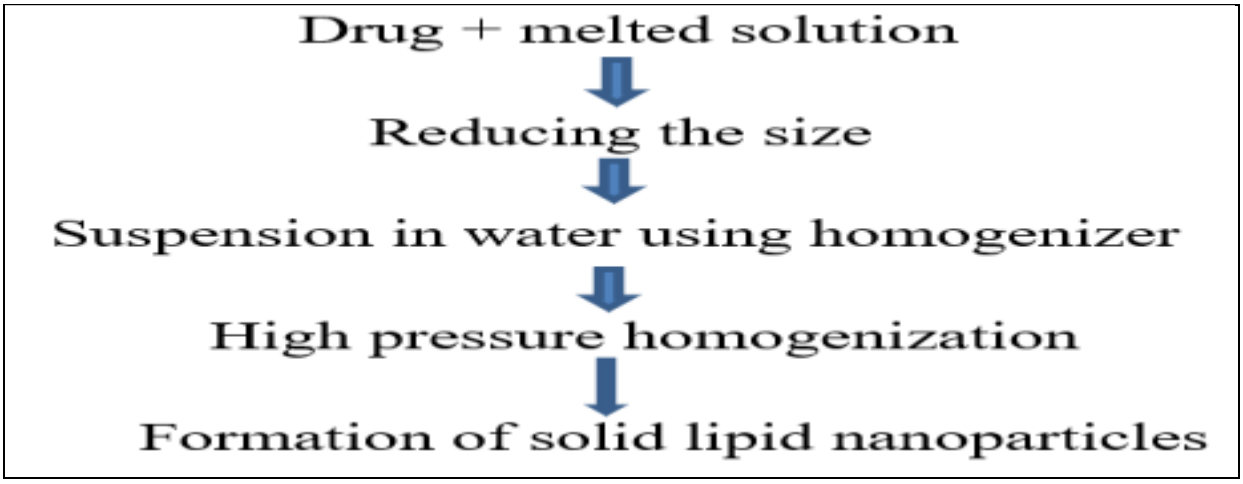
Hot homogenization:

This method is a dependable and potent technology employed in the creation of solid lipid nanoparticles. High pressure homogenizers propel a liquid at elevated pressures (exceeding 200 bar) via a tiny aperture of a few microns. The fluid accelerates over a minimal distance to a significantly high velocity. Excessive shear stress and pressures reduce particles to the submicron range. Typically, a lipid percentage of 5-0% is employed, while a lipid content of 40% has also been examined. [8, 9]



Cold homogenization:

The degradation of the drug caused by elevated temperatures and the inadequate dispersion of the drug in the aqueous phase are notable drawbacks of hot homogenization. The disadvantages can be mitigated by employing the cold homogenization method. This method involves loading the lipid with the medication and subsequently cooling it. The converted lipid is changed into microparticles, which are then transferred into a surfactant-containing solution that is then chilled to generate a pre-suspension. The pre-suspension is transformed into solid lipid nanoparticles by selecting a temperature below room temperature, with gravitational force adequate for the disintegration of microparticles into solid lipid nanoparticles.[10]



B. Ultra sonication:

Ultrasonication is a dynamic process for the creation of solid lipid nanoparticles (SLNs). This technique is also referred to as high-speed homogenization. This approach primarily employs the cavitation mechanism. The initial stage entails the incorporation of the medication into the previously melted lipid. The second step entails the incorporation of the previously heated aqueous phase into the lipid-containing medication, followed by emulsification using a magnetic stirrer. This approach can reduce shear stress; however, physical instability, such as particle development, may occur during storage.[11]

C. Solvent evaporation method:

Solvent evaporation method is lipophilic material dissolved in a water immiscible organic solvent (eg. cyclohexane) that is emulsified in the aqueous phase. Upon the solvent evaporation and dispersion of nanoparticles is formed by precipitation of the lipid medium giving by size of nanoparticles 25nm. The solution emulsified is aqueous phase by high pressure homogenization. It is scalable, mature technique, and commercially demonstrated but the disadvantages are bimolecular damage, poly dispersion distribution.[12]

D. Solvent emulsification- diffusion method:

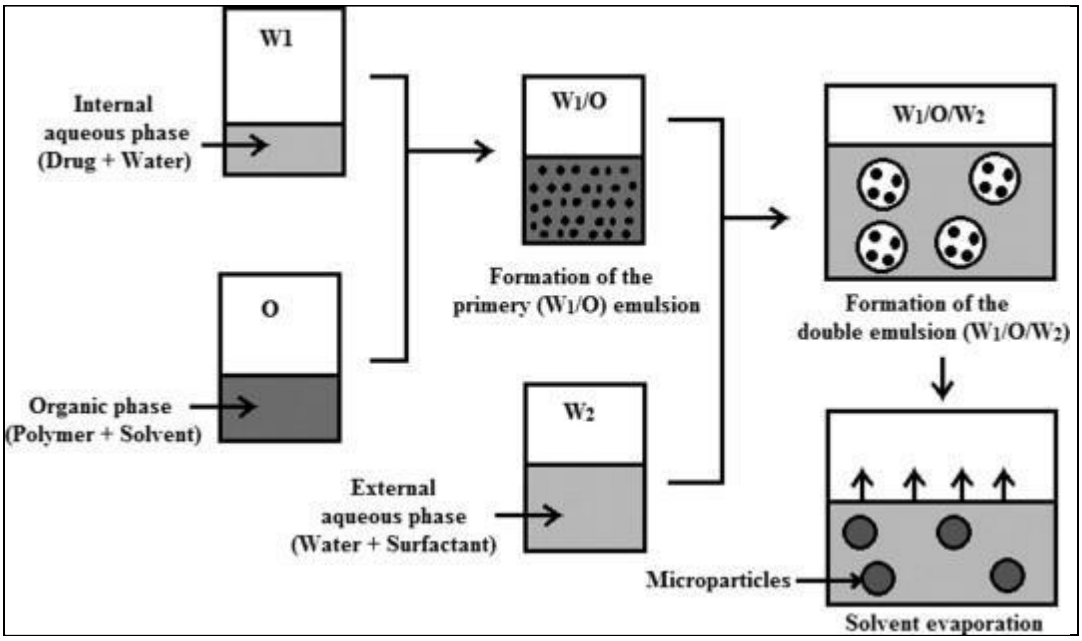
Particles measuring between 30 and 100 nm are produced by this event. The average particle size is contingent upon the lipid concentration in the organic phase and the emulsified phase. One of the primary advantages of this technology is the prevention of heat generation. The initial stage in this process involves the incorporation of a lipid matrix that is distributed in a water-immiscible organic solvent. The second process involves the emulsification of the aqueous phase, followed by solvent evaporation at low pressure. The lipid then precipitates, resulting in the formation of a nanoparticle dispersion.[13]

E. Supercritical fluid method:

This event produces particles ranging from 30 to 100 nm in size. The average particle size depends on the lipid concentration in both the organic and emulsified phases. A key benefit of this technology is the mitigation of heat production. The preliminary phase of this technique entails the integration of a lipid matrix into a water-immiscible organic solvent. The second procedure entails the emulsification of the aqueous phase, succeeded by solvent evaporation under reduced pressure. The lipid subsequently precipitates, leading to the creation of a nanoparticle dispersion.
[13,14]

F. Micro emulsion-based method:

This technique relies on the dilution of microemulsion. The system comprises two phases: an inner phase and an outer phase. The heated microemulsion is dispersed in cold water through agitation. SLN dispersion may serve as a granulation fluid for the conversion into a solid product (tablets, pellets) via the granulation process; however, in instances of low particle content, excessive water removal is required. Elevated temperature gradients facilitate fast lipid crystallization and inhibit aggregation. The final lipid concentration is significantly lower due to the dilution stage compared to HPH-based formulations. It possesses low mechanical energy input, theoretical stability, but low nanoparticle concentrations, rendering it highly susceptible to alterations.[15]



CHARACTERIZATION:

Measurement of particle size and zeta potential:

A variety of methods exist for quantifying particle size. Photon correlation spectroscopy (PCS) and laser diffraction (LD) are the predominant methodologies employed. PCS is often referred to as dynamic light scattering. PCS measures the variation in the intensity of scattered light, which is affected by particle motion. This technique can quantify particles ranging from nanometers to microns. PCS is a superior technique for nanoparticle characterization; nevertheless, it is ineffective for quantifying particle size and shape. In contrast to PCS and LD, electron microscopy is a superior technique for ascertaining the morphology of nanoparticles. The physical stability of solid lipid nanoparticles (SLNs) exceeds 12 months. ZP aids in forecasting the storage stability of colloidal dispersions.[16,17]

Photon Correlation Spectroscopy (PCS):

This method is predicated on the scattering of laser light resulting from the Brownian motion of particles in a solution or suspension. This approach quantifies particle dimensions ranging from 3 nm to 3 mm. The PCS apparatus comprises a laser source, a temperature-controlled sample cell, and a detector. A photomultiplier serves as a detector for identifying scattered light. The PCS diameter is determined by the intensity of light scattering from the particles..[18]

Electron Microscopy:

The morphological characteristics and particle shape of SLNs can be assessed using microscopic techniques such as Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). These approaches are employed to assess the dispersion of medication particles within solid lipid nanoparticles (SLNs). Scanning Electron Microscopy (SEM) focuses on the sample's surface and involves the transmission of electrons, whereas Transmission Electron Microscopy (TEM) examines only the sample through which electrons are conveyed..[19]

Atomic Force Microscopy (AFM):

The properties of the surface of solid lipid nanoparticles (SLNs) can be assessed using an advanced microscopic technique called atomic force microscopy. It is utilized as an innovative instrument

AFM facilitates the visualization of SLNs, allowing for a clear distinction of their original, unaltered shape from other particles. This approach can measure the various forces between the probe and the sample.Twenty The particle surface picture can be acquired by positioning the sample and its probe in proximity, allowing for visualization at a resolution of 0.01 nm.

Determination of Incorporated Drug:

The quantity of drug incorporated into the SLNs significantly influences their features and warrants evaluation. The quantity of medication in solid lipid nanoparticles per unit weight can be ascertained using centrifugation or gel permeation chromatography. These methods quantify the drug by isolating lipids and the free drug contained in the aqueous media. High-Performance Liquid Chromatography (HPLC) and spectrofluorometry are technologies utilized for drug test analysis..[21]

Routes of administration and their biodistribution:

The *in vivo* effects of solid lipid nanoparticles will primarily depend on the following factors: Interchange of solid lipid nanoparticles with biological surroundings, encompassing dispersion processes and enzymatic activities. Various routes of administration exist.[21]

1. Parenteral route of administration:

Protein and peptide drugs were typically available for parenteral use in the market. Their traditional oral structure is unimaginable due to enzymatic degradation in the gastrointestinal tract. The administration of parenteral solid lipid nanoparticles reduces the potential side effects of included medications, therefore enhancing bioavailability. This technique is highly suitable for targeted medication..[23,24]

2. Oral route of administration:
The controlled release behavior of solid lipid nanoparticles facilitates gastric bypass and encapsulated intestinal breakdown of medication, as well as its potential transport and absorption via the intestinal mucosa. Nonetheless, evaluating the colloidal stability barriers in gastrointestinal fluids is crucial for predicting their appropriateness for oral administration.[25]

3. Rectal route of administration:
In situations requiring rapid pharmacological effects, rectal or parenteral administration is employed for pediatric patients due to its ease of usage.[26,27]

4. Nasal route of administration:
The nasal route of administration is preferred due to its rapid absorption and swift onset of therapeutic action, as well as its ability to circumvent the unstable breakdown of drugs in the gastrointestinal tract and the absence of transport across epithelial cell layers.[28]

5. Topical route of administration:
Solid lipid nanoparticles are highly attractive colloidal barrier systems for skin applications due to their various beneficial effects on the skin, in addition to their properties as a colloidal delivery system. It is suitable for use on irritated or compromised skin.[29]

Application of solid lipid nanoparticles:

Tubercular and oral solid lipid nanoparticle chemotherapy:

Medications for insect tuberculosis, such as isoniazid, rifampicin, and pyrazinamide, are loaded. Solid lipid nanoparticle systems can reduce the frequency of dose and enhance patient compliance.

Fifteen This anti-tubercular medicine is manufactured using the solvent emulsion diffusion method to create injected solid lipid nanoparticles.[30]

Utilization of topical solid lipid nanoparticles:

Solid lipid nanoparticles are employed for topical administration of different medications, including Vitamin A, flurbiprofen[31], isotretinoin[32], and anticancer agents. Glyceryl behenate[33] can be employed to create vitamin A-loaded nanoparticles. This technique facilitates the advancement of penetration through assisted discharge. Lipid nanoparticles loaded with isotretinoin are designed for topical drug delivery. Manufacture of the flurbiprofen-loaded Solid lipid nanoparticles gel for topical administration presents a possible advantage in delivering medication directly to the site of action, resulting in enhanced tissue retention. Infused solid lipid nanoparticles are created..[34]

Role of SLNs in vaccines by using adjuvants:

The immune response is enhanced through the utilization of adjuvants. Recently introduced subunit vaccines exhibit insufficient efficacy in vaccination. The adjuvants significantly enhance immunization. Emulsions are the recently identified domains for adjuvants that are rapidly metabolized in the body. The degradation of solid-state lipid components occurs gradually, resulting in prolonged exposure of solid lipid nanoparticles to the immune system..[35,36]

CONCLUSION:

SLN serve as colloidal carriers for drug conglomerates, combining the advantages of polymeric nanoparticles, fat emulsions, and liposomes. These benefits include the capability to incorporate both lipophilic and hydrophilic drugs, enhanced physical stability, cost-effectiveness, ease of scaling up, and a streamlined manufacturing process. SLNs are structured using diverse new methodologies. The site-specific and sustained release effects of the medicine can be more effectively attained by the use of solid lipid nanoparticles (SLNs). Nanoparticles have been extensively utilized in drug discovery, drug delivery, diagnostics, and various other uses within the medical profession. To achieve the extensive uses of lipid-based nanoparticulate formulations, it is imperative that pharmaceutical companies focused on developing new drug delivery systems invest in innovative formulation technologies to facilitate their scaling processes.

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