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A Review on Lipospheres

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ABSTRACT

Lipospheres are made up of lipid based water dispersible solid micro particles ranging from the size between 0.01 to 100 micro meters in diameter. Lipospheres are mainly composed of triglycerides, waxes or fatty acids. It is developed for parenteral and topical drug delivery of bioactive compounds. In lipospheres, a solid hydrophobic fat core stabilized by monolayer of phospholipid molecules instilled in their surface which is a potential entrance enhancer. Lecithin has tendency for epidermal tissue and shows skin hydration. Lipospheres are favourable method for the development of cosmetic preparations. The small size of the lipid particles absorbed through stratum corneum by penetration mechanism. Lipid entrapment plays a major role in the formulation of lipospheres. Among all the methods, melt dispersion technique having highest entrapment efficiency than solvent evaporation method.

Introduction

Lipospheres are made up of lipid based water dispersible solid micro particles ranging from the size between 0.01 to 100 micro meters in diameter. Lipospheres are mainly composed of triglycerides, waxes or fatty acids. It is developed for parenteral and topical drug delivery of bioactive compounds. In lipospheres, a solid hydrophobic fat core stabilized by monolayer of phospholipid molecules instilled in their surface which is a potential entrance enhancer. Lecithin has tendency for epidermal tissue and shows skin hydration.

Lipospheres are favourable method for the development of cosmetic preparations. The small size of the lipid particles absorbed through stratum corneum by penetration mechanism. Poor water soluble components are also suitable for the preparation of lipospheres. Because of captivity with polymeric transportation frame work, broad endeavours are being made to create exchange carriers. Lipids particularly being concentrated on their physico chemical characteristics. Lipospheres like nano particles are carriers of commitment for topical medications. The small size of the lipid particles come in to contact to stratum corneum and can build the measure of the medication entering into the skin. Lipospheres possess a film framing capacity prompting the occlusive properties. Lipospheres containing medications enhances their bio availability with decreased poisonous effect.

Composition of lipospheres

Lipospheres are composed of solid lipid core surrounded by a single unit phospholipid layer that may entrap the drug. The stabilizer is used as coating material of the core and it is also help to facilitate to drug partitioning between the lipid and aqueous phase. PEG containing low molecular weight substances acts as plasticizers and provides tensile strength to the external lipid layer.

Types of lipospheres

Lipospheres are mainly classified into two types based on matrix composition. They are classical lipospheres and polymer lipospheres

Classical lipospheres: For preparation of classical lipospheres lipid based matrix are used and for formation of lipophilic core neutral lipids are used. Examples for classical lipospheres are hydrogenated vegetable oil, ethyl stearate, tri caprin tri Lauren and stearic acid [1].

Polymer lipospheres: Polymer lipospheres are made up of matrices made from bio degradable polymers. Examples for polymer lipospheres are poly lactic acid,

poly capro lactone, poly lactic co glycolide. Poly lipospheres have longer release periods and used for controlled delivery. The major drawbacks of polymer lipospheres are potential toxicological aspects.

Advantages

- Ease of preparation
- Low cost of its components
- Better physical stability
- High entrapment of hydrophobic drug
- High degree of dispersibility in aqueous medium loading of lipophilic drug
- Reduced mobility of entrapped drug
- Extended release of loaded drug
- Better bio compatibility
- Suitable for oral, IM, IV and topical administration

Disadvantages

- Drug degradation due to high pressure
- Variable kinetics
- Insufficient stability
- Low loading capacity of lipophilic proteins [2]

Standard for choice of drugs and excipients

The main aim to develop lipospheres is reaching of the drug to the target site. Increased permeability is achieved by phospholipid coat due to minimizing the solubility problems of the lipophilic substance. In hydrophilic drugs the permeability is limited by bio membrane. This problem can be steer clear of by taking the active component in the lipid core, so that the pair of lipophilic and hydrophilic drugs can be included in the lipospheres. The successful delivery of peptides can reach by lipospheres with increased strength of peptides by bringing down their reach to different pH environmental state.

Flash point is one of the main physical properties of carrier. The melting point of the carrier must be >45^{o}c to decrease the stability problems. Hydrophilic lipophilic balance is the key factor that the HLB rate of centre substance must be <2, because it exist additional affinity for lipids along with elevated prospect for formation of rigid form on the top of the polar substances which form mixture dissipation. Each carrier must possess the ability to dissolve the API and to form particles appearing to ideal measurement [3-6].

Working approach in composition of lipospheres

Following techniques are employed for composition of lipospheres

- Melt dispersion technique
- Solvent evaporation technique
- Multiple micro emulsion technique
- Superior analytical liquid technique
- Spray drying technique
- Spray congealing technique
- Solvent extraction technique

Melt dispersion technique

The mixture of lipospheres containing lipids, phospholipids, cholesterol is prepared with and without lipophilic medication. The mixture is softened by increasing temperature. The emulsion is then mixed by utilizing stirrer furnished with exchange impellers and keeps up the same temperature. Quickly cool the emulsion by putting into ice shower with persistent commotion will give constant scattering of lipospheres. The acquired lipospheres is then washed with water and disconnected by filtration through a paper medium.

Solvent evaporation technique

In this technique, co-solvent exists to enhance the solvability about lipoid and lipophilic drugs to get a fully homogenous lipospheres solution. Choice of solvents and co-solvents was the consequence of miscibility everywhere influences the output. Examples of co-solvents are dichloromethane, Ethyl ethanoate, Propanone, Flavin, tetra hydro furane and aceto nitrile.

Multiple micro emulsion technique

In this technique, the hydrophilic drugs were disband in an aqueous phase and this mixture was added to the lipid part to yield the primary emulsion at high temperature i.e. 70^{o}C. At that time, the mixture was added to the oil phase containing non polar emulsifier to yield uniform size of lipospheres.

Superior analytical liquid technique

In this technique, the lipid and API melt in a acceptable natural solvent to form a mixture which was emulsified in an aqueous phase to form an emulsion that accommodate a intermittent stage of micelles be made up of natural solvent, drug and lipid. Finally the homogenous mixture was treated with a superior analytical fluid under acceptable environment. Now, the removal of the natural solvent

from the micelles and precipitation of the solid compound lipospheres in the aqueous dispersion can occur. Quick transferred pressure causes the super saturation of particles leading to enhanced stability. Use of carbondioxide as a super analytical liquid was favoured due to its low cost, non toxicity, a critical point at 31^{o}C and 74 bars of pressure.

Spray drying technique

This technique provides smaller size particles with homogenous distribution compared to other methods. The shape of the particles was affected by drying rate, viscosity and surface tension of the drying liquid. In this method the key parameters are inlet and outlet temperatures, feeding rate, drying gas medium, gas flow rate, gas humidity and residence time. The rate of particles formation was controlled by these key parameters. As complete removal of solvent was observed, the chance of toxicity was also minimized. This technique was highly applicable in food industry to producing peptide loaded lipospheres.

Spray congealing technique

This technique was employed for preparing lipid micro particles loaded with therapeutics such as clarithromycin, theophylline, verapamil and indomethacin. To flow into the spray congealer specifically into cyclone separator which was maintained at -20^{o}C, which lead to separation of solid particles that were again made to atomize to remove adhered condensed water. The atomization pressure and spraying temperature affect the particles size distribution and also product yield. It was noticed that the increased spraying temperature and pressure in spray congealing cause the result of reduced particle size. This technique can be recommended for scale-up process of sensitive drugs like peptides to favour the stability of the active moiety and to sustain the release. Lipospheres are differ from other nano lipid carrier systems.

Solvent extraction technique

This technique is based on dissolution of tri glycerides and cationic lipid inorganic solvent and an addition of an aqueous poly vinyl alcohol solution 0.5% w/w is used as extraction fluid. The solution and extraction fluid are pumped in static micro channel mixer leading to production of oil in water emulsion. The mixture leads to production of fine lamellae in which subsequently disintegrate into droplets, allowing the formation of lipid microspheres in the extraction medium.

Sterilization of lipospheres

Sterile lipospheres formulations are prepared by sterile filtration of dispersion in hot stage during preparation using 0.2 µm filter at temperature that is 5^{o}C above the flash point of lipospheres composition. Heat sterilization using a standard autoclave cycle is reliable procedure. However, it might decompose the formulation. Gamma sterilization of lipospheres formulations did not affect their physical formulations on the other hand, did not affect their physical properties.

The drug and lipid ratio plays a major role in morphology of lipospheres. By using of drug and lipid ratio as 1:1 to form aggregates during cooling it can leads to irregular in size and shape fluffy and fragile particles. Polar and non polar lipids combinations give satisfactory lipospheres along with uniform in size, shape and recovery [7-9].

Conclusion

Lipid entrapment plays a major role in the formulation of lipospheres. Entrapment depends on the selection of lipid or triglyceride generally long chain triglycerides (Tristearin) and (Tri arachidin) are more hydrophobic than short chain triglycerides like (Tri caprin and Tri laurin). Long chain triglycerides increases the gastro intestinal residence time of the API and it can leads to increased bio availability. Lipid excipients reduce the activity of p-glyco protein and multi drug resistant by down regulating the protein expression and increase in cell membrane permeability in addition to lymphatic uptake. By using ratio of triglyceride:phospholipid at 1:05 to 1:0.25 w/w revealed that 70-90% of phosphatides polar heads were accessible on liposphere surface thus enhancing he entrapment of drug. Among all the methods, melt dispersion technique having highest entrapment efficiency than solvent evaporation method.

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