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A REVIEW ON ORAL LIPOSPHERE OF CANDESARTAN CILEXETIL

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ABSTRACT

Lipospheres are amongst the promising particulate drug delivery systems for improving dissolution rate of water insoluble drugs that were initially reported as a particulate dispersion of solid spherical particles between 0.2-100µm in diameter consisting of solid hydrophobic fat core such as triglycerides or fatty acids derivatives, stabilized by monolayer of phospholipids. The lipospheres are distinct from microspheres of uniformly dispersed material in homogenous polymer since they consist of two layers, the inner solid particle that contains the entrapped drug with phospholipids outer layer. Many of the drug substances are characterized by poor aqueous solubility, which cause many formulation problems. Beside the use of so-solvents, drug complexation and solubilization in surfactant micelles, incorporation in colloidal carrier system represents an alternative way to render poorly water soluble drug applicable for effective therapy.

Keywords:-Lipospheres, surfactant, micelles,solubilization, Polymer Lipospheres

INTRODUCTION

Lipospheres represent a new type of fat based encapsulation system developed for parenteral and topical delivery of bioactive compounds and have been utilized in the delivery of anti-inflammatory compounds, local anaesthetics; antibiotics, anticancer agents, insect repellent, vaccines, proteins and peptides [1, 2]

Advantages of lipid based delivery systems:

Lipid based delivery systems disperse, solubilise and maintain solubility of drug in GI fluids.

- Bioavailability of most of the lipophilic drugs is altered in the presence of lipid content in food.
- Lipid carriers mimic such lipid food and thus reduce the food effect on bioavailability of drugs and render flexibility to dosage regimen.

Transfer drug into bile-salt mixed micelle and promote lymphatic uptake of carrier-drug particles.

- Influence gut wall permeability
- Quantity of excipient required.
- Stability of drug.
- Chemical stability issue like drug and carrier compatibility.

Disadvantages:

Lipospheres suffers from following disadvantage such as

- Low drug loading capacity of lipophilic proteins.
- Variable kinetics.
- Drug degradation due to high pressure.
- Insufficient stability.

Colloidal drug delivery system:

Based on the carrier material the conventional vehicles used drug carries can be divided into 2 groups.

- Polymeric carries
- Lipidic Carriers.
- Liposomes.
- Lipoproteins.
- Lipospheres.

Lipospheres:

Lipospheres were first reported as a particulate dispersion of solid spherical particles between 0.2-100 µm in diameter consisting of solid hydrophobic fat core such as triglycerides or fatty acids

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derivatives, stabilized by monolayer of phospholipids

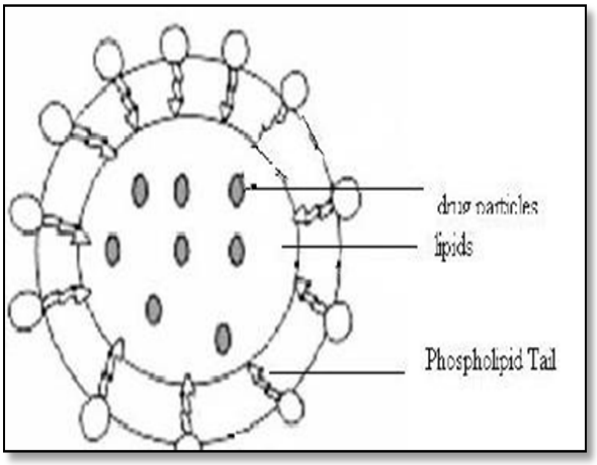

Figure 1: Structure of Liposphere

Types of Lipospheres

a) Based on matrix composition lipospheres are classified as:

- **Classical Lipospheres**

These comprises lipid based matrix and mostly neutral lipid used in their penetration of lipophillic core e.g. Tri Caprin, Tri Lauren, Stearic acid, Hydrogenated vegetable oil, Tri Stearin, Ethyl Stearate.

- **Polymer Lipospheres**

These comprises matrices made from biodegradable polymer e.g. poly lactic acid (PLA), poly caprolactone (PCL), poly lactic-co-glycolide (PLGA). Lipospheres of polymeric matrix have been investigated to achieve longer release periods and considered as efficient tool for controlled delivery. This suffers from major draback including potential toxicology

b) Based on size and composition of lipids:

- Solid lipid microparticles (SLMs) SLMs are micro – and nanoscale drug carries possessing matrix made from fatty acid, glyceride, fatty alcohols, and solid wax with high melting points [27]. SLMs combine many advantages as drug carrier systems.

- The amount of drug encapsulated can vary up to 80 % for lipophilic compound and they are well tolerated in living systems because they are made from physiological or physiologically related material.

- The solid matrix protects loaded labile substances against degradation and they offer possibility of controlled drug release and drug targeting

Formulation

Selection of the solid core of the liposphere

The liposphere contains a core that has a melting temperature equal to or greater than room temperature, approximately 25°C. In the preparation of liposphere meant for topical application, the core is prepared by choosing an agent to be delivered or released that has a melting temperature of approximately 30°C or by incorporating the agent in a carrier to produce a mixture having a melting point of approximately 30°C.

Selection of the phospholipids coating

The solid core of the liposphere is coated with one or more phospholipids that are embedded onto the surface of the solid core during manufacture. Mixtures of two or more phospholipids can be used to vary the surface properties and reactivity of the liposphere

Phospholipids

A phospholipid is a phosphorylated diacylglyceride molecule or its derivative. The parent structure is diacylglycerol phosphate or phosphatidic acid. Phosphatidyl choline (lecithin) is the choline ester of phosphorylated diacylglyceride.

Amphiphiles :

Amphiphiles can be added to the phospholipids coating to alter the surface change on the liposphere.

Surfactants:

The phospholipids can be substituted in part with surfactants such as Tween TM (a hydrophilic class of surfactants), Span TM (a hydrophobic class of surfactants), and polyethylene glycol surfactants.

Method for preparation of Lipospheres:

Melt Dispersion Technique: The blend of lipospheres containing lipids, phospholipids, cholesterol is readied with and without lipophilic medication.

Solvent Evaporation Technique: This is procedure is different option for the melt scattering strategy. The principle target is minimizing the introduction to high temperature of thermo labile mixes, for example, nucleic acids, proteins and so on.

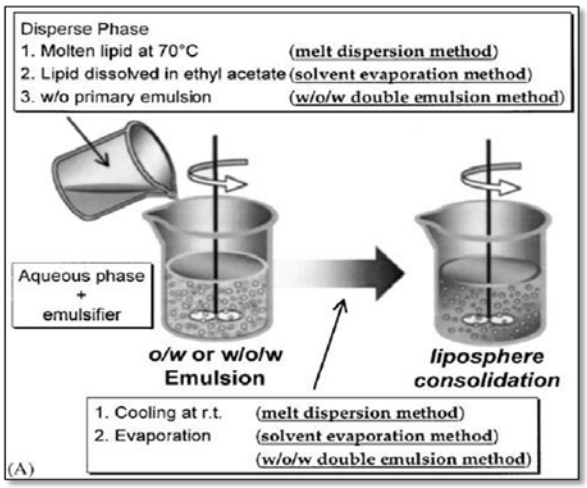

Figure 2: Melt dispersion technique)

Multiple Microemulsion: In this strategy arrangement of peptide is scattered in stearic corrosive melt at 70˚ C taking after by scattering of this essential emulsion into fluid arrangement of egg, lecithin, butaric corrosive and taurodeoxycholate sodium salt at 70˚C.

Sonication Method: In this method drug is mixed with lipid in scintillation vial precoated with phospholipid.

Rota-evaporation Method: On this system lipid arrangement with medication is readied in round base cup (RBF) containing 100 grams of glass dots (3 mm in measurement) blended altogether till clear arrangement is dissipated utilizing rotoevaporator under lessened weight at room temperature.

Micro fluidizer Method: Lipospheres can be prepared by using micro fluidizer which is equipped with two separate entry ports.

Solvent Extraction Method: This method is based on dissolution of triglyceride (e.g. tripalmitin) and cationic lipid inorganic solvent and an addition of an aqueous polyvinyl alcohol (PVA) solution (0.5% w/w) is used as extraction fluid.

Factors Affecting Entrapment Efficiency

- **Type of Lipid:** Entrapment in lipospheres is promoted by lipophilicity of API. Long chain triglycerides (tristearin and triarachidin) are generally more hydrophobic than short chain triglycerides like tricaprin and trilaurin

- **Amount of Phospholipid Triglyceride:** phospholipid at a 1:0.5 to 1: 0.25 w/w revealed that 70-90% of phospholipid polar heads were accessible on liposphere surface thus enhancing the entrapment of drug.

Drug Release influenced by following factors

- **Release Pattern** The release pattern of tetracaine, etomidate and prednisolone entrapped in lipid particles. Tetracaine and etomidate lipospheres have shown explode release and prednisolone lipospheres gave sustained release.

- **Particle size:** Smaller particles have greater surface area exposedto dissolution medium and higher diffusion coefficient. If the drug resides in the outer shell diffusion distance becomes shorter resulting in fast (burst) release.

- **Type of lipid:** Hydroxyl groups of stearic alcohols promote matrix hydration by providing a hydrophilic pathway for water molecules to solubilize the drug and increase in dissolution than the fatty acids like stearic acid.

- **Stabilizer:** Polaxomer 407 releases lipospheres in biphasic pattern (burst release followed by slow release) whereas gelatin releases drug in sigmoid release pattern.

Application

Controlled drug release

Prolonged drug release of lipophilic drugs can be facilitated by lipospheres. Gibaly et al identified that prolonged activity of allopurinol can be achieved by lipospheres and also avoids hepatotoxicity.

Improved physical stability

It was reported that lipospheres containing acelofenac intended for topical delivery, the lipospheres proves as a highly stable and is superior anti-inflammatory activity compared to marketed product [14]

Improved photo stability

The prepared lipospheres in which melatonin was encapsulated into lipid microspheres improve photo stability of melatonin.

Enhancement of drug release

Melt dispersion is considered as ideal for encapsulating fat soluble drugs

Rectal delivery

It has been demonstrated that diazepam incorporated in lipospheres prepared by high pressure homogenization of melted Witepsol dispersed in aqueous lecithin for rectal delivery for infants and children

REFERENCES:

1. Wake M.C. Effects of biodegradable polymer particles on rat marrow-derived Stromal osteoblasts in vitro, Biomaterials. 1998; 19: 1255-1268.
2. Cortesi R. Preparation of liposomes by reverse-phase evaporation using alternative organic solvents, J. Microencapsul. 1999; 16: 251-256.
3. Masters D.B., Domb A.J. Lipospheres local anesthetic timed release for perineural site application. Pharm. Res. 1998; 15:1038 – 1045.
4. Khopade A.J, Jain N.K. Long circulating liposphere targeted to inflamed tissue. Pharmazie. 1997; 52: 165 – 166.
5. Amselem S, Alving C.R, Domb A.J. Lipospheres for vaccine delivery. Drugs Pharm. Sci. 1996; 77: 149 – 168.
6. Rawat M, Saraf S. Liposphere: Emerging carriers in delivery of proteins and peptides. Int. J. Pharm. Sci. and Nanotechnol. 2008; 1: 207 – 214.
7. Lentz B.R, Carpenter T.J, Alford D.R. Spontaneous fusion of phosphatidyl choline small unilameller vesicles. Biochemistry. 1987; 26:5389 – 5392
8. Morels S, Gasco M.R, Cavalli R. Incorporation in lipospheres of [D – TrP – 6] LHRH. Int. J. Pharm. 1994; 105: R1 – R3.
9. Morel S, Ugazio E, Cavalli R, Gasco M.R. Thymopentin in solid lipid nanoparticles: Int. J. Pharm. 1996; 132: 259 – 261.
10. Raisel A., Sheskin, T., Bergelson L., Domb A.J. Phsopholipidscoated poly (lactic acid) microspheres for delivery of LHRH analogues. Polym. Adv. Tech. 2002; 13:127 – 136.
11. Cortesi R., Esposita E., Luca G., Nas – truzzi C. Production of liposphere as carrier for biocactive compounds. Biomaterials. 2003; 23: 2283 -2294.
12. El-Gibaly I, Abdel-Ghaffar S.K. Effect of hexacosanol on characteristics of novel sustained-release allopurinol solid lipospheres (SLS), factorial design application and product evaluation. International Journal of Pharmaceutics. 2005; 294: 33-51.
13. Umeyor E.C, Kenechukwu F.C, Ogbonna J.D, Chime S.A, Attama A.A. Preparation of novel solid lipid microparticles loaded with gentamicin and its evaluation in vitro and in vivo. J. Microencapsul. 2012; 1-12.
14. Maha Nasr. Lipospheres as a carrier for topical delivery for Acelofenac, Preparation, Characterization, and In Vivo Evaluation. AAPS Pharm Sci Tech. 2008; 9(1): 154-62.
15. Malgorzata S, Stainslaw J, Monika Gajewska, Miroslawa K. Investigation of diazepam lipospheres based on Witepsol and lecithin intended for oral or rectal delivery. ActaPoloniaePharmaceutica- Drug Research. 2000; 57(1): 61-64.