Abstract
The new drug molecules (greater than 40%) are lipophilic in nature and showing poor water solubility. Researchers are facing challenges to develop and improve the bioavailability of poor water soluble drugs towards clinical applications. The development of new drug molecule alone is not adequate to assure ample pharmacotherapy of various diseases. Considerable results obtained from in vitro studies are not supported with in vivo data due to inadequate plasma drug concentrations, this may occur due to limited solubility and absorption. To beat these problems, development of new drug delivery systems will be a promising approach. The in vivo studies of the drug are indicating not only by the drug itself, but also by the mode of administration and by the carrier system which should facilitate an optimal drug release profile according to the therapy requirements is very important for drug delivery development. One of the promising pharmaceutical approaches to beat these obstacles is the use of lipospheres drug delivery system to deliver the poorly water soluble drugs. Therefore, the present review articles described about achievements of lipospheres formulation to deliver the drugs in the targeted sites.

INTRODUCTION
Liposphere formulation is an aqueous micro dispersion of solid water insoluble spherical micro particles of particle size between 0.01 and 100 μm in diameter. The lipospheres are made of solid hydrophobic triglycerides with a monolayer of phospholipids embedded on the surface of the particle. Liposphere formulation is appropriate for oral, parenteral and topical drug delivery system (Figure 1). The solid core containing a drug dissolved or dispersed in a solid fat matrix and used as carrier for hydrophobic drugs. Several techniques, such as solvent emulsification evaporation, hot and cold homogenization and high pressure homogenization have been used for the production of liposphere (Rawat et al., 2006; Reithmeier et al., 2001). Benefits of liposphere drug delivery system are; a) improving drug stability; b) possibility for controlled drug release; c) controlled particle size; d) high drug loading. In addition, use of lipospheres for oral administration, it can protect the drug from hydrolysis, as well as improve drug bioavailability (Domb et al., 1996). Therefore, the present review articles focused on achievements of lipospheres formulation to deliver the drugs in the targeted sites.

Lipospheres Drug Delivery System
Injectable depot liposphere delivery system with high loading capacity for controlled delivery of donepezil was developed to decrease dosing frequency and increase patient compliance. Subcutaneous and intramuscular delivery of donepezil glyceryl tripalmitate lipospheres showed depot release and less frequent dosing (Yehia et al., 2012). Buoyant lipospheres containing lercanidipine hydrochloride were prepared by melt dispersion technique using hydrophobic matrix of cetostearyl alcohol (CSA). The formulation factors (stirring speed, lipid:drug ratio, lipid:surfactant polymer composition) on particle size, encapsulation efficiency and in-vitro release characteristics of lipospheres were investigated. The results suggested that buoyant lercanidipine lipospheres was suitable for per-oral administration (Pandit and Patil, 2009). Ceftriaxone sodium lipospheres was investigated for oral administration. Ceftriaxone sodium lipospheres were prepared by melt-emulsification techniques using Phospholipon 90H in Softisan 154 as the lipid matrix containing PEG 4000. Microbiological studies of the ceftriaxone sodium-loaded lipospheres were performed using Escherichia coli. In vitro permeation studies of ceftriaxone sodium lipospheres
through artificial membrane (0.22 microm pore size) was performed using Franz cell and simulated intestinal fluid (SIF). This study results expressed that Ceftriaxone sodium lipospheres was suitable oral administration (Attama et al., 2009). Micrometer-sized gas-filled lipospheres was produced by using digital (droplet-based) microfluidics technology for chemotherapeutic drug delivery. Photolithography techniques are applied to fabricate polydimethylsiloxane (PDMS) based microfluidic devices that give a combined dual hydrodynamic flow-focusing region and expanding nozzle geometry with a narrow orifice. The encapsulation of an extra oil layer between the outer lipid shell and inner bubble gaseous core permits the transport of hydrophobic drugs. Doxorubicin was entrapped in lipospheres and packed in a single ordered layer. The attachment of targeting ligands to the lipid shell showing direct vehicle binding to cancer cells. This study suggested that gas lipospheres was suitable for localization of drug concentration and release the drug with potentially (Hettiarachchi et al., 2009). Lipospheres containing aceclofenac was formulated for topical skin delivery. Lipospheres were prepared using lipid cores and phospholipid coats, implemented to melt and solvent techniques. The study results expressed that liposphere systems were able to entrap high levels (93.1%) of aceclofenac. aceclofenac lipospheres was showed potential anti-inflammatory activity. Therefore, Liposphere systems demonstrated to be a promising topical system for the delivery of aceclofenac with high stability and to sustain the anti-inflammatory effect of aceclofenac (Nasr et al., 2008). Butyl methoxydibenzoylmethane (BMDBM) loaded lipospheres were prepared by melt technique and investigated its skin permeation properties both in vivo (tape stripping method) and in vitro (flow-through diffusion chamber). In vivo human skin application, O/W emulsion containing BMDBM loaded lipospheres, the applied sunscreen was accumulated in the uppermost layers of the stratum corneum without remarkably modifying the skin permeation of the unencapsulated sunscreen. The results indicated that in vitro methodology involving the diffusion of BMDBM lipospheres through a lipophilized synthetic membrane into a hydrophilic receptor phase, simulating the viable epidermis (Iannuccelli et al., 2008). Hydroxypropyl-beta-cyclodextrin (HP-beta-CD) and the sunscreen agent, butyl methoxydibenzoylmethane (BMDBM) were incorporated with lipospheres and investigated the influence of this system on the sunscreen photostability. The results suggested that incorporation in lipid microparticles of BMDBM in the cycloexextrin complex form was potentially effective in enhancing the sunscreen photostability than the complex alone (Scalia et al., 2006). Cyclosporin is an immunosuppressive drug and used to treat autoimmune diseases. But Cyclosporin has poor bioavailability orally. Therefore, oral delivery system for cyclosporin A (CyA) lipospheres were developed and investigated the effect of composition and particle size of the CyA lipospheres on the oral bioavailability. The results indicated that cyclosporin A (CyA) lipospheres formulation significantly improved the oral bioavailability of Cyclosporin (Bekerman et al., 2004). Bupivacaine lipospheres were prepared by hot emulsification and cold resolidification process using natural and synthetic phospholipids. The use of synthetic phospholipids in the formulation produced bupivacaine liposphere dispersions showing prolonged gelation time than natural phospholipids (Toongsuwan et al., 2004). Investigation of effect of lipospheres on the light-induced degradation of melatonin was performed. Lipospheres loaded melatonin were prepared using tristearin or tripalmitin as the lipid material and hydrogenated phosphatidylcholine or polysorbate 60 as the emulsifier. The photolysis experiments indicated that the light-induced decomposition of melatonin was decreased by encapsulation into lipid microparticles based on tristearin and phosphatidylcholine. Thus, incorporation in lipospheres could be considered an effective carrier system to improve the photostability of melatonin (Tursilli et al., 2006).

**CONCLUSION**

The pharmaceutical industry is potentially focused on the development of new drug delivery systems. The drug delivery system must facilitate therapeutic drug concentrations at the drug target site for an adequate time period and avoid the adverse effects in other tissues and organs as possible. In this review article, we have reviewed the achievements and applications for lipospheres drug delivery systems. Lipospheres have the potential to be a major contributor to the search for better oral, parental and topical drug delivery systems due to their improved absorption and penetration. In addition, lipospheres could be suitable for low cost production, clinical and large-scale production. Therefore, Lipospheres could be considered as a promising delivery system for oral, parental and topical delivery of lipophilic drugs. Lipospheres can able to entrap the lipophilic drugs at high levels and showed sustain release over a prolonged period.

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**REFERENCES**


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