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Formulation and in-vitro evaluation of Glipizide (Anti diabetic drug) Liposphere

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ABSTRACT

Objective- The aim of the present study was to formulate and *in- vitro* study of glipizide liposphere by using melt dispersion technique.
Methods- Glipizide Liposphere system composed of paraffin wax, Stearic acid as lipid phase and sodium lauryl sulphate as surfactant. Glipizide lipospheres were prepared by using melt dispersion technique. Formulation of Glipizide was evaluated such as organoleptic properties, particle size, drug content, entrapment efficiency *in-vitro* study and stability of the lipospheres.
Result- The formation of glipizide lipospheres by using melt dispersion technique was done successfully. All the formulations have off- white in colour, characteristic odour and spherical shape. The formulation A4 has particle size 19.65 µm, drug content 84.93 %, entrapment efficiency 80.75 % and the percentage drug release was carried out by using USP type 2 dissolution apparatus in 6.8 pH phosphate buffer solution and drug release of glipizide lipospheres within 12 hrs was found to be 74.06 %.stability study of glipizide lipospheres revealed that the formulation was stable at 5°C ± 3°C.

Keywords- Lipospheres, Glipizide, Paraffin wax, Melt dispersion method, Dissolution Apparatus, Stability study

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INTRODUCTION

Lipospheres were reported for the first time by Domb and Maniar as aqueous micro dispersion of solid water insoluble spherical microparticles of particle size between 0.02 to 100 µm in diameter. Lipospheres are composed of a solid hydrophobic lipid core as triglycerides, stabilized by a layer of phospholipid molecules embedded on their surface. The internal core contains the bioactive compound dissolved or dispersed in the solid fat matrix in fig. 1.[1,2]

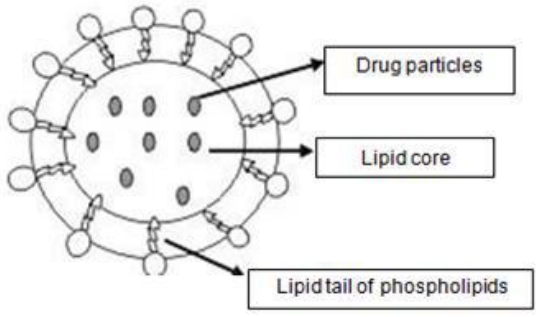

Figure 1: Structure of Liposphere

Around 40 to 70 % of chemical entities are poor water soluble. Several techniques like lyophilisation, drug micronization and microencapsulation used to enhance the dissolution profile of water insoluble drugs. Lipospheres are the most promising drug delivery for the water insoluble drugs. Lipids are used as common excipient and base in creams, ointments and flow modifier. Lipospheres drug delivery technique is suitable for oral, parenteral and topical drug delivery of bioactive compounds and used for the formulation of anti-inflammatory compounds, local anesthetics, antibiotics and anticancer agents, as well as carriers of vaccines and adjuvants.[3]

Advantages

- Liposphere exhibit enhanced physical stability due to avoidance of coalescence.
- High dispersability in an aqueous medium.
- Low cost of ingredients.
- Ease of preparation and scale up.
- High entrapment of hydrophobic drugs.
- Controlled particle size.
- Extended release of entrapped drug after a single injection.

- Static interface facilitates surface modification of carrier particles after solidification of the lipid matrix.
- The liposphere particle size allows administration at many sites, including perineural, subcutaneous, or intramuscular locations. The small particle size of liposphere (< 20 µm) is hypothesized to be well tolerated by a single cell contact , whereas large particle size (> 50 µm) are much more reactive due to attractive forces (e.g. Van der Waals).[2,4]

Disadvantages

- Different lipid modifications and colloidal species coexist that may cause differences in solubility and melting point of active and auxillary species.
- Low drug loading capacity for hydrophilic proteins.
- Variable kinetics of distribution processes.
- High-pressure induced drug degradation.
- Insufficient stability data
- Toxic effects of organic residues after the production of polymers,
- Lack of large industrial scale production.[4]

Glipizide is a sulfonyl urea class that can decrease the blood glucose level in human body by stimulating the release of insulin from the pancreas. It is mainly used in patients with type 2 diabetes, who have failed diet and exercise therapy. It is absorbed from Gastrointestinal tract, having 80-100 % oral bioavaibility and have short half-life is around 3-4.7 hrs that it be administered in two or three doses of 2.5 to 10 mg per day. Here we work towards to control the plasma concentrations level of drug maintained throughout 24 hours dosing interval with less peak trough fluctuation than that observed with twice a day dosing of immediate release Glipizide.[5,6,7] Glipizide lipospheres are prepared by melt dispersion method which is one of the most used and best method for preparation of liposphere because it gives high entrapment efficiency with controlled particle size.

MATERIALS AND METHODS

Materials

Glipizide was gifted by Roorkee Testing Laboratories, Roorkee, India. Sodium Lauryl Sulfate, Paraffin Wax, and Stearic Acid were purchased from CDH, and all other chemicals were used of analytical grade.

Preparation Method

The Glipizide lipospheres may be prepared by the method:-

Melt Dispersion Technique

The lipidic physical mixture containing paraffin wax and stearic acid was prepared with glipizide. The physical mixture was melted at 70°C and then emulsified into a hot external aqueous phase maintained at 70°C containing sodium lauryl sulphate. The emulsion was mechanically stirred by using stirrer equipped with alternate impellers and maintained at 70°C. Then, the emulsion formulation was rapidly cooled to about 20°C by immersing the formulation into an ice bath and continuing the agitation to yield uniform dispersion of LS. The obtained LS was then washed with water and isolated by filtration through 42 number whatman filter paper. [8, 9]

Table 1: Formulation Composition of Glipizide Liposphere Containing Paraffin Wax and Stearic Acid as Carrier.

Formulation Code	Drug (mg)	Lipid Phase			Sodium Lauryl Sulphate (ml) (0.2%)
		Paraffin Wax (mg)	Stearic Acid (mg)	Total	
A1	20	20	20	40	30
A2	20	20	30	50	30
A3	20	30	20	50	30
A4	20	30	30	60	30
A5	20	40	20	60	30

Evaluation of Lipospheres

Determination of Organoleptic properties

Glipizide liposphere batches were evaluated for organoleptic properties such as colour, odour and shape by visual observations.

Particle Size Determination-

Particle size analysis of glipizide-loaded lipospheres was performed by optical microscopy using a compound microscope. A small amount of dry lipospheres was suspended in purified water (10ml). The suspension was shaking for 10 seconds. A small drop of suspension thus obtained was placed on a clean glass slide. The slide containing lipospheres was mounted on the stage of the microscope and 100 particles were measured using a calibrated micrometer.10, 11

Determination of drug content

The drug content of glipizide lipospheres was determined by dissolving accurately 10 mg dried lipospheres in a mixture of 1:9 ratios of chloroform and methanol. Solution was sonicated for 5-10 min by using sonicator (Biomedica, BMI-599). Solution was filtered and analyzed for drug concentration by using UV visible spectrophotometer (Elico, UV SL-210) at wavelength of 225 nm. The drug content was determined by using the straight line equation.3

Drug Entrapment Efficiency

The entrapped drug concentration of glipizide liposphere was determined by lysis of the lipospheres with absolute alcohol and sonication. Accurately weighed amount of loaded lipospheres 50 mg was dissolved in 10 ml absolute alcohol and covered to prevent evaporation .The solution was sonicated for 15 min to obtain a clear solution. Take 1 ml of this solution was added to 9 ml of absolute alcohol. The solution was sonicated for another 15 min. The entrapment efficiency was determined by UV-visible spectrophotometer (Elico, UV SL-210) after suitable dilution at the absorbance 223nm. The entrapment efficiency was determined by the following formula 1, 3, 11

Percentage entrapment efficiency = [Amount of drug in lipospheres/ Initial amount of drug incorporated in formulation] × 100

In-vitro Drug Release

In vitro drug release of glipizide from lipospheres was evaluated in phosphate buffer (pH 6.8). Capsules (cream colour and size no.3) were filled by accurate amount of lipospheres equivalent to 10mg of glipizide liposphere. Then transferred to the pre-warmed dissolution media and maintained at 37±0.5°C under stirring at 50rpm. Samples were withdrawn every hour up to 8 hrs and the volume was replaced immediately by fresh phosphate buffer. The sample solution was filtered and analyzed for glipizide content by measuring absorbance in UV-Spectrophotometer at 223 nm.1, 3

Table 2: Dissolution apparatus & parameters

S. no.	Equipments	Parameters
1.	Dissolution apparatus	USP type-2, paddle
2.	Dissolution media	6.8 pH phosphate buffer
3.	Volume of the media	900 ml
4.	Blank solution	6.8 pH phosphate buffer
5.	Sampling volume	10 ml every 1 hour
6.	Rotation speed	50 rpm
7.	Temperature	37±0.5^{0}c
8.	λmax	223 nm

Stability testing

According to ICH and WHO guidelines stability study of glipizide lipospheres was carried out. Glipizide lipospheres was packed with aluminium foil and exhibit this to different temperature i.e., 5oC ± 3^{o}C, 25 ± 2^{o}C/ 60 ± 5% RH and 40 ± 2^{o}C/ 75 ± 5% RH for a period of two months12.

RESULTS AND DISCUSSION

Determination of Organoleptic properties

The organoleptic properties such as colour, odour and shape of glipizide liposphere batches were evaluated.

Table 3: Organoleptic properties

Organoleptic properties	Result
Colour	Off-White
odour	Faint
Shape	Spherical

Particle Size Determination

Glipizide lipospheres shows particle size distribution in the range of 13.22 µm for A1 batch to 25 µm for A5 batch.

Determination of drug content

Drug content is usually depends on encapsulation of drug in lipid, surfactants and method of preparation.

Glipizide lipospheres shows drug content in the range from 65.47 % for A1 batch to 79.63 % for A5 batch. The drug content of glipizide liposphere batch A4 was found to be 84.93 %.

Table 4: Particle Size Data of Lipospheres

S. NO.	Average Particle Size (µM)
A1	13.22
A2	15.24
A3	18.38
A4	19 .65
A5	22.54

Table 5: % Drug Content

S. NO.	Drug content (%)
A1	65.47
A2	69.35
A3	75.43
A4	84.93
A5	79.63

Drug Entrapment Efficiency

The entrapment efficiency of the drug is important parameter. The method used for the preparation of the liposphere is playing the important role in the entrapment of drug. The commonly used technique for the formation of liposphere was melt dispersion technique. Glipizide liposphere shows entrapment efficiency in the range from 68.21 for batch A1 to 74.64 for batch A5. The entrapment efficiency of glipizide liposphere batch A4 was found to be 80.75. Batch A4 has the high entrapment efficiency among all five glipizide liposphere batches.

Table 6: % Drug Entrapment Efficiency

S. NO.	Drug Entrapment Efficiency (%)
A1	68.21
A2	70.45
A3	72.73
A4	80.75
A5	74.64

In-vitro drug release

All batches of glipizide liposphere from A1 to A5 give a sustained drug release profile. Type 2 paddle dissolution apparatus used in the in-vitro drug release of glipizide lipospheres. All of the drug release could last 12 hrs. Release profile of the glipizide liposphere range from 83.04 for batch A1 to 68.11 for batch A5. Batch A4 has the drug release 74.06.

Table 7: *In-vitro* drug release

Time (hours)	% Drug Release				
	A1	A2	A3	A4	A5
2	3.14	2.89	2.89	2.21	3.08
4	32.31	29.52	30.16	22.91	32.84
6	49.24	49.02	41	45.45	47.27
8	68.53	61.13	56.18	56.82	60.95
10	81.82	78.06	74.05	72.46	66.53
12	83.04	80.13	78.03	74.06	68.11

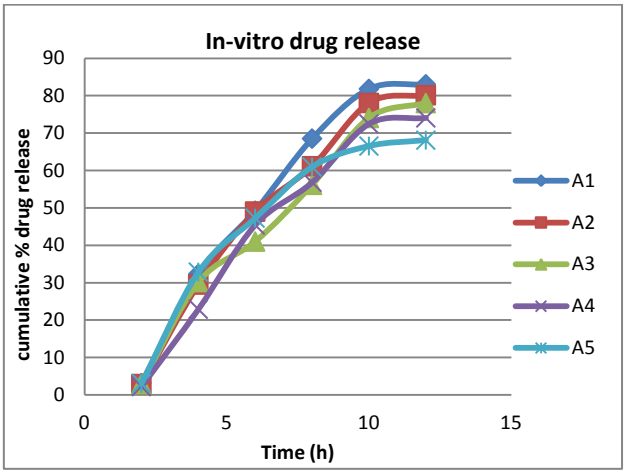

Figure 2: Release Profile of Various Formulations at pH 6.8 Phosphate Buffer

Stability testing

According to ICH and WHO guidelines the optimized batch of glipizide lipospheres A4 was subjected for stability testing. Glipizide liposphere batch A4 was packed in aluminium foil paper and kept in the stability chamber for two month. After two month glipizide lipospheres were stable at 5°C ± 3°C and checked the particle size and entrapment efficiency. Particle size and entrapment efficiency was found to be 18.24 µm and 79.24 % respectively.

CONCLUSION

Glipizide containing liposphere were prepared and evaluated successfully by using melt dispersion method. The evaluated tests were carried out such as organoleptic properties, particle size, drug content, entrapment efficiency, *in-vitro* drug release and stability study. The optimized batch A4 was the best among all five batches and found potential for further development.

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REFERENCES

1. Angilicam A, Karimunnisa SK, Sumathi P, Lipospheres: A Comprehensive Overview, *IJCTPR, 2015, 3(3): 909–915*
2. Chime SA, Kenechukwu FC, Onunkwo GC, Attama AA, Ogbonna JD. Recent advances in lipospheres drug delivery system. J Pharm Res, 2012; 5(3):1743-1748.
3. Galgatte UC, Bhosale UM, Chaudhari PD, Formulation Development, Optimization and *In-vitro* Evaluation of Glimepiride Lipospheres, Int. J. Pharm. Sci. Rev. Res., 2015; 157-162.
4. Satheeshbabu N, Gowthamarajan K. Manufacturing techniques of lipospheres: overview.International Journal of Pharmacy and Pharmaceutical Sciences, 2011; 3(4):17-21.
5. Tripathi KD. Essentials of Medical Pharmacology, Seventh Edition, Volume 4, Jaypee Brothers medical publishers (P) Ltd. Delhi, 2013; 270-72.
6. Lavanya N, Aparna C, Umamahesh B, Formulation and evaluation of glipizide microemulsion, International Journal of Pharmacy and Pharmaceutical Sciences, 2016; *8(8):171-176.*
7. Patel JK, Chavda JR, Formulation and Evaluation of Glipizide Floating-Bioadhesive Tablets, Braz. Arch. Biol. Technol. 2010; 53(5):1073-1085.
8. Momoh MA, Esimone CO. Phospholipon 90H (P90H)-based PEGylated microscopic lipospheres delivery system for Gentamicin: An antibiotic evaluation. Asian Pac J Trop Biomed, 2012; 2(11):889-894.
9. Jadhav S.V., Sadgir D. P., Patil M. P., Jagtap R. M., Lipospheres review: methods and its applications in bio-compatible drug delivery system, world journal of pharmacy and pharmaceutical sciences, 2014; 1023-1043.
10. Khulbe P, Manjal P. Formulation and evaluation of vinpocetine loaded lipospheres. Int J Pharm Pharm Sci, 2012; 4(3):470-473.
11. Shivakumar HN, Patel PB, Desai BG, Ashok P, Arulmozhi S, Design and statistical optimization of glipizide loaded lipospheres using response surface methodology, *Acta Pharm.* 2007; 57:269–285.
12. World Health Organization. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Technical Report Series, No. 2009; 953:87-130.