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FORMULATION AND EVALUATION OF GLIMEPIRIDE LIPOSOMAL DRUG DELIVERY SYSTEM

Dr. Khaja Pasha*[1] and Dr. Shahana Banu[2]

[1]Azad College of Pharmacy, Moinabad, Rangareddy.

[2]Department of Zoology Gulbarga University, Gulbarga.

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***Corresponding Author**
Dr. Khaja Pasha
Azad College of Pharmacy,
Moinabad, Rangareddy.

ABSTRACT

The drug release from Liposomes depends on many factors including the composition of Liposomes, the type of drug encapsulated and nature of the cell. Once it is released a drug that normally crosses the membrane of a cell will enter the cell, other drugs will not enter. Glimepiride is a drug with narrow therapeutic index and short biological half-life. This study aimed at developing and optimizing liposomal formulation of Glimepiride in order to improve its bioavailability. In evaluation study the effect of the varying composition of lipids on the properties such as encapsulation efficiency, particle size and drug release were studied. Phase transition study was carried out to confirm the complete interaction of Glimepiride with bilayer structure of liposome. Moreover, the release of the drug was also modified and extended over a period of 8 h in all formulations. F1 emerged as the most satisfactory formulation in so far as its properties were concerned. Further, release of the drug from the most satisfactory formulation (F1) was evaluated through dialysis membrane to get the idea of drug release.

KEYWORDS: Liposomes, Glimepiride, bioavailability.

INTRODUCTION

Conventional antidiabetic drugs administered either orally or parenterally have several disadvantages. The therapeutic areas of liposomes were widely extended as carriers for antidiabetics, anticancer agents, antibacterial, antifungal drugs and ocular liposomes.[1,2] These studies show that the role of liposomes in satisfying pharmaceutical considerations is unavoidable in the field of medicine. The supporting factors of liposomes include inexpensive material, straightforward and rapid method of generating liposomes,

homogeneous and reproducible size distribution and different efficient techniques for loading liposomes.[3,4,5] In addition, the final liposomal formulation must be highly stable, as both the retention of entrapped drug as well as chemical and dimensional stability of the liposome themselves. For treating patients with type II diabetes mellitus, an oral antidiabetic drug, Glimepiride is commonly prescribed. Glimepiride is a sulfonylureas class drug.[6,7]

MATERIALS AND METHOD[8,9,10]

Materials

Glimepiride was a gift sample from Dr. Reddy's Laboratories, Hyderabad.

Phosphotidylcholine, cholesterol and chloroform were purchased from SD fine chemical Mumbai.

Methods

Preparation of standard graph of glimepiride in 7.4 Phosphate buffer

Accurately weighed amount (100 mg) of the drug was dissolved in distilled water in 100 ml volumetric flask and the volume was made up to 100ml. from this stock solution 10ml is withdrawn in to volumetric flask, made the volume up to 100ml with distilled water. From this second stock solution (100µg/ml), g/mlµconcentrations of 10, 20, 30, 40, 50 solutions were prepared and the corresponding absorbance was measured at wave length (λmax) 245 nm in a UV Visible spectrophotometer.

Preparation of glimepiride liposomes

Liposomes were prepared by physical dispersion method using different ratio of lipids.

In this method the lipids were dissolved in chloroform. This solution of lipids in chloroform was spread over flat bottom conical flask. The solution was then evaporated at room temperature without disturbing the solution. The hydration of lipid film form was carried out with aqueous medium phosphate buffer (pH 7.4). For this the flask was inclined to one side and aqueous medium containing drug to be entrapped was introduced down the side of flask and flask was slowly returned to upright orientation. The fluid was allowed to run gently over lipid layer and flask was allowed to stand for 2 h at 37^0C for complete swelling. After swelling, vesicles are harvested by swirling the contents of flask to yield milky white suspension.[11,12,13] Then formulations were subjected to centrifugation. Different batches of

liposomes were prepared in order to select an optimum formula. All batches of liposomes were prepared as per the general method described above.

Formulation table

Table 1: composition of lipids for preparation of liposome each formulation contain 200 mg of glimepiride.

Ingredients	F1	F2	F3
Phosphatidylcholine	200	250	300
Cholesterol	50	75	100
Solvent(Chloroform)	10	10	10
Drug(Glimepride)	100	100	100
Phosphate buffer pH 7.4	10	10	10

Evaluations of Liposomes[15,16,17,18,19,20]

Drug - excipient compatibility studies (FT-IR)

The compatibility between the drug and the selected lipid and other excipients was evaluated using FTIR peak matching method. There was no appearance or disappearance of peaks in the drug-lipid mixture, which confirmed the absence of any chemical interaction between the drug, lipid and other chemicals.

Drug entrapment efficiency of liposomes

Entrapment efficiency of liposomes were determined by centrifugation method. Aliquots (1 ml) of liposomal dispersion were subjected to centrifugation on a laboratory centrifuge (Remi R4C) at 3500 rpm for a period of 90 min. The clear supernatants were removed carefully to separate non entrapped Glimepiride and absorbance recorded at 245nm. The sediment in the centrifugation tube was diluted to 100 ml with phosphate buffer pH 7.4 and the absorbance of this solution was recorded at 245 nm.

Amount of glimepiride in supernatant and sediment gave a total amount of glimepiride in 1 ml dispersion.

% entrapment of drug was calculated by the following formula

$$\% \text{ Drug Entrapped (PDE)} = \frac{\text{Amount of drug in sediment}}{\text{Total amount of drug}} \times 100$$

Particle size analysis

All the prepared batches of liposomes were viewed under microscope to study their size. Size of liposomal vesicles from each batch was measured at different location on slide by taking a small drop of liposomal dispersion on it and average size of liposomal vesicles were determined.

***In Vitro* Drug release study**

The release studies were carried out in 10 ml Franz diffusion cell containing 10 ml Phosphate buffer. Phosphate buffer pH 7.4 (10ml) was placed in a 10 ml beaker. The beaker was assembled on a magnetic stirrer and the medium was equilibrated at 37±5^{0}C. Dialysis membrane was taken and one end of the membrane was sealed. After separation of non-entrapped Glimepiride liposomal dispersion was filled in the dialysis membrane and other end was closed. The dialysis membrane containing the sample was suspended in the medium. 1sml of aliquots were withdrawn at specific intervals, filtered after withdrawal and the apparatus was immediately replenished with same quantity of fresh buffer medium.

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile.

The prepared Glimepiride liposomes were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2^{o}c and refrigerator 2-8^{o}c for a period of 30 days.

RESULTS AND DISCUSSION

Standard graph of Glimepiride

Standard solution of Glimepiride prepared with phosphate buffer saline of pH 7.4

Table 2: Absorbance of various concentrations of the standard solution prepared with phosphate buffer saline of pH 7.4.

S.No.	Concentration (µg/ml)	Absorbance (245nm)
1.	10	0.146
2.	20	0.216
3.	30	0.347
4.	40	0.498
5.	50	0.590

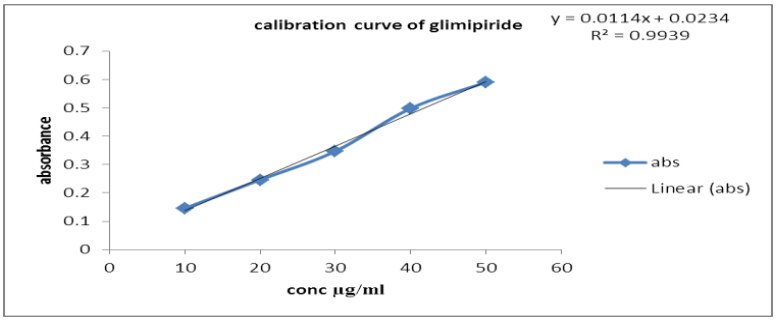


Figure 1: Standard graph and regression value of the standard solution with pH 7.4.

Drug - excipient compatibility studies (FT-IR)

The compatibility between the drug and the selected lipid and other excipients was evaluated using FTIR peak matching method.

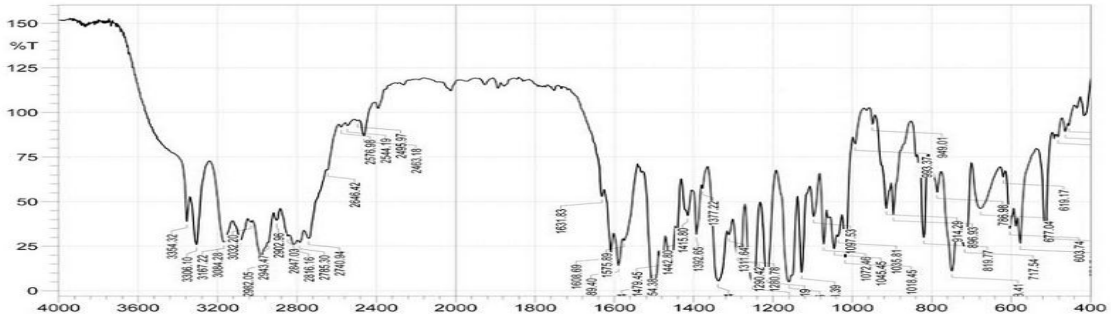


Figure 2: FTIR spectra data for pure Glimepiride.

Table 3: FTIR spectra data for pure Glimepiride.

S. no.	Functional groups	FTIR absorption band of pure Decitabine
1	C-N	1213
2	CH(Alkane)	2863
3	N-H(Bending)	1620
4	OCH_3	1250
5	C=C	3205

Entrapment efficiency

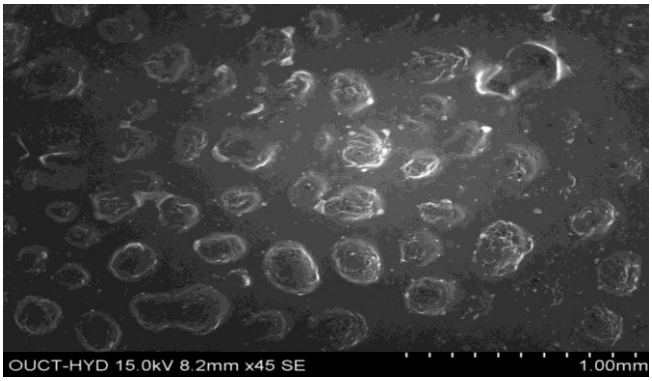
Table 4: Results of entrapment efficiency of liposomes of formulations.

Observations	Batch code		
	F1	F2	F3
1	49.12	47.50	46.47
2	44.59	47.69	49.14
3	47.70	45.80	46.62
Mean	48.33	46.70	48.07
Mean ± S.D.	48.33±1.000	46.70±0.566	48.07±1.525

Now, let H_0 be the hypothesis that there is no significant difference between the batches.

Particle size

Vesicle shape: Vesicle shape of the prepared formulation was found to be spherical from the SEM (scanning electron microscope) analysis at 15.00kV.



2. Vesicle size

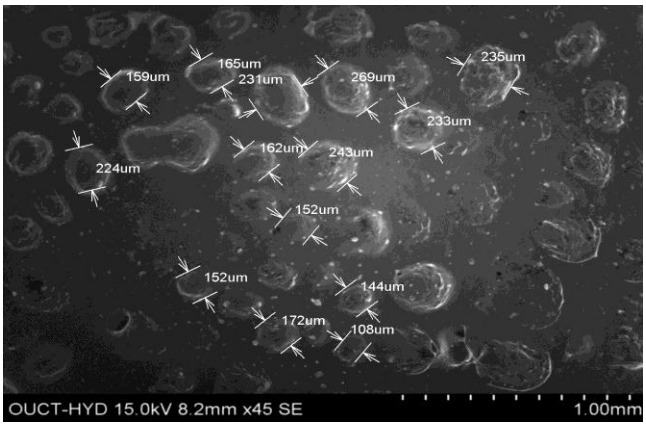


Figure 3: particle size of Glimepiride liposomes.

Table 5: Vesicle Size.

Formulation	Size (µm)
F1	125
F2	119
F3	212

Table 6: Results of particle size of liposomes.

Observations	Batch code		
	F1	F2	F3
1	6.22	7.20	6.07
2	7.12	6.72	7.19
3	6.62	7.32	6.69
Mean	6.68	7.20	6.4
Mean ± S.D.	6.76±0.096	7.24±0.049	6.6±0.062

Now, let H_0 be the hypothesis that there is no significant difference between the batches.

Drug release studies

Table 7: Cumulative percentage drug release from verious formulation of liposomes.

Time (Min)	Batch code		
	F1	F2	F3
0	0	0	0
5	17.35±1.04	19.85±1.16	22.60±1.58
15	23.05±2.26	23.63±3.52	24.18±0.52
30	25.13±0.78	26.10±0.23	27.30±2.22
45	30.38±1.20	29.32±0.10	31.32±1.60
60	31.81±1.08	31.52±0.39	33.24±1.20
90	32.40±1.02	34.23±0.12	35.52±1.04
120	36.16±0.86	35.12±3.50	43.08±0.72
180	45.50±1.42	42.43±0.51`	51.10±0.88
240	52.19±0.77	52.10±3.00	57.25±.80
300	59.18±1.18	60.59±2.12	65.09±1.48
360	78.62±0.79	72.21±9.81	72.38±1.36
420	85.32±1.6	85.33±6.89	80.87 ±0.7
480	98.16±0.30	95.70±2.50	97.63±1.02

(Mean ± S. D., =3)

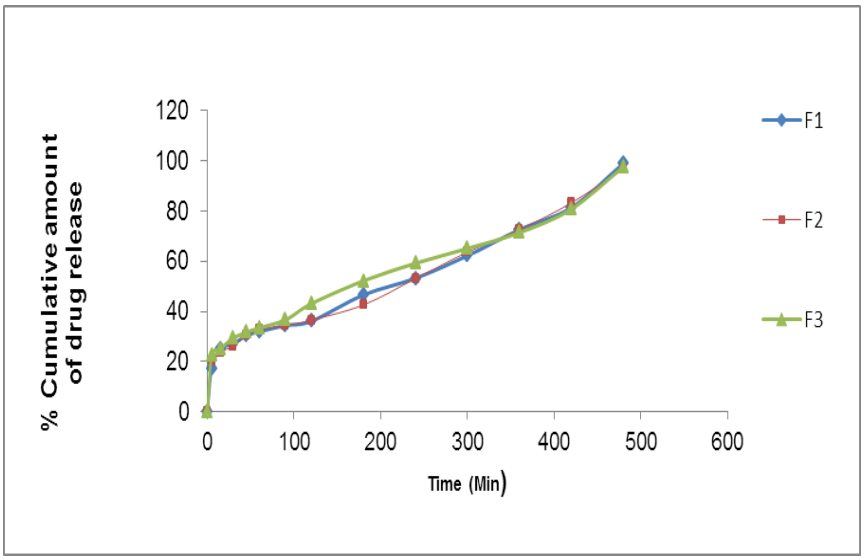


Figure 4: *in vitro* drug release of various formulations.

All the three batches of formulation F1 were found to release the drug in 8 h. The cumulative percentage release was found to be 98.16%.

Stability studies

Stability studies were carried out for a period of two month at 4±2^{0}C, 25±2^{0}C and 37±2^{0}C. The entrapment efficiency was estimated at an interval of 15 days. The results of stability studies are shown in table.

Table 8: Stability studies for the formulation F1.

Sampling Intervals (Days)	% drug entrapped at		
	4 ± 2^0C	25 ± 2^0C	37 ± 2^0C
0	46.72	46.72	47.72
15	47.65	47.65	46.21
30	48.32	42.42	42.12
45	46.05	42.60	38.92
60	47.70	38.12	35.09

CONCLUSION

From the performed work it was concluded that:

1. Glimepiride possesses all requisite qualities required for liposomal drug delivery.
2. Among the various formulation, the combination F1 was found to be most suitable because of high encapsulation efficiency with smaller particle size.
3. The formulation F1 comprising phosphatidylcholine, cholesterol 9:1 ratio, fulfills the requirement of good liposomal formulation. *In vitro* drug release upto 8 h and more than 98.16% drug released. Follows peppas model in release studies. It shows encapsulation efficiency of 48.33% and particle size of 6.76 µm.

REFERENCES

1. Benita S. Microencapsulation Method and Industrial Application, Drug and The Pharmaceutical sciences, 2002; 73: 213.
2. Fuji G. Vesicles, Realization of the Drug Delivery Concept. New York, 1996; 62: 491-495.
3. Bangham AD, Standish MM. Diffusion of univalent ions across the lamella of swollen Phospholipids. J. Mol. Biol. 1965; 13: 238-252.
4. Vyas SP, Khar RK. Targeted and controlled Drug Delivery, Novel Carrier system, CBS Publishers and distributors, 2002; 249.
5. Gregoriadis G. Liposome technology, Liposome preparation and related techniques, 3rd edition, 2007; 1: 21.
6. Singh S, Gulati M. Advances in liposomal therapeutics, Targeting of drugs to lipid bilayer in liposomes: an approach for the success of liposomes as delivery systems. CBS Publishers and distributors. New Delhi, 2001; 4-34.
7. Scherphof G, Morselt H, Regts J. The involvement of the lipid phase transition in the plasma-induced dissolution of multilamellar phosphatidylcholine vesicles. Biochem. Biophys. Acta, 1979; 556: 196–207.

8. Jain NK. Controlled and novel drug Delivery, CBS Publishers and distributors, 2002; 305-326-330.
9. Bangham AD. Techniques in life Science, lipid membrane biochemistry. Elsevier scientific publications. Ireland, 1982; 1-25.
10. Drummond DC, Meyer O, Hong K. Pharmacokinetic study of liposome encapsulated drug. Pharmacological reviews, 1999; 51(4): 691-743-11.
11. Lasic DD**.** Stealth liposomes, Microencapsulation Method and Industrial Applications, 1996; 73: 297-311.
12. Crommelin DJ, Schreier H. Liposomes, Colloidal Drug Delivery Systems. 1996 p. 73-157.
13. Liu R, Cannon JB, Li Y. Liposomes in Solubilization. Water Insoluble Drug Formulation CRC Press, New York, 2000; 355-358.
14. Patel HM, Ryman BR. Systemic and Oral administration of liposomes. Physical Structure to therapeutic applications, 1981; 409-439.
15. Jaggi M, Khar RK. Liposomes as Drug Carriers. Indian Drugs, 1989; 27(8): 404.
16. Krensky AM, Strom TB. Immunomodulators: Immunosuppressive agents, Tolerogens and Immunostimulants. Goodman and Gilman's The Pharmacological Basis of Therapeutics Limbird LE (Ed.) 10th Ed, 2001; 1466-1480.
17. Redziniak G, Perrier P. Cosmetic applications of liposomes. Microencapsulation Methods and industrial applications Simon B (Ed) New York, 1996; 577-579.
18. Bhalerao SS, Harshal AR. Preparation optimization characterization and stability studies of Salicylic acid liposomes. Drug Development and Industrial Pharmacy, 2003; 29(4): 451.
19. Yang D, Ge L. Preparation characterization and pharmacokinetics of sterically stabilized Nimodipine containing liposomes. Drug Development and Industrial Pharmacy, 2006; 32: 219.
20. Ugwu S, Zhang A. Preparation characterization and stability of liposome based formulation of Mitoxantrone. Drug Development and Industrial Pharmacy, 2005; 31: 223.