ejpmr, 2021,8(4), 474-478

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

DEVELOPMENT AND CHARECTERIZATION OF GLIBENCLAMIDE LIPOSOMAL FORMULATION

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Article Received on 28/01/2021 **Article Revised on 18/02/2021** **Article Accepted on 08/03/2021**

ABSTRACT

The aim of the present investigation was to design a liposomes containing glibenclamide. Liposomes were prepared by the thin film hydration method by using chloroform as a solvent. Liposomes containing glibenclamide formulations were prepared by different concentration of lecithin and cholesterol by thin film technique. these formulations were evaluated for entrapment efficiency , zeta potential ,surface morphology and in vitro drug release. Coating of liposomes resulted increases the zeta potential. highest entrapment efficiency was observed in F1and F3 92%and 94%. The percent drug release from F1-F4 and CF1 was observed as follows F1-88.57%, F2-73.31%, F3-76.29%,F4-90.97%, and F1 coated as a CF1-69.85%. release kinetics folows the higuchi plot and non –fickian diffusion mechanism.

KEYWORDS: Glibenclamide, liposomes, thin film hydration method, invitro – diffusion.

INTRODUCTION

Liposomes were discovered by Alec D Bangham in the 1960s at the Babraham Institute, University of Cambridge, and consist of single or multiple concentric lipid bilayers encapsulating an aqueous compartment. The first formulations were composed solely of natural lipids; at present they can include natural and/or synthetic lipids and surfactants. They have the capability of entrapping both lipophilic and hydrophilic agents, in the lipid membrane and in the aqueous core, respectively. The size of these nearly spherical lipid vesicles can range from a few nanometers to several micrometers. However, liposomes applied to medical use range between 50 and 450 nm.[1]

MATERIAL AND METHOD

Glibenclamide was gifted from kavya pharma Ltd, soya lecithin was purchased from pharma sonic biochem extraction Ltd .indore , cholesterol,and other solvents like chloroform and methanol purchased from s d fine chem. Ltd .mumbai, phosphate buffer PH 6.8 were prepared as described in the Indian pharmacopoeia (1996).

PREPARATION OF PREDNISONE LIPOSOME

A. Preparation of liposomes

Cationic multilamellar liposomes can be prepared by hydration of lipid film. The lipid mixture is dissolved in a small amount of chloroform and placed in a rotary evaporator at 40°C until a thin film is obtained, and allowed to stand overnight in a vacuum chamber to ensure complete solvent removal. Phosphate buffer pH 6.8 is used to hydrate the thin film. The hydrated thin film is melted in water bath at 70°C for 1 min and blended to obtain multilamellar liposomes. Then prepared liposome will be sonicated to reduce particle size.[2]

B. Coating of liposomes

Chitosan was previously dissolved in glacial acetic acid overnight at room temperature. In order to coat the liposomes with chitosan, 1 mL of chitosan with a concentration of 1 mg/mL was added dropwise to the same amount liposome volume under continuous magnetic stirring for 1 h. Finally, the liposomes were sonicated for 30 min with an ultrasonic batho produce uniform chitosan-coated liposomes.[3]

Table 1: formulation design for the preparation of uncoated liposomes containing glibenclamide.

Formulation code	Drug	Soya lecithin	Cholesterol
F1	100	200	100
F2	100	300	100
F3	100	400	100
F4	100	500	100

CHARECTERIZATION OF LIPOSOMES

Determination of Entrapment Efficiency

The liposomal formulation was centrifuged at 4000 rpm for 18 min at 4 °C temperature by using ramie cooling centrifuge to separate the free drug. A supernatant contains the liposomes in suspending stage and free drug on the wall of centrifuge tube. The supernatant was again centrifuged at 12000 rpm for 38 min at 4 °C temperature. As a result, a transparent solution of supernatant and liposome pellet was attained. The pellet consisting of liposomes was redispersed in distilled water prior to other studies.

The liposomes devoid of unentrapped free drug were mixed with 10 ml of mixture of methanol: water ratio (7:3 v/v) followed by 5 min of sonication. As a result of sonication, the liposomes were disrupted to discharge the drug. The discharged drug was determined for the drug entrapment. The amount of fenofibrate was estimated by using HPLC system. Percentage entrapment efficiency was determined as

$$\textbf{Percentage Entrapment Efficiency} = W_c / W_t \times 100$$

Where amount of drug content (entrapped) in the liposomes is denoted as W_c and total amount of drug in the dispersion is denoted as W_t.[4]

In vitro diffusion studies

In vitro diffusion studies were carried by using cellophane membrane. The membrane was soaked overnight in phosphate buffer pH 6.8. 10 ml of prepared liposomal dispersion which contains 10 mg of drug was taken and placed in the one end of the open tube. Dialysis tube was placed in 500 ml beaker, containing 250 ml phosphate buffer pH 6.8. The temperature of the receptor phase was maintained at 37 ± 0.5° C and then it was stirred with magnetic stirrer to maintain homogeneous condition. The samples were withdrawn at different time intervals. Fresh medium was used to replace with equal volume of the sample withdrawn. The samples were analyzed at 243. 60 nm in a UV-Visible spectrophotometer and amount of drug released at different time intervals was calculated.[5]

Stability studies

The drug retentive behaviour was assessed by storing the formulationF6 liposomal suspensions and liposomal loaded gels at two different temperature conditions, i.e., 4-8 °C (Refrigerator; RF), 25±2 °C (Room temperature; RT), for a period of 60 days. Samples were withdrawn periodically and analyzed simultaneously for the entrapment efficiency studies.[6]

RESULT AND DISCUSSION

FTIR spectra of pure glibenclamide showed sharp peaks 1715,1618.66,1626.2 and 1160 physical mixture showed all the characteristic peaks of pure drug, confirmed no interaction between the drug and excipient. Comparative studies of FTIR graph are showed in figure 1-2. The surface morphology was studied by scanning electron microscope (SEM) the SEM photographs of liposomes formulation F4 as showen in figure 3. vesicle size distribution of F1-F4-CF1 graph are showed in figure 4. The % entrapment efficiency was found to decresed with increasing cholesterol concentration it is showed in figure 5. In vitro drug release of liposomes in phosphate buffer pH6.8 was performed using dialysis tube diffusion technique. the in vitro drug release profile of liposome formulations obtained from dialysis experiment was shown in figure 6. The release of liposomes chitosan containing coated liposomes was varied according to concentration of soya lecithin and cholesterol. The progressive decresase in the amount of drug diffused through cellophane membrane from formulations F1-F4and CF1 attributed to gradual increase in soya lecithin and cholesterol content. It has been concluded that, if we increase the concentration of soya lecithin and cholesterol, the diffusion of drug also decreases. The amount of drug diffused from formulation CF1 was 68.9%, was lower among the formulations F1 to F4 and CF1.

Release kinetics follows the higuchi plot and non – Fickian diffusion mechanism. it is shown in table 3 and figure7.

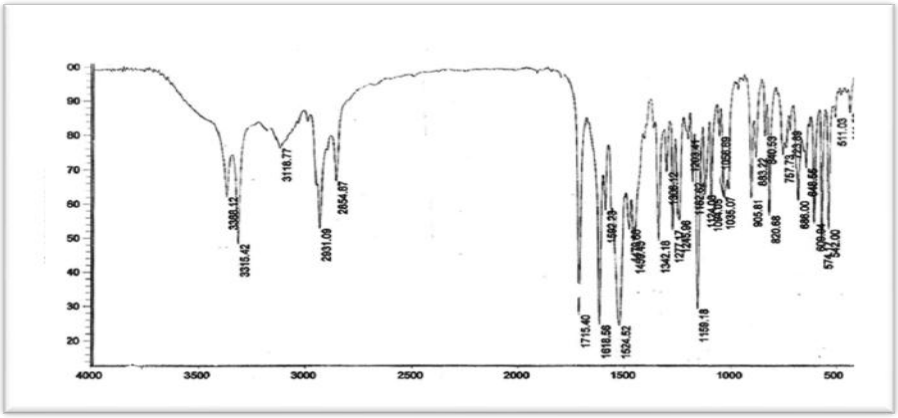

Figure 1: FT IR spectroscopy of glibenclamide.

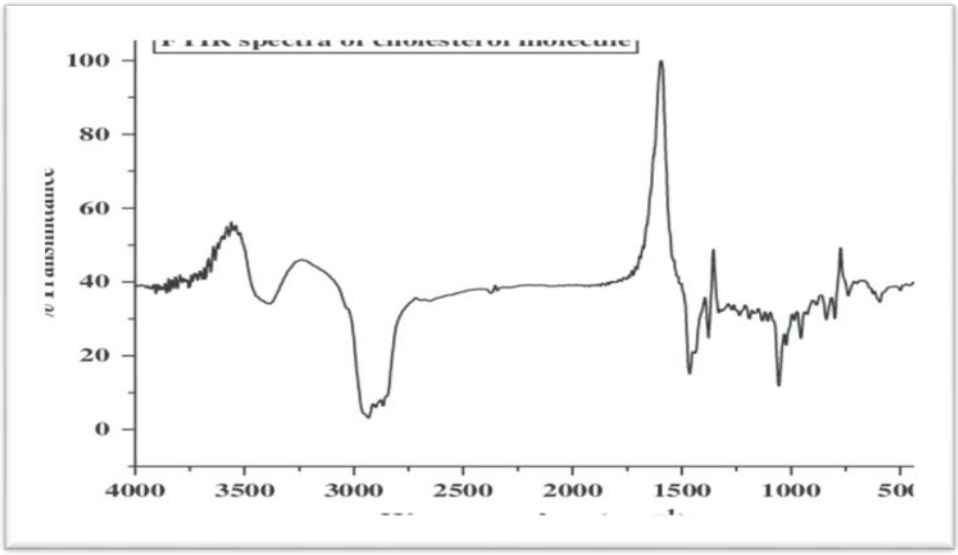

Figure. 2: FT-IR Spectroscopy of cholesterol.

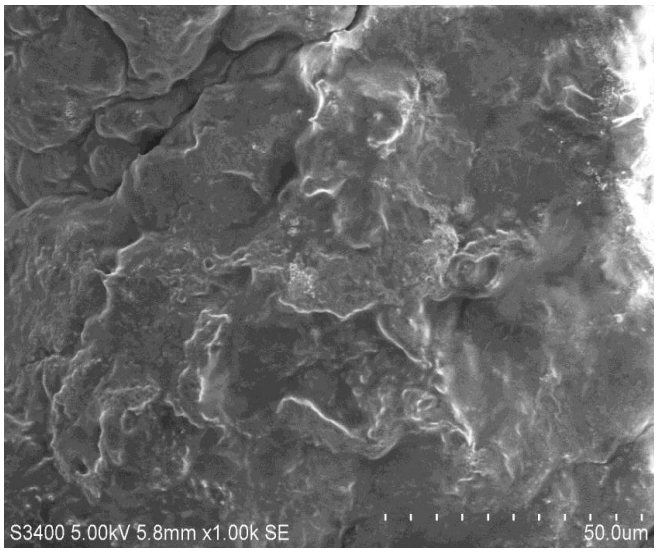

Figure. 3: SEM of liposomes formulation F4.

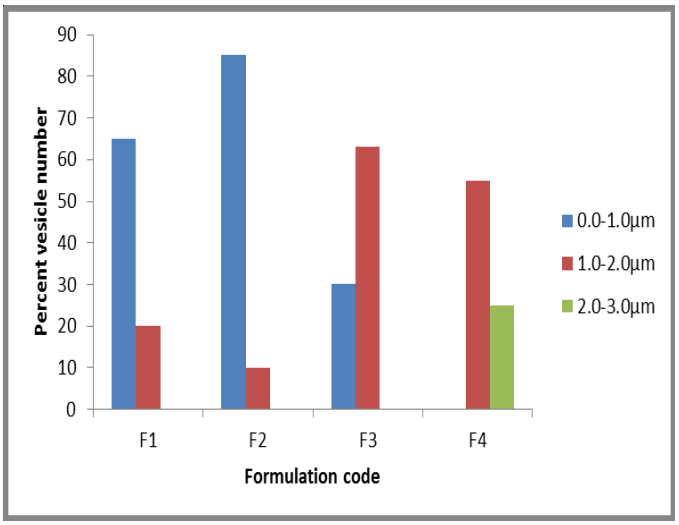

Figure. 4: vesicle size analysis of liposomal formulation.

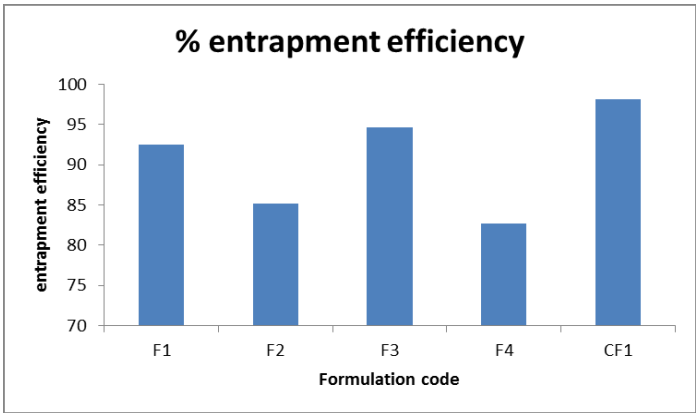

Figure 5: % entrapment efficiency of formulation F1- F4- CF1.

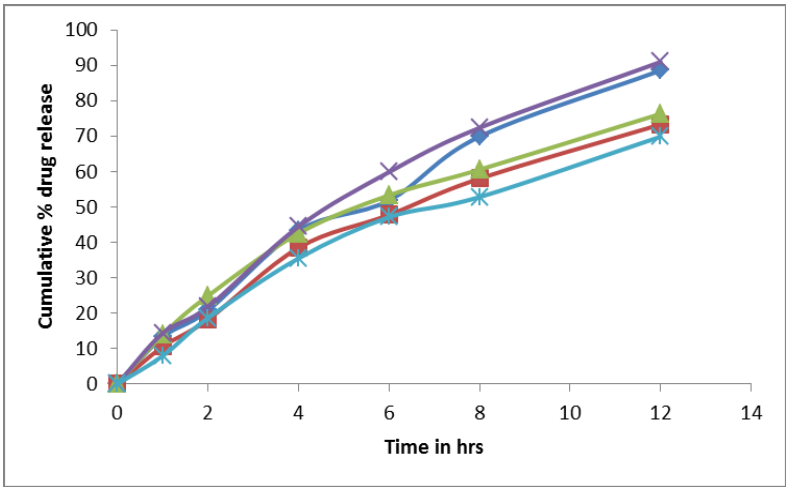

Figure.6: % *in-vitro* drug release of formulation F1- F4-CF1.

RESULT OF MODELLING FITTING

Table 3: Data for different kinetic model.

Formulation code	Zero order	First order	Higuchi plot	Peppas plot	
				r2	'n'
F1	0.963	0.622	0.973	0.714	1.306
F2	0.959	0.478	0.970	0.578	1.166
F3	0.938	0.567	0.987	0.668	1.234
F4	0.966	0.611	0.969	0.705	1.315
CF1	0.920	0.558	0.975	0.659	1.225

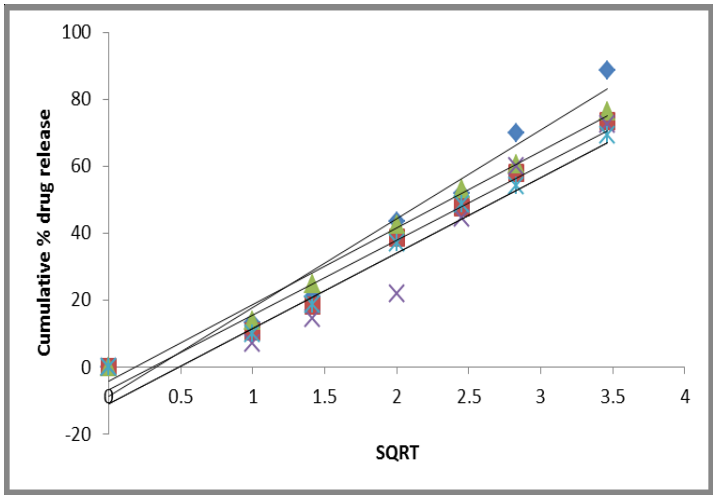

Figure 7: Higuchi drug release kinetics for F1-F4-CF1.

CONCLUSION

In this study ,a liposomal formulation was developed with desirable drug delivery properties.The chitosan-coated liposome had good in vitro stability, and enhances cellular cellular uptake. Therefore, the chitosan –coated carbopol gel formulation appears to have the potential to improve the bioavailability of glibenclamide.

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