Journal of Advanced Pharmacy Education & Research
1(4): 195-200 (2011) ISSN 2249-3379

Microemulsion Drug Delivery System: For Oral Bioavailability Enhancement of Glipizide

Biresh K Sarkar*[1], Shiv S. Hardenia[2]

1. Sri Balaji College of Pharmacy, Jaipur, India.
2. College of Pharmacy, Indore Professional Studies (IPS) Academy, Knowledge Village, Agra-Bombay Road, Rajendra Nagar, Indore (Madhya Pradesh), India.

*Corresponding author: bireshsarkar@gmail.com

ABSTRACT:

Glipizide (GZ) is a widely used oral hypoglycemic drug with very poor water solubility. The purpose of this study was to enhance the dissolution rate and bioavailability of this drug by developing a novel delivery system i.e. microemulsion (ME), and to study effect of microemulsion (ME) on the oral bioavailability of Glipizide. Capmul® MCM-based ME formulation with Cremophor® EL as surfactant and Transcutol® as co-surfactant, was developed for oral delivery of Glipizide. Optimized ME was evaluated for its transparency, viscosity, percentage assay etc. Solubilisation capacity of the ME system was also determined. The prepared ME was compared with the pure drug solution and commercially available tablet for *in vitro* drug release. The optimized ME formulation containing Glipizide, Capmul® MCM (6.5%), Cremophor® EL (25%), Transcutol® P (7.5%) and distilled water, showed higher *in vitro* drug release, as compared to plain drug suspension and the commercially available drug. These results demonstrate the potential use of ME for improving the bioavailability of poor water soluble compounds, such as Glipizide.

Keywords: Glipizide, microemulsion, bioavailability, Solubilisation.

INTRODUCTION:

Glipizide (GZ) is a second-generation sulfonylurea that can acutely lower the blood glucose level in humans by stimulating the release of insulin from the pancreas and is typically prescribed to treat non-insulin-dependent diabetes mellitus. The drug is insoluble in water, and its dissolution is considered to be a rate-determining step (i.e., an effective factor) in its absorption from the gastrointestinal fluids [1]. Microemulsion (ME), a novel drug delivery system, has been reported to improve the rate and extent of

absorption of lipophilic drugs [2-5]. The main aim of this study was to improve the bioavailability of GZ by preparing its ME. *In vitro* stability of formulation was assessed. In the present study, ME formulation was prepared using Capmul® MCM (HLB = 5.5-6.0), Cremophor® EL (HLB = 14), Transcutol® P (HLB = 4) and distilled water by water titration method. The effects of formulation variables on different physicochemical characteristics were studied. An *in vitro* diffusion study was performed using a synthetic membrane.

MATERIALS AND METHODS:

Materials

GZ was obtained from Novopharm Formulations Pvt. Ltd**.** Gujarat, India. Capmul® MCM, Labrafac® CC, Cremophor® EL, Labrasol® and Transcutol® P were obtained from Colorcon Asia (Mumbai). All other chemicals were used of reagent grade.

Preparation of ME

ME formulations were prepared by the water titration method by varying the ratio of oil, surfactant, co-surfactant, and water; keeping the concentration of GZ constant in each case. The drug was mixed in an accurate quantity of oil (Capmul® MCM), and to that, surfactant (Cremophor® EL) and co-surfactant (Transcutol® P) were added and mixed gently for 10 minutes with the help of a magnetic stirrer at room temperature. The mixture was then finally titrated with distilled water until a stable and transparent ME was obtained. ME formulation was optimized through the formulation (oil: surfactant, surfactant: co-surfactant and oil: water ratios) and process variables (time and speed). Percentage transmittance was evaluated during the optimization [6].

Characterization and evaluation of ME

Percentage transmittance

Transparency of both optimized ME formulation and its diluted forms (10 and 100 times with distilled water) was determined by measuring percentage transmittance through ultraviolet (UV) spectrophotometer (UV-1601-220xShimadzu). Percentage transmittance of samples was measured at 276 nm using purified water as blank [7].

Rheological measurements

The rheological behavior of ME (different dilutions) was evaluated using Brookfield LVDV and CP Viscometer (Brookfield, USA) by means of rheological software.

Conductivity study

Electrical conductivity of ME was measured using a conductometer [(CM 180 conductivity meter (Elico, India)] at ambient temperature.

Determination of Drug content in the ME

ME formulation was analyzed for drug content using the UV spectrophotometer.

In vitro release studies

In vitro release studies were performed using a modified Franz diffusion cell at 37 ± 2^0C. A dialysis membrane, with a pore size of 2.4 nm was used. ME of drug (GZ), plain drug suspension and suspension of commercially available GZ were placed in the donor compartment. The receptor compartment was filled with dialysis medium (23 ml of phosphate buffer pH 6.8). At a fixed time interval of one hour, five milliliters of the sample was withdrawn from the receiver compartment through a side tube and analyzed spectrophotometrically [8].

RESULTS AND DISCUSSION:

Solubility study

The solubility data of GZ in various vehicles are provided in Table 1. Capmul® MCM showed higher solubilising capacity compared to other vehicles. Hence, Capmul® MCM was selected as the oil phase. Cremophor® EL and Transcutol® P were selected as the surfactant and co-surfactant respectively for the preparation of optimized ME.

Table 1.Solubility studies in various vehicles

Vehicles	Solubility [(mg/ml) ± standard deviation (SD)]
Capmul® MCM	56.7 ± 1.7
Labrafac® CC	25 ± 2.1
Cremophor® EL	26.3± 2.5
PEG 600	5.52 ± 0.9
Transcutol® P	28.12± 1.3
Optimized ME	115.3 ± 2.4

Percentage transmittance

Percentage transmittance of ME after 10 times and 100 times dilution was 98.59% and 98.82% respectively; indicating transparency and stability of optimized ME.

Determination of drug content

Drug content in the optimized ME formulation was found to be 98.31 %.

Rheological study

The structure and type of ME system was characterized by rheological measurements. Results obtained from the viscosity study reveals that viscosity increased from 52.59 cP to 75.38 cP, with increasing water content which then gradually decreased (Figure 1). This may be due to the fact that the system transforms from W/O through bicontinuous structure to O/W system.

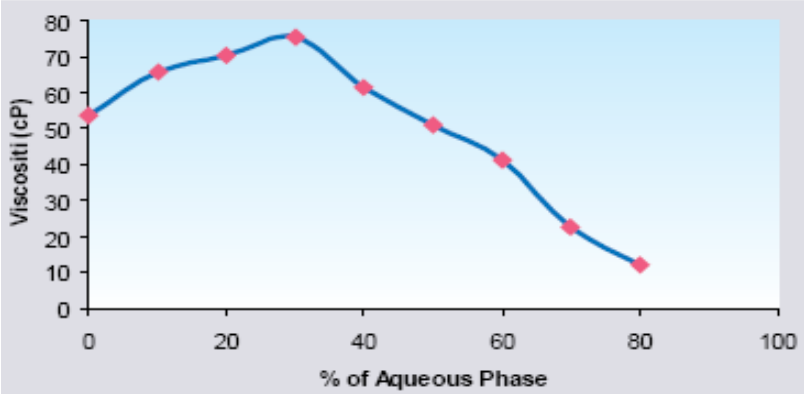

Figure 1: Viscosity changes of ME with increasing water content

Electro-conductivity measurement

Results indicated that electrical conductivity increased rapidly up to 52.94% of the aqueous phase addition. Therefore it was not affected significantly with further addition of the aqueous phase (Figure 2).

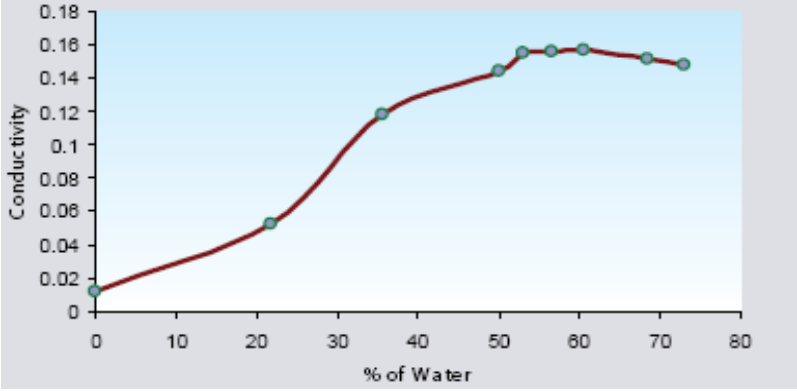

Figure 2: Results of the electro-conductivity study

In vitro release of drug

Results of the *in vitro* drug release from the optimized ME, plain drug suspension and the commercially available drug are shown in Figure 3. Drug release (in hours) from optimized ME, plain drug suspension and the commercially available drug, were found to be 76.14%, 55.11% and 60.15% respectively. ME showed higher drug release as compared to plain drug suspension and the commercially available GZ, which may be due to the solubility-enhancing component of the surfactant and co-surfactant.

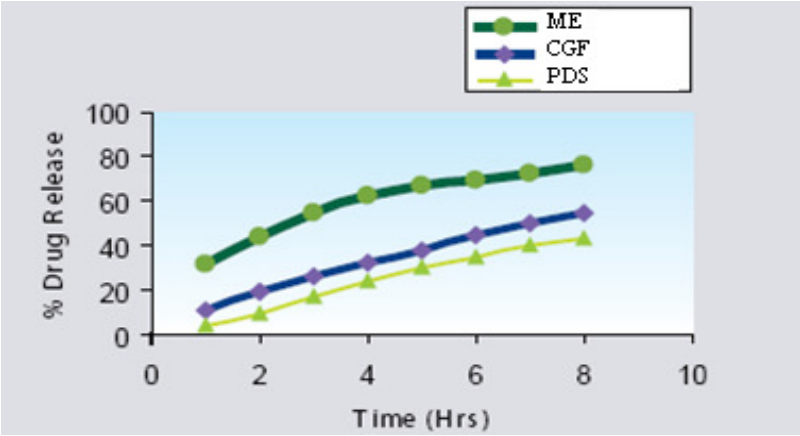

Figure 3: *In vitro* drug release of drug from Microemulsion (ME), Commercially Glipizide Formulation (CGF) and Plain Drug Suspension (PDS)

CONCLUSION:

The developed ME, containing Capmul® MCM (6.5%), Cremophor® EL (25%), Transcutol® P (7.5%), and distilled water, was found to be a transparent fluid. ME showed higher *in vitro* drug release when compared with plain drug suspension and the commercially available drug. Hence, it can be concluded that the ME formulation can be employed to improve the bioavailability of a poorly soluble drug like; Glipizide. However, further studies in higher animals and humans need to be performed before this formulation can be commercially exploited.

REFERENCES:

1. Rx List web site, Description of glipizide, http/www.rxlist.com/cgi/generic/glipxl.htm (Copyright 1998, Mosby Inc.,Mosby's GenRx) (20 May 11).

2. Kang BK, Lee JS, Chon SK, Development of microemulsion drug deliverysystem for oral bioavailability enhancement of simvastatin in beagle dogs. Int J Pharm. 2004; 274:65-73.
3. Dressmann JB, Reppas C. *in vitro-in vivo* correlations for lipophilic, poorly water-soluble drugs. Eur J Pharm Sci, 2000; 11: 73-80.
4. Patel D, Sawant KK. Oral bioavailability enhancement of acyclovir by self microemulsifying drug delivery systems. Drug Dev Ind Pharm. 2007; 33:1318-1326.
5. Abbofazeli R, Lawrence MJ. Investigation into the formation and characterization of phospholipids ME.II: pseudoternary phase diagram of system containing waterlecithin- isopropyl myristate and alcohol: influence of purity of lecithin. Int J Pham. 1994; 106:51-61.
6. Acharya A, Sanyal SK, Moulik SP. Formation and characterization of pharmaceutically useful microemulsion derived from isopropyl myristate, Brij 30, isopropyl alcohol and water. Current Science. 2001; 8:362-370.
7. Kawtikwar PS, Kulkarni NP, Yadav S, Sakarkar DM. Formulation and evaluation of an anti-epileptic, drug-loaded microemulsion for nose to brain delivery. Asian Journal of Pharmaceutics. 2009; 20:143-147.
8. Ghosh PK, Umrethia M, Majithiya RJ, Murthy RSR. Preparation and physicochemical characterization of aprylocapryl macrogol-8-glycerides microemulsion for oral drug delivery. Ars Pharm. 2004; 45:353-372.