

PREPARATION AND *IN VITRO* CHARACTERIZATION OF A NON-EFFERVESCENT FLOATING DRUG DELIVERY SYSTEM FOR POORLY SOLUBLE DRUG, GLIPIZIDE

VENKATA SRIKANTH MEKA^{*}, SHREENI PILLAI, SENTHIL RAJAN DHARMALINGHAM,
RAVI SHESHALA and ADINARAYANA GORAJANA

School of Pharmacy, International Medical University, Bukit Jalil, 57000, Kuala Lumpur, Malaysia

Abstract: The aim of the present study was to formulate a non-effervescent floating drug delivery system of glipizide, a poorly water soluble drug. The solubility of glipizide was initially enhanced using a solid dispersion (SD) strategy with the help of hydrophilic carriers such as poloxamer, cyclodextrin, and povidone. The optimized core material/SD was further formulated into non-effervescent floating tablets (NEFT) by using matrix ballooning inducers, such as crospovidone and release retarding agents including HPMC and PEO. Poloxamer-based solid dispersions prepared by a solvent evaporation technique showed the highest dissolution rate (1 : 10 drug to carrier ratio) compared with all other dispersions. NEFT were evaluated for all physico-chemical properties including *in vitro* buoyancy, dissolution, and release rate. All of the tablets were found to be within pharmacopoeial limits and all of the formulations exhibited good floating behavior. The formulations (F2 and F3) were optimized based on their 12 h drug retardation with continuous buoyancy. The optimized formulations were characterized using FTIR and DSC and no drug and excipient interaction was found. *In-vitro* buoyancy and dissolution studies showed that non-effervescent floating drug delivery systems provide a promising method of achieving prolonged gastric retention time and improved bioavailability of glipizide.

Keywords: non-effervescent, floating system, glipizide, solid dispersion

Oral controlled release drug delivery systems are widely used as they provide prolonged therapeutic effect by releasing the drug at a controlled rate after administration of a single dose. This improves patient compliance, reduces fluctuation of drug levels after multiple doses, reduces the total amount of drug administered, and reduces side effects. However, these systems are limited by the short gastrointestinal (GI) transit time, which prevents the drug from being completely released, leading to low bioavailability. To overcome this limitation, gastroretentive drug delivery systems were developed to retain the dosage form in the stomach (1, 2).

Although different types of gastroretentive systems are available, the floating drug delivery system (FDDS) has been described in detail. Floating drug delivery can be approached by either effervescent or non-effervescent techniques. Optimized effervescent FDDS of propranolol HCl prepared using polyethylene oxide (PEO) had good buoyancy and controlled drug release for up to 12 h (3). Ofloxacin effervescent floating tablets showed controlled drug

release for more than 12 h with excellent buoyancy properties (floating lag time < 1 min, floating duration > 16 h) (4).

FDDS have a bulk density < 1 g/mL, allowing them to float on the surface of the stomach contents (2). Effervescent FDDS incorporate gas generating agents, which provides buoyancy, whereas in non-effervescent systems, the swelling of polymers entraps air within the polymeric matrix, providing buoyancy to the dosage form (1, 2). While there has been much work on the development of effervescent drug delivery, non-effervescent technology is limited. The main drawback of the effervescent drug delivery is patient compliance, due to discomfort in the stomach after administration caused by the continuous liberation of gas.

Studies on non-effervescent systems include that of Garse et al. who formulated non-effervescent FDDS of labetalol hydrochloride using HPMC. Tablets had an insignificant floating lag time, a floating time > 12 h, and complete drug release (5). Patel et al. also designed a non-effervescent floating

^{*} Corresponding author: e-mail: venkatasrikanthmeke@gmail.com

tablet for captopril. Combination of different viscosity grades HPMC showed > 96% drug release after 24 h (6). Sawicki and Łunio prepared floating pellets with verapamil hydrochloride and studied the influence of type of tablet press on the tableting of floating pellets and releasing rate of active substance (7). Development of gastroretentive drug delivery for poorly soluble drug presents a significant challenge. It is inadequate to formulate gastroretentive drug delivery of a poorly soluble drug without improving its solubility at the gastric pH. Hence, the present study targeted glipizide, a poorly soluble compound, as a model drug for the development of a gastroretentive drug delivery system. Solid dispersion is the best approach for the enhancement of solubility of the drugs.

Glipizide is a short acting antidiabetic sulfonylurea. It has a short half life (2–7.3 h) which requires it to be administered in 2–3 divided doses per day. Like all sulfonylureas, it may cause dose-dependent hypoglycemia (8). Therefore, a controlled release system is expected to provide more stable plasma glucose levels, reduce the dosing frequency and decrease the incidence of hypoglycemia. Moreover, the FDDS will be retained longer in the GI tract, providing sufficient time for the drug to be completely released.

Glipizide is a Class II drug according to the Biopharmaceutics Classification System; thus, its absorption is dissolution rate limited (9). Therefore, a solid dispersion approach was applied to improve the solubility and dissolution rate of the drug, followed by formulation into non-effervescent floating

tablets. Dehghan et al. concluded that the order of drug dissolution from different carriers is PEG > PVP > mannitol (10). Batra et al. showed that poloxamer 188 had a higher solubility enhancement effect than poloxamer 407 (11). In both studies, solid dispersions showed a higher dissolution compared with plain drug, or with a physical mixture of drug and carriers (10, 11). The objective of this study was to create a platform technology that enables the incorporation of poorly soluble drugs into FDDS.

EXPERIMENTAL

Materials

Glipizide was obtained from Dr. Reddy's Laboratories Ltd. (Hyderabad, India). Poloxamer 188, PVP K30, β -cyclodextrin, gelucire, PEO, HPMC, magnesium stearate, crospovidone, and lactose were obtained from Labchem Sdn. Bhd. Malaysia. All other reagents were of analytical grade.

Methods

UV analytical method development

Glipizide (100 mg) was dissolved in minimal quantity of methanol and volume was made up to 100 mL with 0.1 M HCl solution. From this, 10 mL of the solution was withdrawn and diluted to 100 mL using 0.1 M HCl solution, which yielded 100 μ g/mL of stock solution. Stock solution was scanned in a UV-Visible spectrometer at the wavelength range of 400–200 nm. Standard solutions of various concentrations of glipizide were prepared by subsequently

Table 1. Solid dispersions prepared by solvent evaporation and melt granulation.

Solid dispersion	Carrier	Drug-Polymer Ratio	Technique
G-PL-S 1:1	Poloxamer 188	1:1	Solvent evaporation
G-PL-S 1:2	Poloxamer 188	1:2	Solvent evaporation
G-PL-S 1:4	Poloxamer 188	1:4	Solvent evaporation
G-PL-S 1:6	Poloxamer 188	1:6	Solvent evaporation
G-PL-M 1:1	Poloxamer 188	1:1	Melt granulation
G-PL-M 1:2	Poloxamer 188	1:2	Melt granulation
G-PL-M 1:4	Poloxamer 188	1:4	Melt granulation
G-PL-M 1:6	Poloxamer 188	1:6	Melt granulation
G-PVP 1:6	PVP K30	1:6	Solvent evaporation
G-BCD 1:6	β -Cyclodextrin	1:6	Kneading
G-GEL 1:6	Gelucire	1:6	Melt granulation
G-PL-S 1:8	Poloxamer 188	1:8	Solvent evaporation
G-PL-S 1:10	Poloxamer 188	1:10	Solvent evaporation

*PL – poloxamer; PVP – polyvinylpyrrolidone; BCD – β -cyclodextrin; GEL – gelucire

Table 2. Formulae of glipizide non-effervescent floating tablets.

Ingredients	F1	F2	F3	F4	F5	F6
Solid dispersion (1 : 10 ratio)	55	55	55	55	55	55
HPMC K100M	15	30	40	–	–	–
PEO N12K	–	–	–	30	50	70
Crospovidone	50	50	50	50	50	50
Lactose	28.5	13.5	–	63	43	23
Mg Stearate	1.5	1.5	1.5	2	2	2
Tablet weight (mg)	150	150	150	200	200	200

Table 3. Mathematical models of drug release (12).

Model	Equation
Zero order	$Q_t = Q_0 + k_0 t$
First order	$\log Q_t = \log Q_0 - k_1 t$
Higuchi	$Q_t = k_H(t)^{1/2}$
Hixson-Crowell	$Q_0^{1/3} - Q_t^{1/3} = k_s t$
Korsmeyer-Peppas	$Q/Q_s = k_n t^n$

Q_t = amount of drug released in time t ; Q_0 = initial amount of drug in the tablet; t/Q_s = fraction of drug released at times t ; k_0 , k_1 , k_H , k_s , k_n = release rate constants; n = the release exponent indicative of the mechanism of drug release.

diluting suitable quantities of stock solution with respective media to obtain a series of standard solutions containing 10, 20, 30, 40, and 50 mg/mL of glipizide. The absorbances of these standard solutions of glipizide in respective media were measured individually at a wavelength of 275 nm against 0.1 M HCl as blank using UV-Visible spectrophotometer (UV-VIS Perkin-Elmer double beam spectrophotometer). A calibration curve was constructed by plotting the absorbance against the concentration of glipizide. The regression equation and the correlation coefficient value were derived from the plot and were used for the estimation of glipizide in 0.1 M HCl solution.

Preparation of solid dispersions

Solid dispersions were prepared using different carriers, techniques, and ratios, as summarized in Table 1.

Solvent evaporation

Glipizide and carrier were dissolved separately using the minimum quantity of methanol, and the two solutions combined. The resulting solution was evaporated at 50°C under reduced pressure in a rota evaporator and they were further dried in desiccator

over silica gel for 24 h to remove all the residual solvents. The dried mass was collected and packed in a closed container.

Kneading technique

Glipizide and β -cyclodextrin were mixed in a mortar. A drop of water was added, and the mixture was kneaded until a homogenous paste was obtained. The mixture was then placed in an oven at 50°C for 30 min, to remove water.

Melt granulation

The carrier was melted on a hot plate. Glipizide was added to the molten carrier with constant stirring to obtain a uniform melt, which was directly cooled in a refrigerator for 24 h to make it solidify. The final product was packed in a closed container for further use.

In vitro drug release of solid dispersions

Drug release studies were carried out using a USP type II (paddle) apparatus at 50 rpm. Solid dispersions equivalent to 5 mg of glipizide were tested in 900 mL of 0.1 M HCl (pH 1.2). Aliquots (5 mL) were withdrawn and filtered with cotton-filled canulae at predetermined intervals with replacement of equal volumes of fresh dissolution medium. Samples were tested spectrophotometrically at 275 nm, and compared against a calibration curve. Percent drug release *versus* time profiles were constructed.

Optimization of solid dispersion

The dissolution profiles of all the solid dispersions were compared. The technique, carrier and ratio were optimized based on the highest dissolution rate.

Preparation of floating tablets

The optimized solid dispersion was incorporated into floating tablets as the tablet core. Tablets were

prepared by direct compression. The ingredients used for each formulation are shown in Table 2. All excipients except magnesium stearate were passed through a 0.5 mm mesh sieve, while the dispersion was screened through a 1 mm mesh sieve. The pre-sifted ingredients were then manually blended in a polybag. The pre-lubricated blend was then mixed with magnesium stearate in the polybag for 3 min. Accurately weighed quantities of the final blend were manually fed into the die of an 8-station rotary tablet press, and then compressed with 8 mm punches.

Evaluation of tablet parameters

Tablets were evaluated for hardness (Monsanto hardness tester), weight variation, and friability (Roche friabilator, 100 revolutions in 4 min).

In vitro buoyancy

Tablets were placed in the dissolution vessel containing 900 mL of 0.1 M HCl. The time taken for the tablet to rise to the surface of the dissolution media (floating lag time) and total duration that the tablet remained on the surface (total floating time) were recorded.

In vitro drug release of floating tablets

Tablets were placed into dissolution vessels containing 900 mL of 0.1 M HCl (pH 1.2). Dissolution studies were carried out for 12 h, with samples withdrawn at predetermined intervals. The apparatus used and procedure is as described in step 4 (*in-vitro* drug release of solid dispersions).

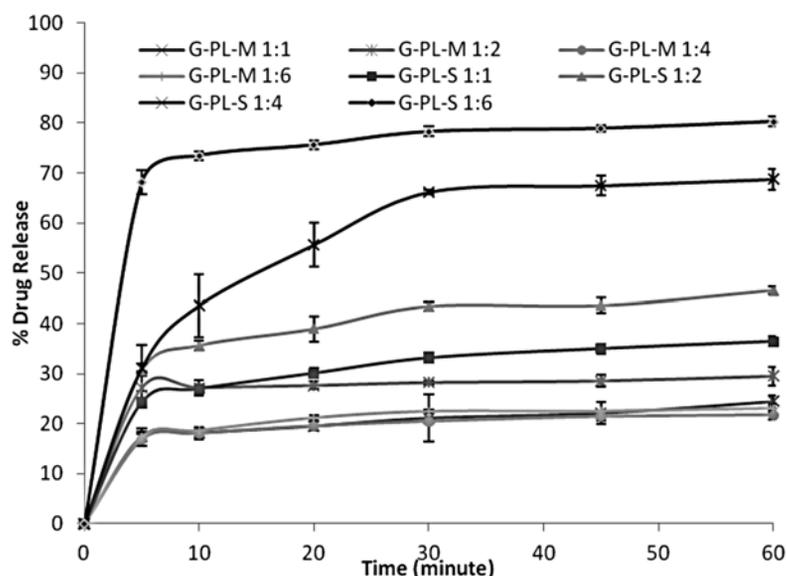


Figure 1. Dissolution profiles of poloxamer solid dispersions

Table 4. *In-vitro* drug release of pure drug and Poloxamer 188 solid dispersions.

Solid dispersion	% drug release					
	5 min	10 min	20 min	30 min	45 min	60 min
G-PL-S 1 : 1	24.29 ± 1.21	26.92 ± 2.89	30.05 ± 1.11	33.11 ± 0.96	34.96 ± 0.28	35.40 ± 1.55
G-PL-S 1 : 2	30.70 ± 1.22	35.60 ± 0.88	38.89 ± 2.56	43.39 ± 0.88	43.55 ± 1.53	46.53 ± 0.74
G-PL-S 1 : 4	31.10 ± 4.66	43.55 ± 6.19	55.61 ± 4.43	66.13 ± 0.46	67.42 ± 1.94	68.71 ± 2.16
G-PL-S 1 : 6	68.22 ± 2.44	73.45 ± 0.91	75.62 ± 0.91	78.27 ± 1.03	78.91 ± 0.74	80.06 ± 1.03
G-PL-M 1 : 1	17.44 ± 0.96	18.16 ± 0.88	19.53 ± 0.91	21.13 ± 4.66	22.10 ± 2.16	24.43 ± 1.14
G-PL-M 1 : 2	27.24 ± 3.11	27.24 ± 1.53	27.64 ± 0.74	28.21 ± 0.28	28.53 ± 1.20	29.49 ± 1.80
G-PL-M 1 : 4	16.79 ± 1.14	18.00 ± 1.20	19.53 ± 0.96	20.41 ± 0.34	21.38 ± 0.85	21.70 ± 0.97
G-PL-M 1 : 6	17.28 ± 1.82	18.64 ± 0.28	21.13 ± 0.51	22.42 ± 0.28	22.50 ± 0.00	23.06 ± 0.74

Table 5. *In vitro* drug release of solid dispersions prepared with different carriers.

Solid dispersion	% drug release					
	5 min	10 min	0 min	30 min	45 min	60 min
G-PL-S 1 : 6	68.22 ± 2.44	73.45 ± 0.91	75.62 ± 0.91	78.27 ± 1.03	78.91 ± 0.74	80.06 ± 1.03
Gel 1 : 6	13.42 ± 2.84	23.38 ± 1.08	33.35 ± 3.86	35.12 ± 0.34	39.70 ± 3.24	44.04 ± 1.48
BCD 1 : 6	14.06 ± 3.13	36.00 ± 2.39	44.60 ± 1.82	48.07 ± 1.25	50.30 ± 3.07	52.79 ± 3.30
PVP 1 : 6	46.93 ± 2.28	59.22 ± 3.24	62.28 ± 0.40	63.48 ± 0.74	64.37 ± 1.25	65.73 ± 1.31

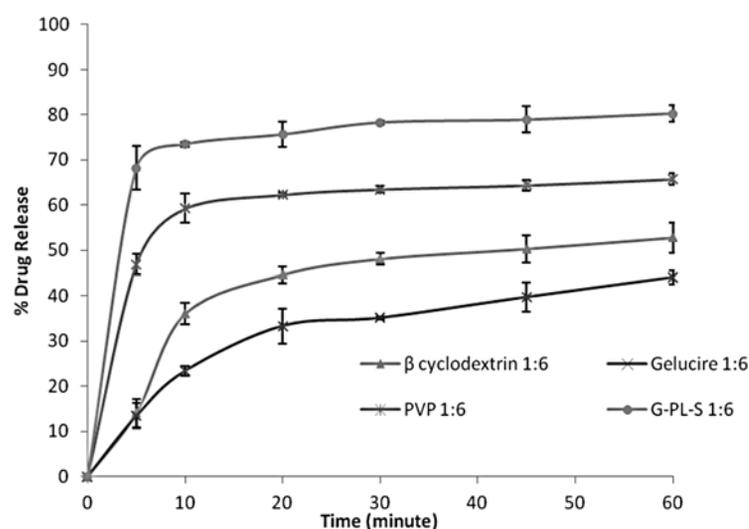


Figure 2. Dissolution profiles of dispersions prepared with different carriers

Determination of drug release kinetics

The dissolution data were fitted into various models of drug release as detailed in Table 3.

Optimization of floating tablets

Formulations with minimum floating lag time, maximum total floating time, and controlled drug release up to 12 h were selected as the optimized formulations.

Drug interaction studies

Fourier transformed infrared radiation (FTIR)

FTIR was performed on the drug, polymer, optimized solid dispersion, and optimized formulations. Samples were analyzed using the potassium bromide (KBr) pellet method (Shimadzu FTIR, scanning range 4000–400 cm^{-1}).

Differential scanning calorimetry (DSC)

DSC was performed with a Mettler Toledo DSC apparatus. Samples (3–10 mg) were heated in

nitrogen atmosphere from 10 to 250°C (heating rate 10°C per min).

RESULTS AND DISCUSSION

UV analytical method development

Glipizide λ_{max} was 275 nm. The calibration curve was linear (equation: $y = 0.0224x + 0.0072$) with regression (r^2) value of 0.9996.

In vitro drug release of solid dispersions

Poloxamer 188 solid dispersions prepared by solvent evaporation have a higher % drug release than melt granulation at all ratios (Table 4 and Fig. 1). In addition, higher drug: carrier ratios provided a higher % drug release. Therefore, solvent evaporation was selected as the optimized technique.

In melt granulation, maximum drug release was observed at 1 : 2 ratio (29.49%). Higher drug : carrier ratios did not increase the % drug release. This could be because the carrier formed a concentrated

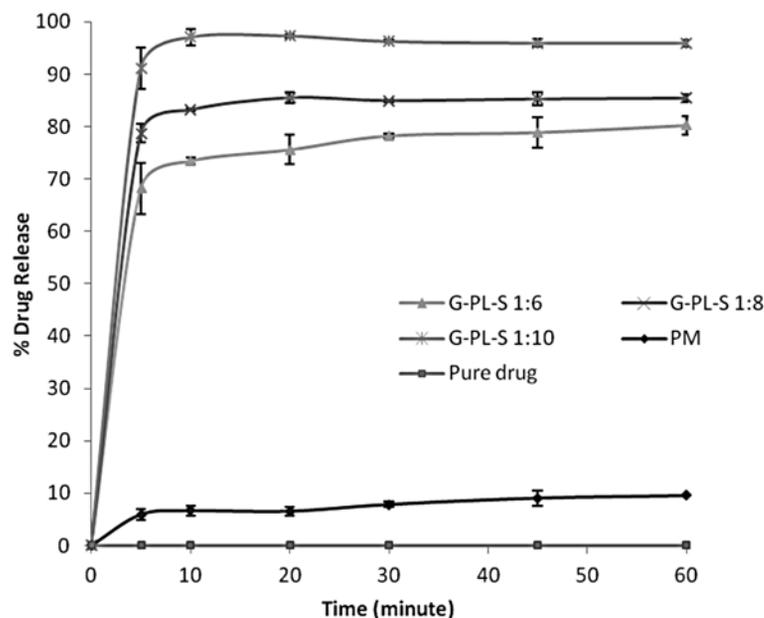


Figure 3. Dissolution profiles of pure drug, physical mixture and dispersions with different drug : poloxamer ratios

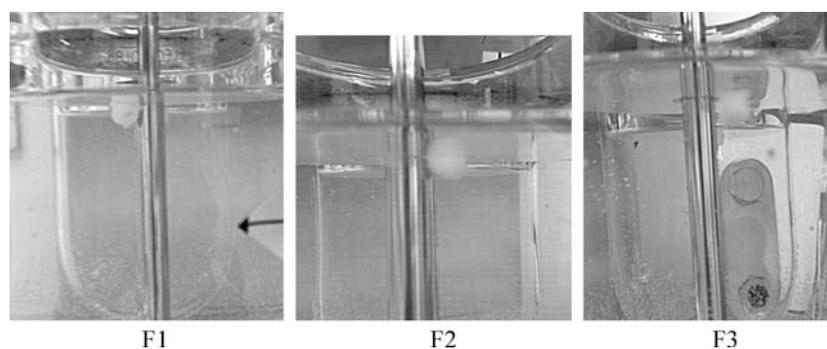


Figure 4. Floating tablets of glipizide at 2 h

layer surrounding the drug particles, acting as a diffusion barrier and slowing drug release (13). However, drug release of dispersions prepared by solvent evaporation at 1 : 6 ratio is only 80.6%. Therefore, different carriers were tried at 1 : 6 ratio to determine if they could further increase the drug release.

The order of drug release for different carriers was gelucire < β -cyclodextrin < PVP < poloxamer (Table 5 and Fig. 2). At 1 : 6 ratio, the other carriers could not provide higher drug release than poloxamer. Therefore, poloxamer 188 was selected as the optimized carrier. Higher drug : poloxamer ratios were investigated to obtain higher drug release.

As shown in Table 6 and Figure 3, 1 : 8 and 1 : 10 ratios released 85.42 and 95.95% of drug, respectively. The ratio 1 : 10 was selected as the optimized ratio as it had the highest % drug release. All dispersions had higher % drug release than pure drug and physical mixture.

The increased solubility of solid dispersions may be due to various mechanisms, including formation of eutectic mixtures or solid solutions, increased wetting by hydrophilic carriers, amorphization of drug, or particle size reduction (13). For example, gelucire decreases interfacial tension between drug particles and water by microemulsifi-

cation, while PVP systems may have formed interstitial solid solutions or an amorphous state; poloxamer systems increases dissolution by micellar solubilization (14), and cyclodextrin systems by formation of inclusion complexes (15). However, poloxamer systems seem to be the most efficient in increasing the solubility of glipizide.

Tableting parameters and *in vitro* buoyancy

The limits of weight variation for all formulations were less than 7.5% (Table 7). The hardness of

all formulations was between 3–4 kg/cm² and the % weight loss after friability was less than 1% (Table 7). Thus, all formulations fulfilled pharmacopoeial requirements.

All tablets floated (Fig. 4). The floating properties of HPMC formulations (F1, F2 and F3) were better than that of PEO (F3–F6), as shown by the shorter floating lag time and longer floating duration (Table 7). This could be due to the higher inherent swelling property of HPMC compared to that of PEO (8). Also, PEO based tablets floated for 8–10 h

Table 6. *In vitro* drug release of physical mixture and solid dispersions with different drug:carrier ratios.

Solid dispersion	% drug release					
	5 min	10 min	0 min	30 min	45 min	60 min
G-PL-S 1 : 6	68.22 ± 2.44	73.45 ± 0.91	75.62 ± 0.91	78.27 ± 1.03	78.91 ± 0.74	80.06 ± 1.03
G-PL-S 1 : 8	78.67 ± 1.76	83.17 ± 0.23	85.50 ± 1.08	84.94 ± 0.17	85.26 ± 1.20	85.42 ± 0.74
G-PL-S 1 : 10	91.13 ± 4.04	97.07 ± 1.59	97.31 ± 0.28	96.27 ± 0.17	95.95 ± 0.74	95.95 ± 0.63
Pure drug	< 1	< 1	< 1	< 1	< 1	< 1
Physical mixture (PM)	5.95 ± 1.08	6.67 ± 0.96	6.59 ± 0.79	7.88 ± 0.52	9.08 ± 1.41	9.56 ± 0.06

Table 7. Tableting and buoyancy characteristics of non-effervescent floating tablets.

Formulation	F1	F2	F3	F4	F5	F6
Hardness (kg/cm ²)	3–4	3–4	3–4	3–4	3–4	3–4
Weight variation (mg)	149.6 + 1.84	150.5 + 1.70	149.2 + 0.94	198.33 + 1.24	200.3 + 2.78	200.01 + 0.25
Friability (%)	0.3	0.6	0.4	0.5	0.02	0.1
Floating lag time (s)	< 1	< 1	< 1	25–30	10–11	5–9
Total floating time (h)	12	12	13	8	8	10

Table 8. Correlation coefficient values and drug release kinetics.

Formulation	Zero order		First order		Higuchi	Hixson-Crowell	Korsmeyer-Peppas	
	K ₀	r	K ₁	r	r	r	n	r
F1	3.8908	0.8882	0.1990	0.9573	0.9498	0.8556	0.2222	0.9710
F2	7.3383	0.9965	0.1338	0.9120	0.9925	0.9786	0.5798	0.9918
F3	7.815	0.9837	0.186	0.8516	0.9699	0.8416	0.4564	0.9826
F4	16.35	0.9001	0.1957	0.9252	0.9536	0.9854	1.0632	0.9912
F5	7.4484	0.9154	0.19	0.9041	0.9652	0.8773	0.9777	0.9991
F6	7.45	0.9254	0.197	0.8813	0.9531	0.8239	1.167	0.9887

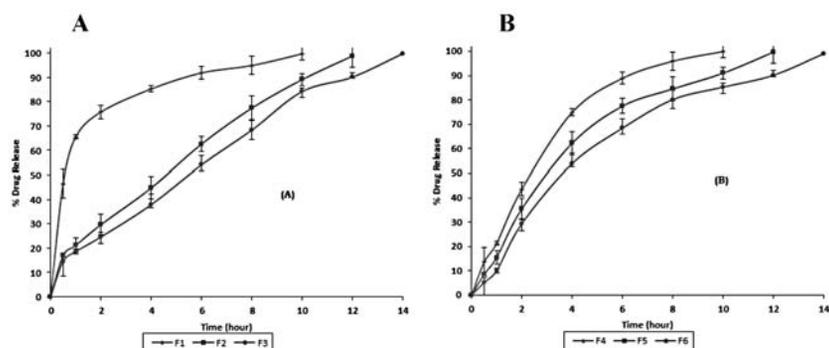


Figure 5. Dissolution profile of non-effervescent floating tablets prepared with A – HPMC; B – PEO

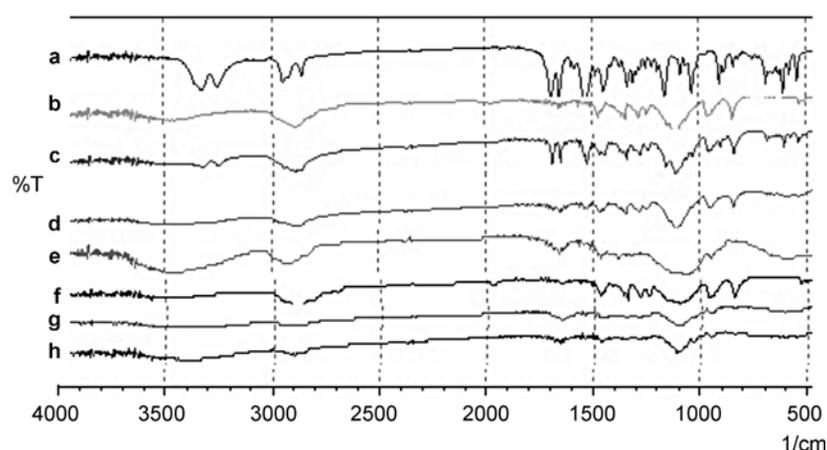


Figure 6. FTIR spectra of compounds. a) glipizide; b) poloxamers 188; c) physical mixture; d) solid dispersion (1 : 10); e) HPMC; f) formulation F2; g) PEO; h) formulation F5

as surface erosion of polymer took place (8), and the tablet was completely eroded by the end of 8 h, with insoluble residues visible at the bottom of the dissolution vessel.

Buoyancy of the tablets was provided by crospovidone. The quantity of crospovidone was constant in all the formulations based upon the preliminary studies. It is a super-disintegrant /matrix ballooning inducer, which swells and increases water uptake capacity of tablets. In the presence of hydrophilic polymers, it exhibits controlled swelling. Thus, the porosity of the matrix increased, and air bubbles were entrapped within the polymeric matrix, causing buoyancy of the dosage form (16, 17).

In vitro drug release

From Figure 5, drug release after 12 h reached > 90% for all formulations. F2 formulation showed

better controlled release than F1, which released > 90% of drug within 6 h. A higher HPMC content causes greater amount of gel to be formed, which increases the diffusion path length of the drug. This might lead to drug retardation. PEO based formulations also have good retardation properties. Lactose was the chosen diluent due to its water soluble and hydrophilic nature. It enables better matrix hydration, gel formation, and promotes free volume, which may have facilitated the drug release (8). When the dosage form is exposed to the dissolution medium, the medium can penetrate readily into the spaces between chains of the polymer. After polymer chain solvation, the dimensions of the polymer molecule increase due to the polymer relaxation by the stress of the penetrated solvent. This will form a gel-like network surrounding the tablet. This hydration property of the hydrophilic polymers such as HPMC and PEO can cause an immediate formation

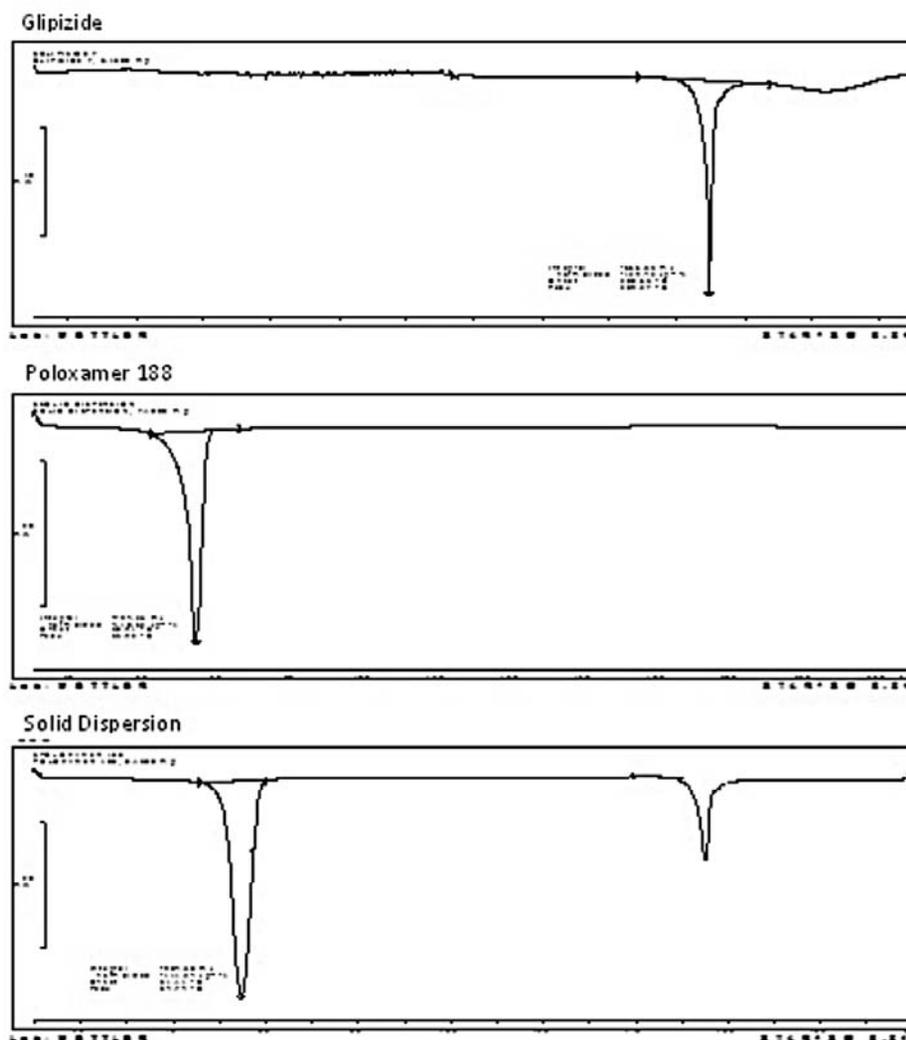


Figure 7. DSC spectra of glipizide, poloxamer 188 and solid dispersion

Table 9. FTIR assignment of bands of compounds (3, 18–21).

Compound	Major peaks (cm ⁻¹)	Assignment of bands
Glipizide	3325, 3250	N-H stretching
	1689, 1651	C = O stretching
	1159, 1132	S = O
	1527	Aromatic vibrations
	1444	Cyclohexane C-H bending
Poloxamer 188	2887	O-H stretch
	1109	C-O stretch
HPMC K100M	3437	O-H stretch
	1062	C-O (ether) stretch
PEO WSR N12K	3233	O-H stretch
	1097	C-O-C symmetric stretch
	1262	C-O-C asymmetric stretch

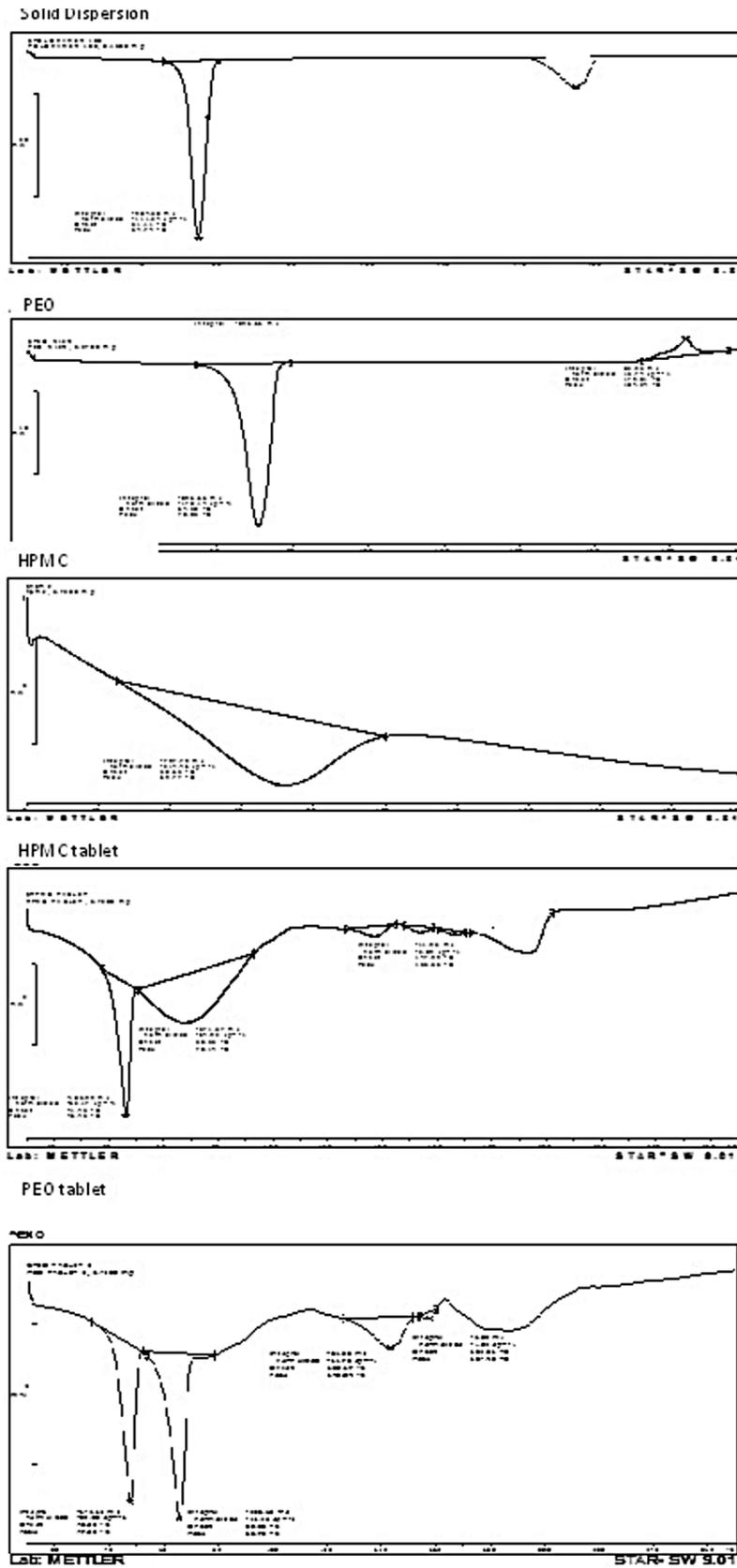


Figure 8. DSC thermograms of compounds

Table 10. DSC endothermic peaks.

Compound	DSC peak (°C)
Glipizide	209.27
Poloxamer	54.74
Solid dispersion	53.89
HPMC	69.77
PEO	70.83
Lactose	146.41
HPMC tablet	46.43, 70.14, 137.20
PEO tablet	47.60, 65.72, 143.04

of a surface barrier around the non-effervescent floating tablet that eliminates the burst release.

F2 and F5 were selected as optimized formulations based upon their drug retardation up to 12 h with continuous buoyancy properties.

Drug release kinetics

Among the HPMC based formulations, F1 followed first order rate kinetics and F2 and F3 followed zero order rate kinetics (Table 8). All HPMC based formulations follow the Higuchi model, indicating diffusion mechanisms. F1 follows Fickian diffusion, while F2 and F3 shows non-Fickian diffusion. This can be concluded from the higher correlation coefficient (*r* value) (12). The PEO based formulations F4 followed first order rate kinetics with erosion mechanism, which might be due to the lower concentration of the polymer. Other formulations F5 and F6 followed zero order kinetics with super case-II transport diffusion mechanism. The rate and mechanism of drug release depends on the type of polymer and the polymer concentration. For HPMC as well as PEO based formulations, higher polymer concentrations changed the rate from first order to zero order and the mechanism from Fickian to non-Fickian diffusion.

FTIR

Table 9 shows the major peaks of the compounds. From Figure 6 it can be seen that the physical mixture still retains the characteristic peaks of glipizide (3250, 3325, 1689, 1649, 1527, 1448 and 1159 cm^{-1}) and poloxamer (1112 and 2891 cm^{-1}). The solid dispersion spectrum also shows some peaks of glipizide (1527, 1637, and 1452 cm^{-1}) and poloxamer (1114 and 2877 cm^{-1}). However, the intensity of glipizide peaks are significantly reduced

(some to obscurity), and band broadening was observed at approximately 3600–3200 cm^{-1} (N-H stretching). The absence of any significant change in the IR spectral pattern in the physical mixture and solid dispersion indicate the absence of interaction between glipizide and carrier.

F2 tablets showed peaks at 1112 and 1097 cm^{-1} due to C-O of poloxamer and HPMC. A broad peak centered around 3375 cm^{-1} indicates the O-H group of HPMC. F3 tablets show a broad, high intensity peak from 3600 to 3000 cm^{-1} indicative of the O-H group of PEO. A peak at 1114 cm^{-1} indicates the C-O group of poloxamer and the 1097 cm^{-1} peak indicates C-O-C symmetric stretch of PEO. The absence of new, unidentified peaks indicates no drug- excipient interactions.

DSC

The endothermic peaks shown in Table 10 correspond to the melting points of glipizide, poloxamer, HPMC, PEO, and lactose. From Figure 7 and 8, the drug endothermic peak was suppressed in the solid dispersion, probably due to the small amount of drug compared to carrier, or due to the drug dissolving partially in the carrier to form a solid solution. This observation could also be due to the amorphous form of the drug in solid dispersion. The peaks of tablets F2 and F3 result from the superposition of their individual component DSC curves. The slight change in melting points could be due to a change in purity of the individual components in the tablets.

CONCLUSION

Incorporation of solid dispersion into floating tablets is a promising approach to enhance the solubility of poorly soluble drugs and achieve controlled release through gastric retention. Poloxamer 188 provided significant increase in solubility of glipizide. HPMC and PEO were able to provide *in vitro* buoyancy as well as controlled the drug release. Crospovidone was used successfully as a swelling agent.

Competing interests

The authors declare that they have no competing interests.

Acknowledgment

The authors would like to thank International Medical University for providing the necessary facilities for conducting the research.

REFERENCES

1. Arora S., Ali J., Ahuja A., Khar R.K., Baboota S.: AAPS PharmSciTech 6, 372 (2005).
2. Singh B.N., Kim K.H.: J. Control. Release 63, 235 (2000).
3. Srikanth M.V., Songa A.S., Nali S.R., Battu J.R., Kolapalli V.R.M.: Invest. Clin. 53, 60 (2012).
4. Shakya R., Thapa P., Saha R.N.: Asian J. Pharm. Sci. 8, 191 (2013).
5. Garse H., Vij M., Yamgar M., Kadam V., Hirlekar R.: Arch. Pharm. Res. 33, 405 (2010).
6. Patel P., Dand N., Somwanshi A., Kadam V.J., Hirlekar R.S.: AAPS PharmSciTech 9, 839 (2008).
7. Sawicki W., Łunio R.: Acta Pol. Pharm. Drug Res. 67, 103 (2010).
8. American Hospital Formulary Service. McEvoy G.K.: Antidiabetic agents. AHFS drug information. American Society of Health-System Pharmacists, Bethesda 2013.
9. Jamzad S., Fassihi R.: Int. J. Pharm. 312, 24 (2006).
10. Dehghan M.H.G., Saifee M., Hanwate R.M.: J. Pharm. Sci. Technol. 2, 293 (2010).
11. Batra V., Shirolkar V.S., Mahaparale P.R., Kasture P.V., Teshpande A.D.: Indian J. Pharm. Educ. Res. 42, 371 (2008).
12. Costa P., Lobo J.M.S.: Eur. J. Pharm. Sci. 13, 123 (2001).
13. Vo C.L.N., Park C., Lee B.J.: Eur. J. Pharm. Biopharm. 85, 799 (2013).
14. Ahuja N., Katare O.P, Singh B.: Eur. J. Pharm. Biopharm. 65, 26 (2007).
15. Martin Del Valle E.M.: Process Biochem. 39, 1033 (2004).
16. Ratnaparkhi M.P., Bhabad V.S., Chaudhari S.P.: Int. J. Pharm. Tech. Res. 4, 1041 (2012).
17. Mohamed M., Talari M.K., Tripathy M., Majeed A.B.A.: IJDFR 3, 13 (2012).
18. Tiwari G., Tiwari R., Srivastava B., Rai A.K.: Research J. Pharm. and Tech. 1, 14 (2008).
19. Kolašinac N., Kachrimanis K., Homšek I., Grujić B., Durić Z., Ibrić C.S.: Int. J. Pharm. 436, 161 (2012).
20. Patil S.A., Kuchekar B.S., Chabukswar A.R., Jagdale S.C.: J. Young Pharm. 2, 121 (2010).
21. Coates J.: Interpretation of Infrared Spectra, A Practical Approach, in Encyclopedia of Analytical Chemistry. Meyers R.A. Ed., p. 10815, John Wiley & Sons, Chichester 2000.

Received: 11. 12. 2013