GLIBENCLAMIDE SOLUBILITY ENHANCEMENT BY MODIFIED NATURAL CARRIERS USING THE SOLID DISPERSION TECHNIQUE

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Abstract

The present study was undertaken to explore the potential of natural carriers such as locust bean gum and guar gum for dissolution enhancement of glibenclamide. The locust bean gum and guar gum were modified by heating at 120^{o}C for 2h. Solid dispersions were prepared by the solvent evaporation method using modified gums individually at 1:2, 1:4, 1:6, 1:8, 1:10 and 1:12 drug to carrier ratio. The prepared solid dispersions were evaluated for equilibrium solubility studies, content uniformity, *in vitro* dissolution testing, thermal analysis and *in vivo* studies. The solubility studies showed an increase in the solubility of glibenclamide with the increase in the concentration of carriers but it was up to 1:8 and 1:10 in the case of modified locust bean gum and modified guar gum respectively. All the batches lie within limits for content uniformity according to the United States Pharmacopeia (USP). The decrease in peak intensity and a slight shift in peak of drug in differential scanning calorimetry (DSC) thermograms of solid dispersions batches indicated a slight conversion of crystalline to amorphous form. Fourier Transform Infrared Spectroscopy (FTIR) studies indicated no interaction between drug and carriers, which was further confirmed by X-Ray diffraction (X-RD) studies. The dissolution rate of glibenclamide from solid dispersions was maximum in L4 and G5 batches with a cumulative release of 96.17% and 96.78% in 2h respectively. *In vivo* results showed a superior activity of L4, G5 as compared to plain glibenclamide in alloxan-induced diabetic rat model.

Rezumat

Prezentul studiu a avut ca scop evaluarea substanţelor naturale cu rol de transport, cum sunt guma de roşcove şi guma guar, în creşterea solubilităţii glibenclamidului.

S-au realizat dispersii solide prim metoda evaporării solventului, folosind forme modificate ale gumelor, în diferite rapoarte substanţă activă: transportor. Acestea au fost analizate cu ajutorul studiilor de solubilitate la echilibru, s-a determinat uniformitatea conţinutului, au fost efectuate teste de dizolvare *in vitro*, analiza termică şi studii *in vivo*.

Rezultatele obţinute demonstrează că formele modificate ale transportorilor naturali (gume) pot fi folosite cu succes pentru creşterea solubilităţii medicamentelor greu solubile cum este glibenclamidul.

Keywords: Solid dispersions, modified locust bean gum, modified guar gum, solvent evaporation.

Introduction

The oral route of drug delivery system is regarded as the safest, most convenient and most economical method of drug delivery possessing the highest patient compliance [1]**.** Most of the new chemical entities (NCE) under development or developed recently are preferred to be used as a solid oral dosage form that will produce an effective dissolution rate and bioavailability after oral administration [2,4]. An essential physicochemical factor affecting absorption of a drug and its therapeutic effectiveness is its solubility. Today, more than 40% of all new chemical entities have poor aqueous solubility. In the absorption of poorly water soluble drug from gastrointestinal (GI) tract, low solubility and dissolution become the rate limiting steps. Therefore, the enhancement of solubility and dissolution rate of poorly water soluble drugs after oral administration is one of the most necessary aspects of modern pharmaceutics [14]. Various conventional techniques for dissolution enhancement of these drug candidates include salt formation, micronization, addition of surfactants or surface active agents, super critical processing, pro-drug [12], complexation and solid dispersion [11]. However, all the above mentioned techniques have some potential limitations. Solid Dispersions technique exhibit great potential toward dissolution enhancement via dispersion of drugs in inert carriers or matrix at solid state [3,10]. Melting and solvent evaporation methods are the two major processes of preparing solid dispersions. The use of natural polymers in preparation of solid dispersions is more beneficial because of their low cost, biocompatibility, and biodegradability, but the high viscosity of natural polymers appears to be a limitation, particularly for large scale manufacturing. Modified forms of natural polymers (with low viscosity and high swelling capacity) have been utilized in solid dispersions for solubility enhancement of poorly water soluble drugs. The present work examines the influence of modified locust bean gum (MLBG) and modified guar gum (MGG) on dissolution enhancement of poorly water soluble drug Glibenclamide (GLB). Glibenclamide is a second generation sulphonyl urea. It is a very potent oral hypoglycemic agent with long duration of action [9]. Apparent solubility, *in vitro* dissolution study, infrared spectroscopy, scanning electron microscopy (SEM), differential scanning calorimetry (DSC), and X-ray diffraction (XRD) study were used to explain the phenomenon.

Materials and Methods

Glibenclamide was obtained as a gift sample from Piramal Healthcare Ltd., Baddi, India and Locust Bean Gum was obtained as a gift sample from Taiyo Lucid Pvt. Ltd., Mumbai, India and Guar Gum was

purchased from Yarrow Chem Products, India. All other materials used were of analytical grade.

Preparation of Modified Polymers

The Locust Bean Gum and Guar Gum were modified by the method reported in literature [7]. Powdered gums were placed in a porcelain bowl and subjected to heating at 120^{o}C for 2h using sand bath. The prepared MLBG and MGG were finally resieved (100 mesh) and stored in an airtight container at room temperature till further characterization.

Physicochemical characterization of polymers

Swelling Index (SI)

Both gums were accurately weighed (1g) and transferred to 100 mL measuring cylinders. The initial volume of the gums in the measuring cylinders was noted. The volume was made up to 100mL mark with distilled water and was shaken gently and set aside for 24 hours at room temperature and ambient humidity. The final volume of the gums in the measuring cylinders was noted after 24 hours. The swelling index was expressed as percentage and calculated according to the following equation:

$$SI = [(X_t - X_0) / X_0] \times 100$$

where X_0 is the initial height of the powder in a graduated cylinder and X_t denotes the height occupied by the swollen gum after 24 hours.

Viscosity Measurement

The viscosities of 1% (w/v) gums solutions were measured according to the United States Pharmacopeia (USP) specification, using a Brookfield DV-E Viscometer (Middleboro, MA, USA).

Hydration Capacity (HC)

The weighed quantity of gums was taken in the 15mL tare centrifuge tube and allowed to centrifuge for 10 min at 1,000 rpm using a laboratory centrifuge (REMI). After the centrifugation process, the tared centrifuge tube was taken out and inverted to remove the supernatant. The decanted tube was then weighed on a digital balance (Citizen) and the hydration capacity was calculated using the following equation:

$$HC = Weight\ of\ hydrated\ sample / Weight\ of\ dry\ sample$$

Density

Gums were poured into calibrated measuring cylinders (10mL capacity) and the initial volume was noted. Then, the cylinder was allowed to fall under its own weight onto the hard surface from the height of 2.5 cm at 2 sec intervals. Loose Bulk Density (LBD) and Tapped Bulk Density (TBD) was calculated using the following equations:

$$LBD = Weight\ of\ the\ powder / Volume\ of\ the\ packing$$

$$TBD = Weight\ of\ the\ powder / Tapped\ volume\ of\ the\ packing$$

Angle of Repose

The angle of repose was determined by the funnel method. The diameter of the powder heap was measured and the angle of repose was calculated using the following equation:

$$\tan(\theta) = \frac{H}{R}$$

where, H is the height of powder heap and R is the radius of powder heap

Compressibility Index (CI)

Compressibility index (Carr's index) was determined by using the following equation:

$$CI\ (\%) = [(TBD - LBD) \times 100 / TBD]$$

Preparation of solid dispersions: Various solid dispersion batches were prepared by the method reported in literature [6]. The drug (Glibenclamide) was first dissolved in 70% v/v ethanol (up to its saturation solubility). The natural carriers in specified ratios (MLBG and MGG) were then added in the drug solution. The entire solvent was evaporated using a rotary evaporator at 60ºC under reduced pressure. The resultant solid residue was allowed to dry under vacuum, passed through sieve (#80) and stored in desiccator till further use. The composition of different batches (L1-L6 with MLBG and G1-G6 with MGG) of solid dispersion is given in table I.

Table I

Composition for solid dispersions batches

Batch No.	Ratio (Drug: Polymer)	Drug (mg)	MLBG (mg)	MGG (mg)
L1	1:2	100	200	-
L2	1:4	100	400	-
L3	1:6	100	600	-
L4	1:8	100	800	-
L5	1:10	100	1000	-
L6	1:12	100	1200	-
G1	1:2	100	-	200
G2	1:4	100	-	400
G3	1:6	100	-	600
G4	1:8	100	-	800
G5	1:10	100	-	1000
G6	1:12	100	-	1200

Characterization and evaluation of solid dispersions

Solubility Studies

The apparent solubility of pure drug and solid dispersions was determined in phosphate buffer pH 7.4. Pure drug and solid dispersions (equivalent to 5 mg of drug) were weighed accurately and added to phosphate buffer pH 7.4 in volumetric flasks. The flasks were then mixed for 24h at 37^{o}C on a shaker incubator. The samples were then filtered and assayed spectrophotometrically at 300 nm.

Differential Scanning Calorimetry

Thermal properties of pure glibenclamide, hydrophilic carriers and solid dispersions were analyzed by differential scanning calorimetry, (Mettler Toledo, DSC 821^{e}). Samples were sealed in aluminium pans and scanned from 25 to 350^{o}C at a heating rate of 10^{o}C/min in nitrogen atmosphere.

Fourier Transform Infrared Spectroscopy

Infrared absorption spectra of pure glibenclamide, hydrophilic carriers and prepared solid dispersions were obtained using potassium bromide disk method, under static air using FTIR Spectrophotometer (NICOLET, Impect-410). The scanning range was 450cm^{-1} to 4000cm^{-1} and the resolution was 1cm^{-1}.

***In vitro* Dissolution Rate Studies**

The dissolution test was performed by using a sample of solid dispersions equivalent to 20 mg of glibenclamide in 900mL phosphate buffer pH 7.4 as dissolution medium. USP dissolution apparatus Type II was used at the speed of 75 rpm at 37±0.5^{o}C. Samples with volume equal to 5mL were withdrawn at regular intervals for 2 hr and analysed for drug concentration at 300 nm using an UV spectrophotometer (Systronics Double Beam Spectrophotometer, AU-2701).

Content Uniformity

Accurately weighed amounts of solid dispersions (equivalent to 5 mg) were dissolved in 10mL methanol in 100 mL volumetric flasks and the volume was made up to mark with phosphate buffer pH 7.4. The solution was filtered and content uniformity was analysed spectrophotometerically.

***In vitro* Release Kinetics Study**

To analyze the *in vitro* release data various mathematical models were applied. Various plots were prepared using different kinetics models such as: cumulative % drug release vs. time (zero order kinetic model); log

cumulative of % drug remaining vs. time (first order kinetic model); cumulative % drug release vs. square root of time (Higuchi model) and cube root of drug % remaining in matrix vs. time (Hixson-Crowell cube root law). The mechanism of drug release from polymeric system was determined by applying Korsmeyer Peppas equation where log cumulative % drug release vs. log time was plotted.

X-Ray Diffraction

Powder X-ray diffraction patterns were traced employing an X-ray diffractometer (XPERT-PRO, PW3050/60 Goniometer) using Ni filtered Cu (K-α) radiation, a voltage of 45 kV, a current of 40 mA. The sample was analyzed over 2θ range of 0-50^o with scan step size of 0.0170^o (2θ) and scan step time 25 s.

Scanning Electron Microscopy

Sample of pure drug and the solid dispersions formulations were mounted onto the stubs using double-sided adhesive tape and then coated with gold palladium alloy (150-200 A^o) using fine coat ion sputter (Joel, fine coat ion sputter, JFC-1100). The samples were subsequently analyzed under the scanning electron microscope (JSM-6100 SEM) for external morphology.

***In Vivo* Glucose Estimation Studies**

In the present study alloxan was used for inducing diabetes to Wistar rats of either sex. All researches were conducted in accordance with the European Directive 86/609/EEC/24.11.1986 regarding the protection of animals used for experimental and other scientific purposes. Animals were kept overnight fasted, then weighed and the blood glucose level of the animals was measured using Accu-Check Active Glucometer. The animals were injected with alloxan (150mg/kg i.p.). The blood glucose level of the animals was measured after 72 hours. Rats with a blood glucose level of above 250mg/dL were considered as diabetic and were further subjected to the study. The diabetic animals were divided into four groups, each group consisting of six rats. To group 1 it was administered the vehicle, to group 2 it was administered glibenclamide, to group 3 and 4 optimized formulations (L4 and G5) of both polymers were administered. The blood glucose level was measured hourly for next 5 hours by using the Accu-Check Active Glucometer. The *in vivo* results were analysed by applying One-Way-ANOVA followed by Tukey's Post-hoc test.

Results and Discussion

The results of the physicochemical characterization of LBG, MLBG, GG, and MGG are given in Table II.

Table II

Physicochemical characterization of LBG, MLBG, GG, and MGG

Parameters	LBG	MLBG	GG	MGG
Swelling index (%)	58.7±7.02	55.5±2.00	64.00±9.54	62.92±3.06
Viscosity (cps)	1635±56.90	558±44.52	3947±52.5	1356±34.6
Hydration capacity	2.22±0.006	1.83±0.005	2.60±0.022	1.65±0.061
Angle of repose	34.93±4.11	33.96±4.75	35.25±1.08	30.02±2.28
Density (g/cm^3) **LBD** **TBD**	 0.51±0.15 0.68±0.17	 0.51±0.04 0.6±0.05	 0.45±.01 0.60±.04	 0.51±0.03 0.59±0.05
CI (%)	24.50±1.47	13.90±1.77	24.52±3.92	13.89±2.41

(Mean ± SD), n=3

The modified forms of both polymers (MLBG and MGG) showed no significant change in the swelling and hydration capacity whereas viscosity showed a marked decrease as compared to the unmodified form of polymers. The swelling nature of the carrier may lead to an increase in the extensive surface of the carrier during dissolution and the dissolution rate of the drug is markedly enhanced. The modified form of polymers exhibited improved flow properties as compared to unmodified form as indicated by CI values. The improved flow properties and decreased viscosity of modified gums may be helpful in further formulation development.

Solubility studies

As depicted in table III, the solubility of pure drug is very low (26µg/mL). The increase in solubility of the drug was observed with the increasing concentration of polymers, but it was up to a certain limit. After that, the increase in concentration of polymers lead to a decrease in solubility of the pure drug. The optimum ratio of drug to MLBG was 1:8 and for MGG was 1:10. The decrease in solubility in batches L5, L6 and G6 may be due to the formation of a viscous layer of polymer around the drug particles at high concentrations.

Table III

Solubility and content uniformity data of glibenclamide, marketed formulation and solid dispersions batches

Products	**Solubility (µg/mL)** (Mean ± SD), n=3	**Content Uniformity**
Marketed formulation	-	98.8±0.007
GLB	26.0±0.334	-
L1	40.7±0.126	101.6±0.026
L2	62.3±0.386	101.6±0.021
L3	73.5±0.334	99±0.007
L4	97.2±0.633	100.2±0.007
L5	81.2±0.379	100.4±0.012
L6	80.9±0.193	100.4±0.007
G1	53.4±0.571	97.8±0.007
G2	68.2±0.649	93.2±0.007
G3	88.9±0.146	102±0.012
G4	93.0±0.456	101.4±0.019
G5	95.2±0.292	100.4±0.007
G6	93.8±0.292	92.6±0.007

Differential Scanning Calorimetry

The DSC thermogram of Glibenclamide, MLBG, MGG and solid dispersions batches (L4and G5) are shown in figure 1. Glibenclamide showed a sharp endothermic peak at 176.18^{o}C with enthalpy of fusion 86.98J/g corresponding to its melting point, which indicates its crystalline nature. The DSC thermogram of MLBG exhibited a broad endothermic peak at 106.01^{o}C with enthalpy of fusion 155.40J/g owing to its amorphous nature. The DSC thermogram of MGG exhibited no endothermic peak owing to its totally amorphous nature. The DSC thermograms of solid dispersion batches (L4and G5) showed identical peaks with decreased intensity. A slight shift in the endothermic peak of pure drug was also observed.

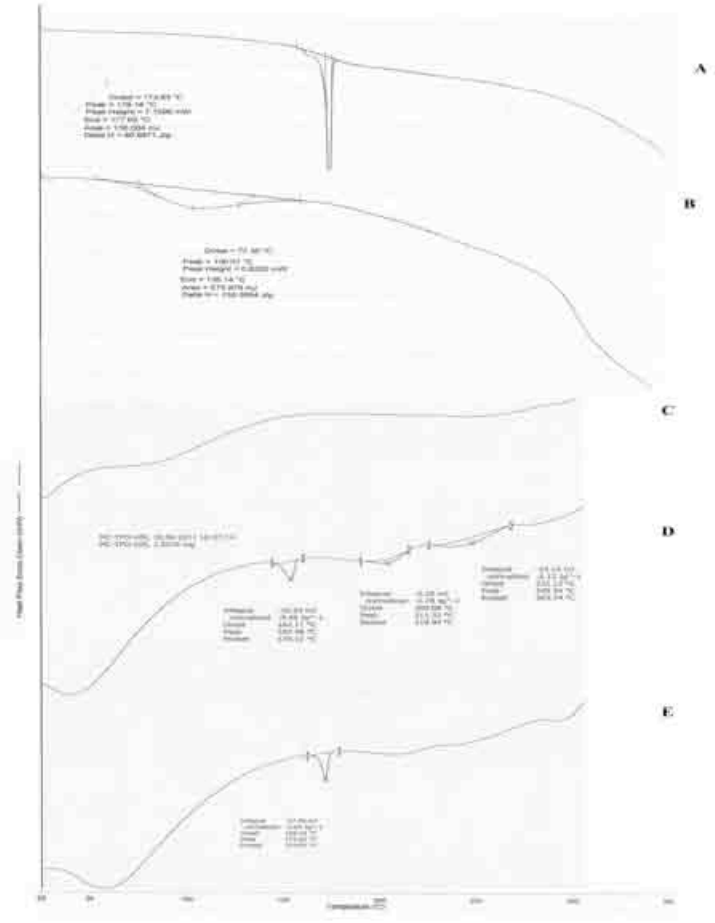


Figure 1
DSC thermograms of A) GLB, B) MLBG, C) MGG, solid dispersion batches D) L4, E) G5.

Fourier Transform Infrared Spectroscopy

The FTIR spectrum of sample was recorded as to ascertain the presence of different functional groups. The FTIR spectrum of pure drug, MLBG, MGG and solid dispersions are shown in figure 2. The FTIR analysis of drug shows some characteristic peaks, it gives sharp peak at 3313cm^{-1} due to N-H stretching, 1718cm^{-1} due to carbonyl group stretching, 1340cm^{-1} showing C-H bending vibration, 1155cm^{-1} showing S=O_2 stretching vibration. FTIR spectrum of MLBG shows O-H stretching at 3460.49cm^{-1} and C-H stretching at 2916.73cm^{-1}. FTIR spectrum of MGG shows O-H stretching at 3352.94cm^{-1} and C-H stretching at 2918.82cm^{-1}. FTIR spectrum of solid dispersions batches showed almost all the characteristic peaks, but with decreased intensity. Slight shifts in the peaks were also observed.

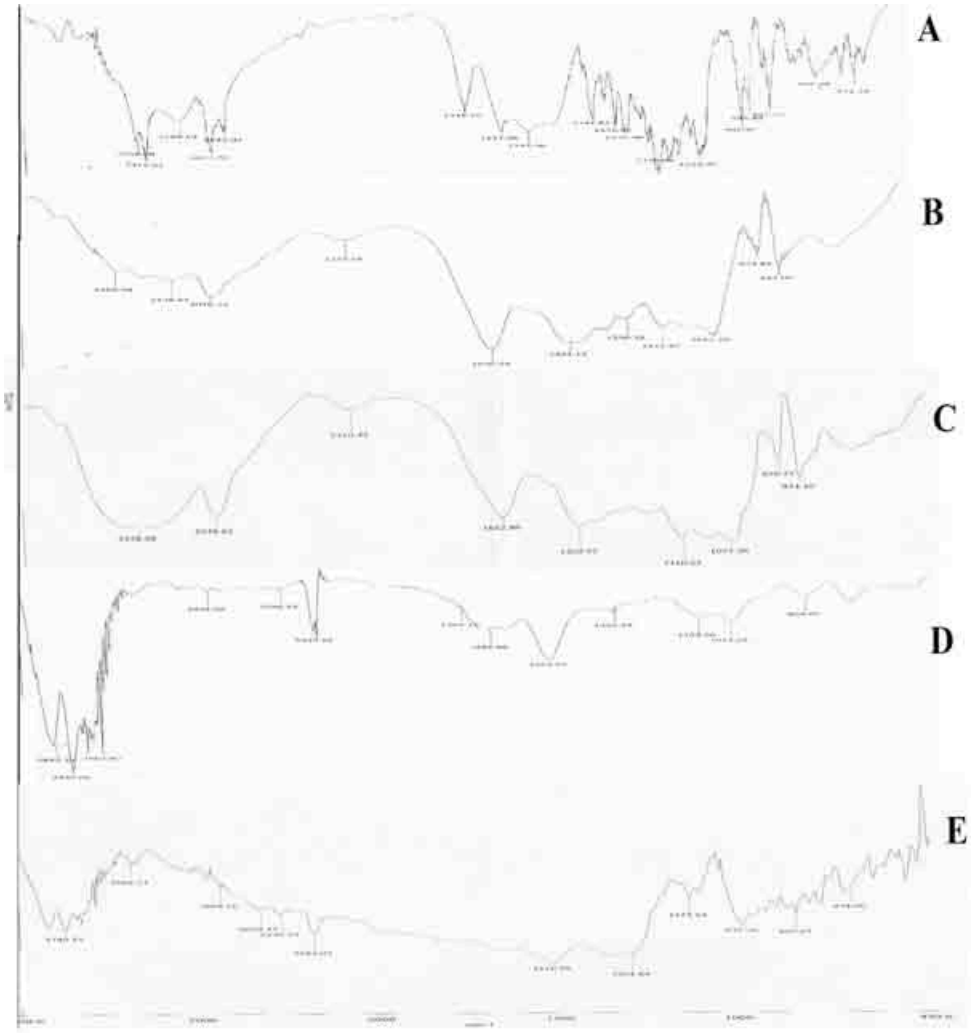


Figure 2
FTIR spectra of A) GLB, B) MLBG, C) MGG, solid dispersion batches D) L4 E) G5.

Content uniformity

Content uniformity of various batches of solid dispersions (L1-L6 and G1-G6) and marketed formulation (Daonil®) was found to be within the USP limit (85-115%) (Table III).

***In vitro* dissolution rate**

The dissolution profile of pure drug and solid dispersions batches (L1-L6 and G1-G6) in 7.4 pH buffer at 37±0.5°C are shown in Figure 3 and Figure 4 respectively. Solid dispersion batches L4 and G5 exhibited a maximum dissolution rate within 10 minutes as well as maximum extent of

drug release (i.e. 96.17% and 97.78% respectively) was achieved with both batches after 2 hours. During the process of dissolution, solid dispersion particles expose a greater surface area leading to a rapid drug release. Greater and rapid dispersion may occur using modified forms of natural carriers due to their less viscous nature. It is initiated the formation of a gelatinous layer (less viscous as compared to unmodified forms) of carrier around the particle as dissolution media enters into drug carrier particle interface and dissolved drug is released by diffusion. However, the increase in viscosity was observed using higher ratios of polymers (L5, L6 and G6) which may decrease the drug release. Figure 5 shows the comparative *in vitro* drug release profile of L4 and G5 with the marketed formulation. Formulations L4 and G5 exhibited higher dissolution rates in comparison to marketed formulation. The extensive surface of carrier is increased during dissolution due to its swelling nature which is responsible for enhanced dissolution characteristics of solid dispersion particles. No effect of particle size on the dissolution characteristics as solid dispersion particles and triturated marketed formulation were passed through the same sieve (#100). G5 batch showed a slight better dissolution rate with the same extent of drug release as compared to L4 batch.

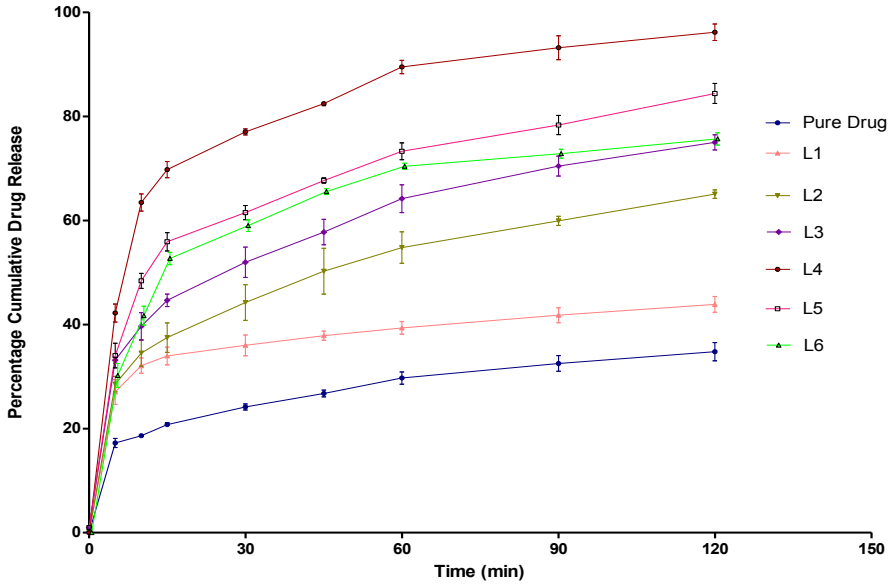


Figure 3
Comparison of dissolution profile of glibenclamide with solid dispersions batches (L1-L6)

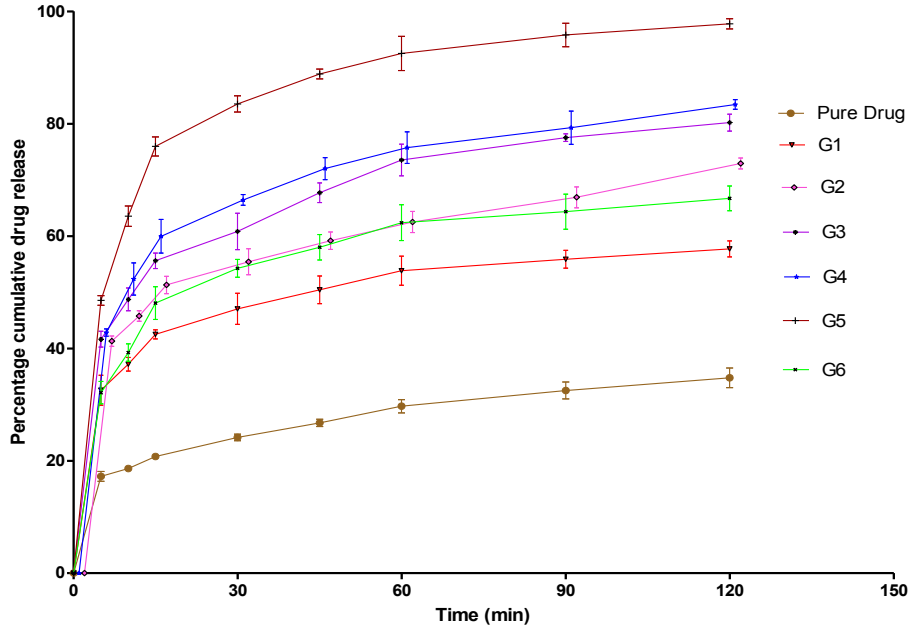


Figure 4
Comparison of dissolution profile of glibenclamide with solid dispersions batches (G1-G6)

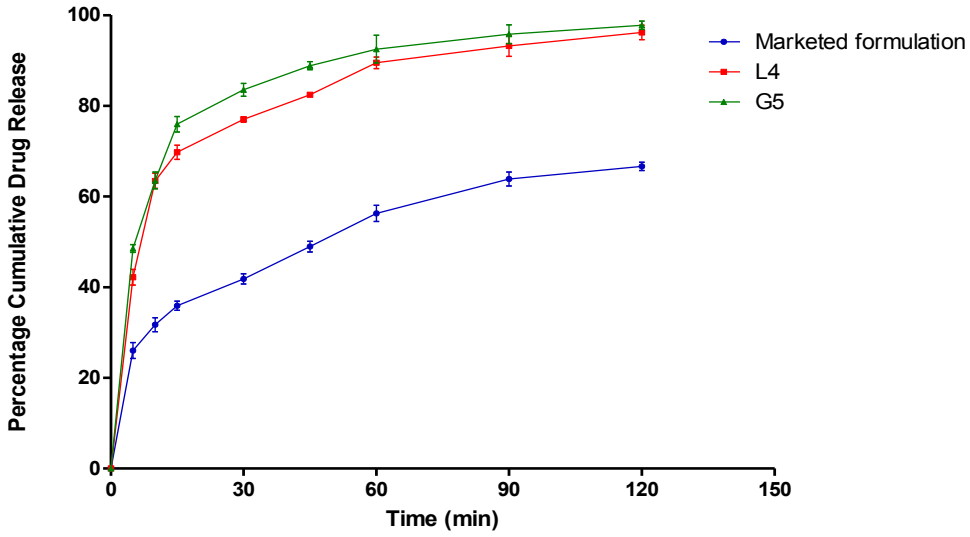


Figure 5
Comparison of dissolution profile of marketed formulation, L4 and G5

In vitro Release Kinetics Study

The drug release data obtained after the *in vitro* release study was further analysed by various kinetic models plotted i.e. zero order, first order, Higuchi equation and Hixson Crowell cube root law. The drug release from all the formulations was observed to follow Higuchi kinetics followed by Koresmeyer Peppas model (as shown by highest r^2 values). The value of the release exponent n for all the batches (less than 0.45 in all batches and more than 0.89 in one batch) is beyond the limits of Korsmeyer model so-called power law in the case of $n < 0.45$ and super case–II transport in the case of $n > 0.89$. This could not reveal the exact release mechanism of the drug from solid dispersions (Table IV). A combination of mechanisms is supposed for the drug release.

Table IV

Regressed values of release profiles of different solid dispersions batches

Formulation code	Zero Order (r^2)	First Order (r^2)	Hixson Crowell (r^2)	Higuchi (r^2)	Koresmeyer Peppas (r^2)	n
L1	0.4531	0.5363	0.5077	0.9904	0.9871	0.130
L2	0.71	0.8522	0.8086	0.9122	0.9983	0.258
L3	0.7107	0.8831	0.8321	0.914	0.9982	0.256
L4	0.5657	0.9308	0.8261	0.814	1	1.00
L5	0.6479	0.8697	0.8023	0.8745	0.8839	0.368
L6	0.6206	0.7908	0.7368	0.8602	0.9613	0.405
G1	0.5324	0.6573	0.6157	0.784	0.9834	0.182
G2	0.5583	0.7618	0.6953	0.7921	0.9841	0.193
G3	0.5952	0.8215	0.7512	0.8338	0.9736	0.217
G4	0.5607	0.8092	0.7297	0.8085	0.9987	0.304
G5	0.5171	0.9292	0.8039	0.7771	1	0.388
G6	0.5768	0.7219	0.6747	0.8258	0.9656	0.273

X-RAY Powder Diffraction

The X-Ray diffractogram of glibenclamide showed sharp peaks of the diffraction angle of 2θ at 11.8599, 19.0642, 21.1106, and 23.2968 with peak intensities of 52.91, 100.00, 67.57, and 52.23 and area 243.89, 395.08, 266.96, 275.11 respectively. All the characteristic peaks (but decreased intensity) appear in the diffractogram of solid dispersion batches (L4 and G5) as shown in figure 6.

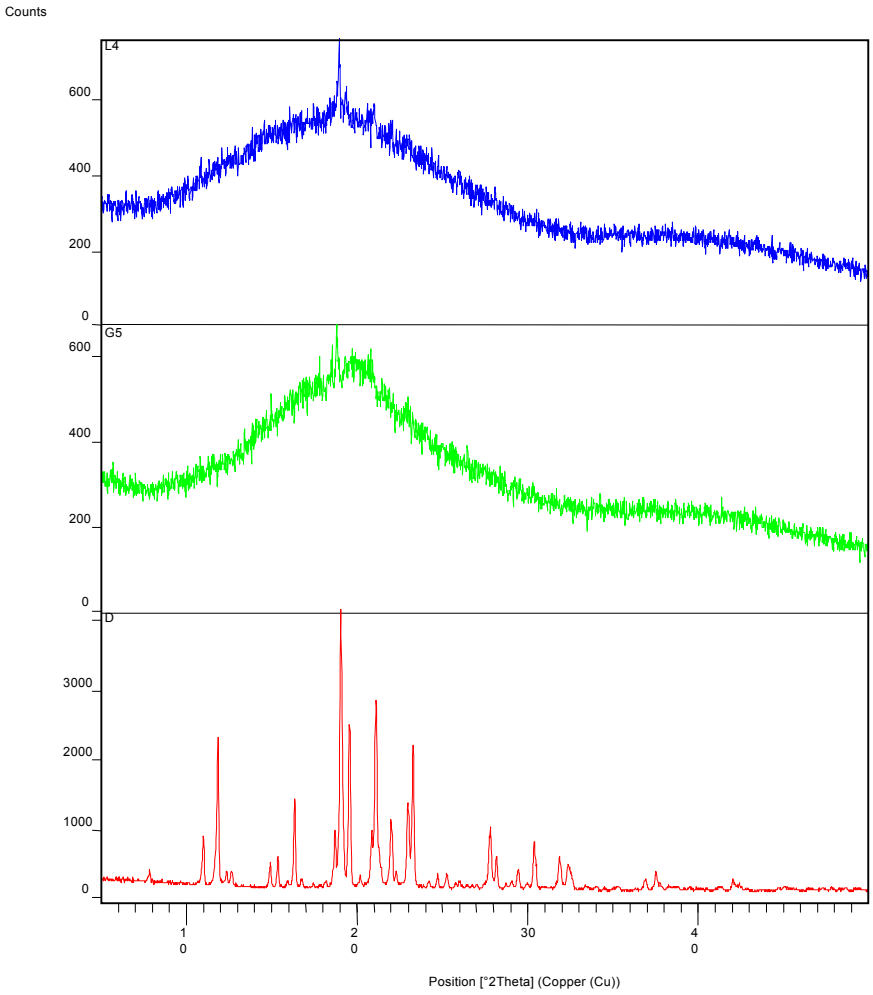
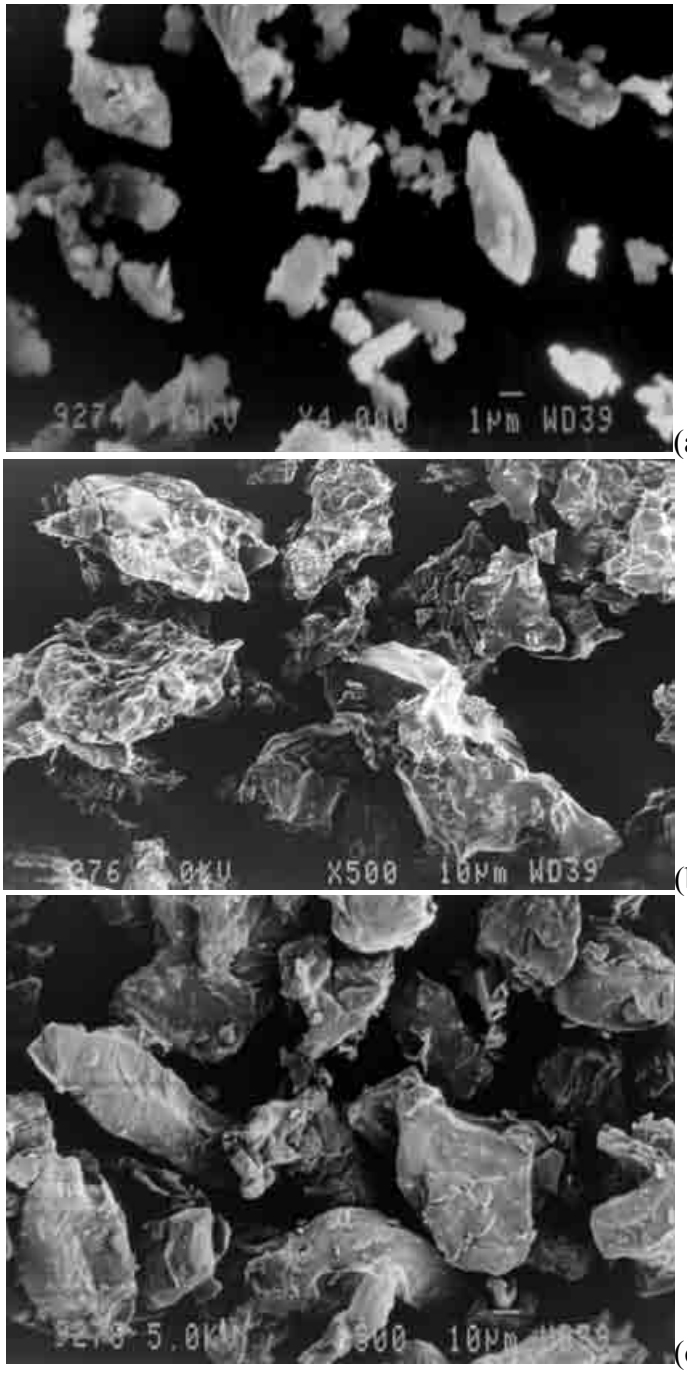


Figure 6
Over lay of X-RD of glibenclamide (GLB), solid dispersion of batch G5, L4

Scanning Electron Microscopy

The scanning electron micrographs of glibenclamide and the best solid dispersions batches (L4 and G5) are shown in figure 7 (a), 7 (b) and 7 (c). Drug particles appeared as smooth-surfaced rectangular crystalline structure (figure 8). On the other hand, in solid dispersions batches the drug surface seems to be more porous in nature. The solid dispersions appeared as an uniform and homogeneously mixed mass with wrinkled surface, indicating a decrease in crystallinity.



(a)

(b)

(c)

Figure 7 (a)
SEM photograph of (a) glibenclamide at 4000X (b) batch L4 at 500X
(c) batch G5 at 500X

In Vivo Glucose Estimation Studies

The *in vivo* results are mentioned in table V and the comparison of blood glucose levels in diabetic rats after administration of glibenclamide, solid dispersions batches (L4 and G5) is shown in figure 8.

Table V

Blood glucose levels in diabetic rats after administration of glibenclamide, solid dispersions batches (L4 and G5)

Group	Dose kg^{-1}	0 hr	1 hr	2 hr	3 hr	4 hr	5 hr
Control	5mg	298.5 ± 3.17	300.2 ± 2.91	295.3 ± 3.43	303.1 ± 1.82	302.3 ± 3.21	306.2 ± 2.39
Pure drug	5mg	304.2 ± 2.98	243.1 ± 1.99[a]	105.2 ± 1.90[c]	109.8 ± 2.01[d]	111.2 ± 2.54[e]	125.1 ± 1.94[f]
L4	Eq. to 5mg	293.4 ± 3.57	115.5 ± 2.14[a,b]	110.8 ± 2.09[c]	121.2 ± 2.23[d]	125.3 ± 2.11[e]	130.6 ± 2.21[f]
G5	Eq. to 5mg	309.3 ± 2.76	108.4 ± 1.85[a,b]	112.5 ± 2.34[c]	110.3 ± 2.81[d]	113.5 ± 1.81[e]	118.3 ± 1.42[f]

n=5 in each group, Values are expressed as Mean ± SEM.

$p<0.05$ was considered as significant.

Where a, c, d, e and f represents the significant decrease in blood glucose level as compared to control group at 1h, 2h, 3h, 4h and 5h. And b represents the significant decrease in blood glucose level as compared to pure drug treated group at 1h.

Significant decrease in blood glucose level was observed within 1 hour for both formulations (L4 and G5) as compared to pure drug. This was also supported by *in vitro* drug release studies. After 2 hours, the increase in blood glucose level in the case of pure drug, formulations L4 and G5 may be due to their clearance or decrease in their absorption.

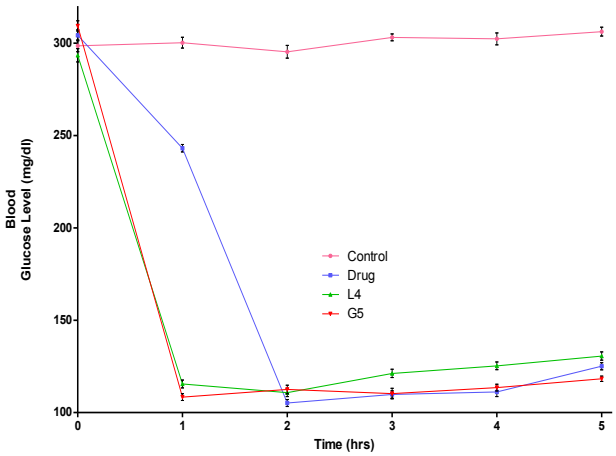


Figure 8

Comparative blood glucose levels in diabetic rats after administration of GLB, solid dispersions batches (L4 and G5).

Conclusion

The study showed that modified forms of natural carriers could be potential carriers in dissolution rate enhancement of poorly soluble drugs. Decreased viscosity with comparable swelling characteristics of these modified polymers and increased wettability, dispersibility of drug markedly increase the solubility of solid dispersions. The results indicated optimum levels of drug to polymer were 1:8 in the case of MLBG and 1:10 in the case of MGG. *In vivo* results showed better activity of solid dispersions batches L4 and G5 as compared to plain GLB in alloxan-induced diabetic rat model.

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References

1. Bhowmik D., Chiranjib, Jaiswal J., Dubey V., Chandira M., Fast dissolving tablet: A review on revolution of novel drug delivery system and new market opportunities. *Der Pharmacia Lettre*, 2009, 1(2), 262-276.
2. Charman S.A., Charman W.N., (2003), Modified Release Drug Delivery Technology, Marcel Dekker, 1–10.
3. Ibolya F., Gyéresi A., Szabó-Révész P., Aigner Z., Solid dispersions of flufenamic acid with PEG 4000 and PEG 6000. *Farmacia* 2011, 59(1), 60-69.
4. Ikegami K., Tagawa K., Osawa T., Bioavailability and *in vivo* release behavior of controlled release multiple-unit theophylline dosage forms in beagle dogs, cynomolgus monkeys, and gottingen minipigs*, J. Pharm. Sci*, 2006, 95, 1888–1895.
5. Kumar V.K., Kumar N.A., Verma P.R.P., Rani C., Preparation and *in vitro* characterization of Valsartan solid dispersions using skimmed milk powder as carrier, *International Journal of Pharm Tech Research*, 2009, 1(3), 431-437.
6. Murali Mohan Babu G.V., Prasad CHDS and Raman Murthy KV. Evaluation of Modified Gum Karaya as a Carrier for dissolution enhancement of poorly water soluble drug nimodipine, *Int. J. Pharm*., 2002, 234, 1-17.
7. Murali Mohan Babu G.V., Prasad C.H.D.S., Ravi Kumar N., Raman Murthy K.V., Studies on the modified form of gum karaya and its applicability as a tablet disintegrant. *Int. J.Pharm. Excip*. 2000, 2(2), 185-191.
8. Patel M., Tekade A., Gattani S., Surana S., Solubility Enhancement of Lovastatin by Modified Locust Bean Gum Using Solid Dispersion Techniques, *AAPS Pharm Sci Tech*, 2008, 9(4), 1262-1269.
9. Ranetti M.C., Ionescu M., Hinescu L., Ionică E., Anuţa V., Ranetti A.E., Stecoza C.E., Mircioiu C., Validation of a HPLC method for the simultaneous analysis of metformin and gliclazide in human plasma, *Farmacia* 2009, 57(6), 728-735.
10. Sekiguchi K. Obi N., Studies on absorption of eutectic mixture: A comparison of the behavior of eutectic mixture of sulfathiazole and that of ordinary sulfatriazole in man, *Chem. Pharm. Bull*.,1961, 9, 866-872.

11. Serajuddin T.M., Solid dispersion of poorly soluble drugs-Early promises, subsequent problems, and recent breakthroughs, *J. Pharm Sci*., 1999, 88(10), 1058-1066.
12. Sharma D.K., Joshi S.B., Solubility enhancement strategies for poorly water-soluble drugs in solid dispersions: A Review, *Asian J. of Pharmaceutics*, 2007, 1(1), 1-19.
13. Shoaib M.H., Tazeen J., Merchant H.A., Yousuf R.I., Evaluation of drug release kinetics from Ibuprofen matrix tablets using HPMC. *Pak. J. Pharm. Sci*., 2006, 19(2), 119-124.
14. Ye G, Wang S, Heng PWS, Chen L and Wang C. Development and optimization of solid dispersion containing pellets of itraconazole prepared by high shear pelletization. *Int. J. Pharm*., 2007, 337, 80–87.
15. Shah V., Patel D., Sandeep M., Upadhyay U., Solubility and dissolution rate enhancement of licofelone by using modified guar gum, *Int. J Pharm. Tech. Res*. 2010, 2(3), 1847-54.

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