

# An Overview on Techniques Implemented for Dissolution Enhancement of Glipizide

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## ABSTRACT

Glipizide is one of the most commonly used anti-diabetic drugs for treatment of type 2 diabetes mellitus. It is effective in pancreatic secretion of insulin. Glipizide is used for patients with type 2 diabetes who have failed diet and exercise therapy and it appears to be the most effective in first phase insulin secretion. The poor aqueous solubility of the drug leads to the poor bioavailability. As it is anti-diabetic drug it has to be absorbed rapidly, so enhancement of the solubility of drug is important. In order to improve solubility and dissolution of poorly water-soluble drug many methods are used. Enhancing the bioavailability of poorly water-soluble drug, selection of the carriers is of the most challenging aspect of drug development. Now a days different techniques are available to enhance the solubility of drug like co-solvent, solid dispersion, chemical modification of drug, liquisolid technique etc. The review article comprises of the research materialized in the field of solubility and dissolution enhancement of glipizide.

**Keywords:** Diabetes, Dissolution Enhancement, Glipizide, Solubility, Solid Dispersion.

## INTRODUCTION

Glipizide is a medium to long acting antidiabetic drug belonging to second generation sulphonyl urea. It lowers the blood glucose level in patients with diabetes mellitus II diabetes (non-insulin dependent diabetes mellitus) in humans by stimulating the release of insulin from the pancreas<sup>1</sup>.

Oral bioavailability of glipizide is around 100% and makes the gastrointestinal absorption uniform, rapid, and essentially complete. The urinary excretion of the drug is 80%, 98-99% protein binding and half life about 2-5 hours<sup>2</sup>.

Dose of drug is 5-20 mg in once or twice daily. The hepatic metabolism leads to the aromatic hydroxylation, as major metabolite, which does not have any hypoglycemic activity. A minor metabolite which accounts for less than 2% of a dose, an acetyl amino ethyl benzene derivatives, is reported to have little hypoglycemic activity. The primary metabolites are excreted mainly in the urine<sup>3,4</sup>.

The glipizide belongs to Biopharmaceutics Classification System (BCS) class II having low solubility and high permeability. It is practically insoluble in water (1.4µg/ml), sparingly soluble in acetone and soluble in methylene chloride (Dichloromethane)<sup>2</sup>. Being a weak acid (pka=5.9), glipizide is better absorbed from basic medium; however, at very low pH levels, the solubility of glipizide is minimal<sup>1</sup>. The melting point of glipizide is approx. 208-209°C<sup>2,3</sup>.

## Solubility and Dissolution Rate Enhancement of Glipizide

The poor solubility causes decreased absorption of the drug. The bioavailability thus depends on the solubility makes the solubility as rate limiting step. The solubility of the drug can be increased by several techniques. The research arises in the enhancement of the solubility and dissolution of glipizide is discussed herewith.

Hitendra S. Mahajan et al, 2011 prepared immediate release glipizide liquisolid tablets using Avicel PH-102 and Aerosil 200 as the carrier and coating material respectively to increase dissolution rate of poorly soluble glipizide. The dissolution patterns of glipizide liquisolid tablets, carried out according to USP paddle method, and were compared with their commercial counterparts. The results obtained shows that all glipizide liquisolid tablets exhibits higher dissolution rates than those of marketed glipizide tablets. Dissolution rates increases with increasing concentration of liquid vehicles and maximum drug release achieved by formulations containing Polyethylene glycol 400 (PEG 400) as a liquid vehicle. In order to attain optimal glipizide solubility in the liquisolid formulations, the concentration of the all three vehicles varied as, 5, 7.5, and 10% (W/W). The wettability of the compacts by the dissolution media was the reason for enhanced dissolution rate of glipizide from liquisolid tablets. The

mathematical models for calculating amounts of excipients were applied in optimizing the formulations. PEG 400 was found the best liquid vehicles to increase solubility of glipizide among three used. The formulations treated with gellan gum were reported to be an excellent disintegrating agent as compared to sodium starch glycolate<sup>1</sup>.

Adel M. Aly et al, 2003 reported the interaction between Glipizide and  $\alpha$ - and  $\beta$ -Cyclodextrins (CDs). Some additives and CDs play an effective role on the drug dissolution rate.

Complexes of glipizide with  $\alpha$ - and  $\beta$ -CDs in aqueous solution were prepared by adding an excess amount of glipizide to sealed glass containers of serial concentrations of CD (from 1 to 12 mmol of each  $\alpha$ - and  $\beta$ -CD) that were equilibrated with electromagnetic stirring at a constant rate at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$  for 7 h. Aliquots were withdrawn, filtered, and analyzed spectrophotometrically at  $\lambda_{\text{max}} 276$  nm for glipizide. The Glipizide- $\beta$ -CD inclusion complex was prepared by the kneading method. Glipizide- $\beta$ -CD was weighed accurately in a molar ratio (1:2). The  $\beta$  CD was more effective than the  $\alpha$  CD in enhancing the dissolution rate of glipizide, and the addition of Sodium Carboxy Methylcellulose (NaCMC) enhanced the dissolution rate of the glipizide  $\beta$  CD complex more than Poly Vinyl Pyrrolidone or PEG6000.

Tablet formulations containing pure glipizide, glipizide - $\beta$ -CD complex, and glipizide- $\beta$ -CD complex with NaCMC were prepared and all showed acceptable physical properties. Tablets containing NaCMC showed a better dissolution rate, tablets containing the glipizide- $\beta$ -CD complex showed the next greatest dissolution rate, and the pure glipizide formulation exhibited the lowest dissolution rate<sup>6</sup>.

Dehghan M H G et al, 2010 prepared solid dispersion of glipizide using water soluble carriers such as polyethylene glycol (PEG) and mannitol by fusion method and PVP K 30 by solvent evaporation method. Physical mixture (PM) of Glipizide with PEG-6000, mannitol and PVP K 30 in ratio 1:1, 1:2, 1:3, 1:4, 1:5 ratio was prepared. The result showed that Glipizide: PEG 6000 solid dispersion had faster dissolution rate than Glipizide itself. In contrast with carriers, it seems that interaction of solid dispersion had not occurred in Glipizide and carriers. Finally it was concluded that PEG-6000 shows greater dissolution enhancing capacity than mannitol and PVP K 30<sup>7</sup>.

Adel M. Aly et al, 2010 prepared Glipizide-Polyethylene glycol (PEG 4000 and 6000) solid dispersions with different ratios, (using

melting and solvent evaporation method), as well as, coprecipitate containing Glipizide with polymethyl-methacrylate (PMMA) were prepared. Four tablet formulations were prepared containing viz glipizide alone, glipizide: PEG6000, 1:10, glipizide: PMMA 1:3 and both glipizide: PEG6000 1:10 and glipizide: PMMA 1:3.

Generally, PEG6000 showed more enhancement of dissolution than PEG4000 especially at 1:10 drug: polymer ratio as the most enhancing formula. The most effective formula in decreasing the blood glucose level, through the first 6 hours, was that containing Glipizide and PEG6000, 1:10. However, formula containing the combination of enhanced and sustained Glipizide was the most effective in decreasing the blood glucose level through 16 hours. Successful in-vitro in-vivo correlations could be detected between the percent released and the percent decreasing of blood glucose level after 0.5 hours<sup>8</sup>.

Sachin Shivaji Kusharea et al, 2012 described the solubility enhancement by formation of bio nano composites (BNCs) using microwave-induced diffusion (MIND), which ultimately resulted in bioavailability enhancement. BNCs were formed by using natural carriers such as gelatin, acacia, cassia and ghatti gum, with the help of microwaves. Selection of carriers was based on their surfactant and wetting properties.

A physical mixture of glipizide and individual carrier (ghatti gum, cassia gum, Gelatin and acacia gum) was prepared by homogeneous mixing. The weight-to-weight (w/w) ratio of drug to the carrier was taken from 1 to 9 keeping amount of mixture constant. To this mixture, 4 ml of water was added for each gram of the drug-carrier mixture to make homogeneous slurry. A fixed amount of the slurry (5g) was placed in a glass beaker with a Teflon stirrer (transparent to microwaves) and treated with microwave irradiation for different times at power of 560 W. The temperature of the mixture at the end of treatment was recorded using an inbuilt temperature measurement probe. The samples were then ground in a glass mortar and sieved. It was found that as the concentration of polymer in the composite increased the solubility and dissolution of glipizide were enhanced. The optimised ratio (drug: polymer) for all the composites was found to be 1:9<sup>9</sup>.

Biresh K Sarkar et al, 2011 developed a novel delivery system i.e. microemulsion (ME), and studied the 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. Bioavailability of glipizide was done by preparing its ME. In vitro stability of formulation was assessed. 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 developed ME, containing Capmul® MCM (6.5%), Cremophor® EL (25%), Transcutol® P (7.5%), and distilled water, was found to be a transparent fluid. Micro Emulsion 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<sup>10</sup>.

Shahla Jamzadand Reza Fassihi, 2006 studied the saturation solubility of fenofibrate and glipizide in different media. A pH 6.8 phosphate buffer medium is appropriate for glipizide 10-mg tablet dissolution study, when formulation ingredients include excipients with surface activity (eg, Hydroxy Proryl Methyl Cellulose).

It is well known that the nature of the drug formulation can also influence the dissolution process. To investigate this effect, solubility of glipizide at different concentrations of HPMC (the release modifying ingredient of the developed formulation) was studied. Polymer dissolution during the time course of study changes the surface tension of the medium and increases drug solubility. A significant increase in solubility was observed. This can be attributed to the surface activity of the polymer. The surface tension of water (at 20°C) is ~72 mN/m and that of HPMC polymer class at the same temperature ranges from 42 to 64 mN/m. This reduction in surface tension can increase the wetting of the drug particles and as a result, increase the solubility. The change in the solubility at levels above 0.05 mg/mL HPMC may be attributed to the change in the viscosity of the medium<sup>11</sup>.

Hemant Rote et al, 2012 enhanced the solubility and bioavailability of glipizide by formulating physical mixtures and solid dispersions (SDs) using spray drying technique with PVP K30 and PEG 6000 and with Skimmed Milk (SM) by kneading technique in ratios of 1:1 to 1:8. The SDs prepared exhibited better dissolution rates in comparison to physical mixtures and intact drug. It was found that the optimum weight ratio for drug: carrier is 1:8 in all cases. But with glipizide: PEG solid dispersion, the solubility enhancement was achieved to

greater extent up to 90.70% in terms of Cumulative percent drug release and solubility of Glipizide was increased up to 7.15 folds. All physical mixtures and solid dispersions SDs were easy to prepare and reproducible<sup>12</sup>.

Hanwate R M et al, 2012 prepared the solid dispersion of glipizide with PVP K30. Solvent evaporation method was employed to prepare solid dispersion. The solid dispersion prepared was found to have higher dissolution rate and solubility compared to plain drug and physical mixture of drug and carriers.

Accurately weighed quantity of carriers PVP K 30 in various 1:1, 1:2, 1:3, 1:4, 1:5 (drug: carrier) proportion were carefully transferred into glass flask and dissolved in dichloromethane. To these solutions, accurately weighed quantities of glipizide were added and allowed to dissolve. Then solvent was removed by evaporation at 40°C under reduced pressure. The mass obtained in each flask was scraped, crushed, pulverized and sifted through mesh No. 100. It was found that the optimum weight ratio 1.5 for PVP K30 shows higher solubility and dissolution rate. In contrast with carriers, it seems that interaction of solid dispersion had not occurred in Glipizide and carriers<sup>13</sup>.

Meenakshi Shukla et al, 2010 studied the effect of solubility of glipizide by using different solubilization techniques such as Solid dispersion, hydrotropy and micellarsolubilization. Solid dispersion of glipizide was prepared by solvent evaporation method; PEG (Polyethylene glycol) 4000, mannitol and urea were used as carriers. Hydrotropic studies were carried out using different hydrotropic agents (sodium acetate, sodium benzoate and salicylate) and Micellar solubilization was carried out using different surfactant solutions (sodium lauryl sulphate, tween 80 and cetrimide).

The solubility was increased with the increase in the concentration of hydrotropic agents and amongst the various hydrotropic agents used the solubility of glipizide was enhanced greatest with sodium salicylate. This increase may be attributed due to aggregation of the hydrotropic molecules and inclusion of aggregates at high concentration probably by reacting to form an associated product as a result of hydrogen bonding. It was also evaluated and compared solubility enhancement of glipizide using three different surfactants i.e. sodium lauryl sulphate, tween 80 and cetrimide. Tween 80 was found to be the most efficient surface active agent, improving solubility by nearly to 36 folds<sup>14</sup>.

Dhaval Patel et al, 2012 prepared the nanoparticles of glipizide by anti-solvent precipitation method using various drug-to-stabilizers ratio. The present investigation focuses on formulation strategy of glipizide nanoparticles and investigates the improvement of solubility and dissolution rate. Different stabilizers in various ratio and anti-solvent precipitation method were effective in nano sizing the drug. The nanosuspension showed improved solubility and dissolution compared to micronized suspension. Saturation solubility of glipizide was increased 22.63 times than that of pure drug by nanosuspension formulation. Formulation containing HPMC-E15 in ratio of 1:1 showed significant improvement in decrease in particle size and higher saturation solubility leads to increased dissolution rate. The nanosuspension formulation was stable for one month at room temperature condition. A significant enhancement was observed in solubility of glipizide in phosphate buffer (pH 6.8) using nanosuspension approach<sup>15</sup>.

D Choudhary et al, 2009 enhanced the solubility of Glipizide by solid dispersion (SDs) technique with Poloxamer (PXM) 188 and Poloxamer (PXM) 407 by using the kneading method. It was found that the optimum weight ratio for drug: Carrier is 1:5 for PXM 188 and 1:6 for PXM 407. Solid dispersion of Glipizide-PXM 188 showed faster release than from that of PXM 407 solid dispersions<sup>16</sup>.

KPR Chowdary et al 2012 studied the complexation of glipizide, biopharmaceutical classification system class II drug with  $\beta$ -cyclodextrin ( $\beta$ -CD) and evaluate the feasibility of enhancing its solubility, dissolution rate and bioavailability by  $\beta$ -cyclodextrin complexation. Complexation of glipizide with  $\beta$ -cyclodextrin was evaluated by phase solubility, TLC, DSC, XRD and IR spectral studies. Solid inclusion complexes of glipizide and  $\beta$ -cyclodextrin were prepared by kneading method and were evaluated by in vitro and in vivo methods. The aqueous solubility of glipizide was increased linearly as a function of concentration of the  $\beta$ -cyclodextrin. The phase solubility studies indicated the formation of glipizide- $\beta$ -cyclodextrin inclusion complex at a 1:1 M ratio in solution. The complexes formed were quite stable<sup>17</sup>.

Hanwate R M et al, 2011 prepared the complex of glipizide with cyclodextrin by kneading method using different molar proportion of  $\beta$  cyclodextrin. Complex prepared was found to have higher dissolution rate compared to plain drug. A maximum increase in dissolution rate was found with

glipizide:  $\beta$  cyclodextrin complex with a molar ratio 1:5<sup>18</sup>.

Yogesh L. Jadhav et al, 2012 prepared the mouth dissolving tablet of glipizide. Drugs are more frequently taken by oral administration. The solubility of Glipizide enhanced with different ratios of CCS by the kneading method. In-vitro release profile of solid dispersion obtained in Ph 6.8 phosphate buffer indicate that 100% drug release found within 20 min. These solid dispersions were directly compressed into tablets using sodium starch glycolate, croscopolidone and pregelatinised starch in different concentrations as a superdisintegrants. The aim of improving drug dissolution and bioavailability of poorly soluble glipizide was achieved successfully because of increased wettability and increased surface area available for dissolution<sup>19</sup>.

Batra, V. et al, 2008 prepared the solid dispersion using solvent evaporation techniques of glipizide with Poloxamer 188 and Poloxamer 407. The dissolution rate of glipizide was directly proportional to increment in proportion of surface active carrier. The 100 % drug release was obtained from the solid dispersions (prepared by solvent evaporation method) of glipizide: poloxamer 188 and glipizide: poloxamer 407 (1:9) in 10 and 20 minutes respectively. The physical mixtures prepared from glipizide: poloxamer 188 (1:9) and glipizide: poloxamer 407 (1:9) showed complete release in 20 and 30 minutes respectively. The enhanced dissolution rate with poloxamer may be attributed to their surfactant activity, which facilitates wetting and subsequent solubilization of drug<sup>20</sup>.

Steffy B Manjila et al, 2013 Formulated the Glipizide micro crystals using different polymers. The results showed that mean particle size and dissolution is highest for microcrystals prepared with Tween 80 whereas microcrystals prepared with PVA have highest solubility. Solvent precipitation was developed in recent years producing microcrystals with enhanced solubility. As there is surface adsorption of excipients, surface inhibits particle growth and thus size reduction is achieved. Morphology can be changed by preferential adsorption of stabilizing agent.

The method followed is emulsion solvent diffusion method. Glipizide was dissolved homogeneously in acetone. This organic phase was added drop wise (using asyringe) to 0.25% w/v of each of stabilizer (PVA, Tween 80 and PEG 200) while stirring in a magnetic stirrer. Continued stirring for 30 minutes. Obtained microcrystals were filtered in a Whatmann No.1 filter paper and dried at room

temperature. The technique has the following advantages that it is a direct process, easy to perform, rapid and doesn't require any sophisticated equipments<sup>21</sup>.

### CONCLUSION

To achieve the immediate effect in diabetes i.e. hyperglycemias the drug availability must be ensured in the body. The immediate release formulation attempted with different investigators mentioned above may be used commercially. The release of the drug

especially BCS class II, dissolution is the rate limiting step. With an improvement in the dissolution in the formulation the availability of drug can be improved. Thus the area of the improvement in dissolution of the drug is widely exploited in case of drug with low solubility and high permeability. Further there is desperate requirement in the development of the immediate release formulations of the glipizide to improve the dissolution and bioavailability therefore.

**Table 1: Research Materialized in Solubility Enhancement of Glipizide**

S. NO.	TECHNIQUE	POLYMER	MECHANISM	REFERENCE
1.	LIQUISOLID	Avicel PH-102 and Aerosil 200	Liquisolid	Hitendra S. Mahajan et al 2011
2.	CYCLODEXTRIN INCLUSION COMPLEX	$\alpha$ - and $\beta$ -Cyclodextrins	Complexes of glipizide with $\alpha$ - and $\beta$ -cyclic dextrins in aqueous solution	Adel M. Aly,* Mazen K. Qato, and Mahrous O. Ahmad, 2003
3.	SOLID DISPERSION	polyethylene glycol (PEG) and mannitol	Fusion method	Dehghan M H G, Saifee M, et al
4.	SOLID DISPERSIONS	PEG 4000 and 6000	Melting and solvent evaporation method	Adel M. Aly, and Ahmed S. Ali, 2010
5.	FORMATION OF BIO NANO COMPOSITES	gelatin, acacia, cassia and ghatti gum	Microwave-induced diffusion (mind)	Sachin Shivaji Kushare and Surendra G. Gattani b, 2012
6.	MICROEMULSION DRUG DELIVERY SYSTEM	Cremophor® EL as surfactant and Transcutol® as co-surfactant	Microemulsion	Biresh K Sarkar*, Shiv S. Hardenia, 2011
7.	ROLE OF SURFACTANT	Hydroxy Propyl Methyl Cellulose		Shahla Jamzad and Reza Fassihi, 2006
8.	SOLID DISPERSION	PVP K30 and PEG 6000 and with Skimmed Milk (SM)	Kneading technique	Hemant Rote*, V.M. Thakare 2012
9.	SOLID DISPERSION	PVP K30	Solvent evaporation method	Hanwate R M*, Dehghan M H G, Saifee M et al 2012
10.	SOLID DISPERSION	PEG (Polyethylene glycol) 4000, mannitol and urea	Solvent evaporation method	Meenakshi Shukla*, Priyanka Rathore et al 2010
11.	ANTI-SOLVENT PRECIPITATION METHOD	HPMC	Enhancement of glipizide dissolution rate through nanoparticles	Dhaval Patel*, Priyanka Chaudhary et al 2012
12.	SOLID DISPERSION	Poloxamer (PXM) 188 and Poloxamer (PXM) 407	Kneading method	D Choudhary, S Kumar, GD Gupta, 2009
13.	COMPLEXATION	$\beta$ -cyclodextrin	Kneading method	Chowdary, K. P. R.; Raga, Sunil, 2012
14.	COMPLEXATION	$\beta$ cyclodextrin	Kneading method	Hanwate R M *, Dehghan M H G 2011
15.	SOLID DISPERSION	Cros Carmellose Sodium	Kneading method	Yogesh L. Jadhav* and Parashar Bharat, 2012
16.	SOLID DISPERSION	Poloxamer 188 and Poloxamer 407	Solvent evaporation techniques	Batra, V. 1 Shirolkar V.S. 1 2008
17.	MICROCRYSTALLIATION	PVA, Tween 80 and PEG 200	Emulsion solvent diffusion method	Steffy B Manjila, Jomon N Baby 2013

### REFERENCES

1. Mahajan HS, Dhamne MR, Gattani SG, Rasal AD and Shaikh HT. Enhanced Dissolution Rate of Glipizide by a Liquisolid Technique.

2. British Pharmacopoeia. Department of Health Scottish Office Welsh Office International Journal of Pharmaceutical Sciences and Nanotechnology. 2011;3(4):1205-1213

- Department of Health and Social Services for Northern Ireland, first Edition, Vol 1, Published by London: The Stationery Office. 1999;701
3. Glipizide. Drug Bank. Open Data Drug & Drug Target Database. Drug created on June 13, 2005, Updated on February 08, 2013. Available at [www.drugbank.ca/drugs/DB01067] Accessed on [SEP, 02 2013]
  4. Shivraj KN. Formulation and In-Vitro Evaluation of Glipizide Floating Microsphere Prepared Using Polymethacrylate Polymers. Rajiv Gandhi University of Health Sciences, Bangalore, Karnataka. 2011;52-53
  5. Mahajan HS, Dhamne MR, Gattani SG, Rasal AD and Shaikh HT. Enhanced Dissolution Rate of Glipizide by a Liquisolid Technique. International Journal of Pharmaceutical Sciences and Nanotechnology. 2011;3(4):1205-1213.
  6. Aly AM, Qato MK and Ahmad MO. Enhancement of the Dissolution Rate and Bioavailability of Glipizide through Cyclodextrin Inclusion Complex. Pharmaceutical Technology. 2003. Available at [www.pharmtech.com]. [SEP, 02 2013]
  7. Dehghan MHG, Saifee M and Hanwate RM. Comparative Dissolution Study of Glipizide by Solid Dispersion Technique. Journal of Pharmaceutical Science and Technology. 2010;2(9):293-297.
  8. Adel MA and Ahmed SA. Preparation and Evaluation of Glipizide Tablets Containing both Enhanced and Sustained Release Solid Dispersions. International Journal of Pharmaceutical Sciences and Nanotechnology. 2010;2 (4):714-725.
  9. Kushare SS and Gattani SG. Microwave-generated bionanocomposites for solubility and dissolution enhancement of poorly water-soluble drug glipizide: in-vitro and in-vivo studies. Journal of Pharmacy and Pharmacology. 2012;79-93.
  10. Sarkar BK and Hardenia SS. Microemulsion Drug Delivery System: For Oral Bioavailability Enhancement of Glipizide. Journal of Advanced Pharmacy Education and Research. 2011;1(4):195-200.
  11. Jamzad S and Fassihi R. Role of Surfactant and pH on Dissolution Properties of Fenofibrate and Glipizide—A Technical Note. AAPS PharmSciTech 2006;7(2):E3-E6.
  12. Rote H, Thakare VM, Tekade BW, Zope RP, Chaudhari RY and Patil VR. Solubility enhancement of glipizide using solid dispersion technique. World Journal of Pharmaceutical research. 2012;1(4):1096-1115.
  13. Hanwate RM, Dehghan MHG, Saifee M and Kondapure AA. Study of dissolution behaviour of glipizide pvp k 30 solid dispersion prepared by solvent evaporation method. International Journal of Universal Pharmacy and Life Sciences. 2012;2(1):2249-6793.
  14. Shukla M, Rathore P, Jain A and Nayak S. Enhanced solubility study of glipizide using different solubilization techniques. International Journal of Pharmacy and Pharmaceutical Sciences. 2010;2(2):46-48.
  15. Patel D, Chaudhary P, Mohan S and Khatri H. Enhancement of glipizide dissolution rate through nanoparticles: Formulation and In vitro evaluation. e-Journal of Science & Technology (e-JST). 2012;4(7):19-31.
  16. Chaudhary D, Kumar S and Gupta GD. Enhancement of solubility and dissolution of glipizide by solid dispersion (kneading) technique. Asian Journal of Pharmaceutics. 2009;3(3):245-251.
  17. Chowdary KPR and Raga S. Studies on Enhancement of Solubility Dissolution Rate and Bioavailability of Glipizide by Complexation with  $\beta$ -Cyclodextrin. Asian Journal of Chemistry. 2012;24(4):1693.
  18. Hanwate RM, Dehghan MHG, Saifee M and Kondapure AA. Solubility and dissolution enhancement of glipizide using  $\beta$  cyclodextrin inclusion complex. International Journal of Institutional Pharmacy and Life Sciences. 2011;1(3):163-168.
  19. Jadhav YL and Bharat P. Formulation and evaluation of mouth dissolving tablet of glipizide by solid dispersion. International Journal of pharmaceutical sciences and research. 2012;3(12):4929-4937.
  20. Batra V, Shirolkar VS, Mahaparale PR, Kasture PV and Deshpande AD. Solubility and Dissolution Enhancement of Glipizide by Solid Dispersion Technique. Indian Journal

of Pharmaceutical Education and Research. 2008;42(4):371-378.

21. Steffy B Manjila, Jomon N Baby, EN Bijin, Icey Constantine, K Pramod and Valsalakumari J. Microcrystalliation of Glipizide: Effect of type of Stabilizer on

Particle Size, Solubility and Dissolution. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2013;4(2):405-409.