Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

COMPARARISSION OF SOLUBILITY IMPROVEMENT OF CEFIXIME AND OMEPRAZOLE MAGNESIUM BY SOLID DISPERSION AND SLUGGING METHOD

S. Shahid Mohammed*[1], G. Venkatarajagopal Reddy[1], K. Viswaganga Pranush[1]

[1*]Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupati-517561, Andhrapradesh, India.

ABSTRACT

The formulation of poorly soluble compounds for oral delivery at present is one of the most frequent and greatest challenges to formulation scientists in the pharmaceutical industry. Omeprazole magnesium comes under class II of BCS classification which means low solubility and high permeability. Cefixime comes under class IV of BCS classification which means for low solubility and low permeability. Low solubility of omeprazole magnesium and cefixime leads to bioavailability problems. Increasing the solubility of omeprazole magnesium and cefixime can increase the bioavailability of the drug. Solid dispersion and slugging method is employed to increase solubility of drug. The solid dispersion by solvent evaporation, and fusion method were prepared using PVPK-30, urea and PEG 6000, in ratios 1:1, 1:2 and 1:3 .Slugging using excipient like lactose and sodium chloride in different ratios 1:1, 1:2 and 1:3 also enhances solubility of the drug. Solid dispersion with solvent evaporation technique (PVP-K: ethanol) showed higher drug solubility in comparison to other technique like slugging method and fusion method. Slugging method is next better alternative to improve solubility of the given drug.

KEYWORDS

Solid dispersion, Omeprazole magnesium, Cefixime and Slugging.

Author for Correspondence:

S. Shahid Mohammed,
Department of Pharmaceutics,
Seven Hills College of Pharmacy,
Tirupati-517561, Andhrapradesh, India.

Email: shahith_md@yahoo.co.in

INTRODUCTION [1-5]

The enhancement of oral bioavailability of poor water soluble drugs remains one of the most challenging aspects of drug development[1].Together with the permeability; the solubility behavior of a drug is a key determinant of its oral bioavailability. There have always been certain drugs for which solubility has presented a challenge to the development of a suitable formulation for oral administration. The formulation of poorly soluble

compounds for oral delivery at present is one of the most frequent and greatest challenges to formulation scientists in the pharmaceutical industry. However, the most attractive option for increasing the release rate is improvement of the solubility through formulation approaches. Although salt formation, solubilization and particle size reduction have commonly been used to increase dissolution rate and thereby oral absorption and bioavailability of low water soluble drugs[2-4], there are practical limitation of these techniques.

In 1961, Sekiguchiand Obi[5] developed a practical method whereby many of the limitations with the bioavailability enhancement of poorly water soluble drugs can be overcome. This method, which was later, termed solid dispersion which involved the formation of eutectic mixture of drugs with water-soluble carriers by the melting of their physical mixtures. The present research was undertaken to improve solubility of omeprazole magnesium and cefixime by solid dispersion and slugging method.

Cefixime comes under class IV of BCS classification which stands for low solubility and low permeability. Low solubility of cefixime leads to bioavailability problems of cefixime. Increasing the solubility of cefixime can increase the bioavailability of cefixime.

Omeprazole magnesium comes under class II of BCS classification which stands for low solubility and high permeability. Low solubility of omeprazole magnesium leads to bioavailability problems of omeprazole magnesium .Increasing the solubility of omeprazole magnesium can increase the bioavailability of omeprazole magnesium.

MATERIAL AND METHODS [6-8]

Material

Cefixime and Omeprazole magnesium was obtained as a gift sample from DRL laboratories, Hyderabad. All other chemicals and reagents were of analytical grade.

Method of estimation of Cefixime [6]

A simple, fast, reproducible and precise method of estimation for cefixime was carried based on the solubility of cefixime in ethanol. The absorption maximum was found to be 234 nm. Beers range was found to be 2-26 µg/ml. Solubility measurements of cefixime were performed according to a published method. An excess amount of cefixime (50 mg) was added to 10 ml of aqueous solution of water soluble carriers like, PVPK 30, Urea and PEG-6000 and slugs of lactose and sodium chloride in the various ratios such as 1:1, 1:2, and 1:3 in screw capped bottles. Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with ethanol. The diluted solution analyzed for the cefixime in UV 234 nm.

Estimation of Omeprazole magnesium [6]

A simple, fast, reproducible and precise method of estimation for Omeprazole magnesium was carried based on the solubility of omeprazole magnesium in ethanol. The absorption maximum was found to be 302nm. Beers range was found to be 2-26 µg/ml. Solubility measurements of Omeprazole magnesium were performed according to a published method (Higuchi and Connors, 1965). An excess amount of cefixime (50 mg) was added to 10 ml of aqueous solution of water soluble carriers like, PVPK 30, Urea and PEG-6000 and slugs of lactose and sodium chloride in the various ratios such as 1:1, 1:2, and 1:3 in screw capped bottles Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with ethanol. The diluted solution analyzed for the Omeprazole magnesium in UV 302 nm.

Preliminary solubility studies of Cefixime[7]

Solubility measurements of cefixime were performed according to a published method Higuchi and Connors. An excess amount of cefixime (25mg) was added to 10 ml of aqueous solution of water in screw capped bottles. Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with distilled water. The diluted solution analyzed for the cefixime in UV 234 nm.

Preliminary solubility studies of Omeprazole magnesium [7]

Solubility measurements of Omeprazole magnesium were performed according to a published method Higuchi and Connor. An excess amount of Omeprazole magnesium (25mg) was added to 10 ml of aqueous solution of water in screw capped bottles. Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with distilled water. The diluted solution analyzed for the Omeprazole magnesium in UV 302 nm.

Preparation of solid dispersions of Cefixime and Omeprazole magnesium [7-8]

Solid dispersion is one of the most commonly used techniques to improve the solubility of water insoluble drugs which in turn improves the bioavailability. Solid dispersions were prepared by hot melt method (PEG 6000) and solvent evaporation methods (PVPK-30, Urea). In hot melt method, the insoluble drug is dispersed into a molten carrier and cooled immediately. In solvent evaporation method, both drug and the carrier were dissolved in a common volatile solvent (ethanol), and the solvent was evaporated to get solid dispersions. The drug is practically water insoluble molecule. In order to improve its solubility in water solid dispersions were prepared.

Hot melt method [7-9]

In hot melt method, the carriers such as PEG 6000 were selected based on the preliminary solubility study. The drug to polymer ratio was kept 1:1, 1:2, and 1:3. The carrier was first melted in the water bath at about 60^{o}C and the drug was dispersed when molten mass is being cooled in cooled water bath with constant stirring. The dispersion was poured and cooled immediately. The solid dispersions obtained from this method were tacky enough.

Solvent evaporation method[7-9]

In solvent evaporation method, drug and the carrier were dissolved in ethanol and were dispersed in the same medium with constant stirring. Solution was evaporated under low pressure to get the solid dispersion. In this method PVP-K-30 and urea was used as carriers. Drug: carrier ratio was kept 1: 1, 1: 2 and 1:3 respectively.

Slugging method [7-9]

Drug (cefixime and omeprazole magnesium) were mixed with excipient (lactose and sodium chloride) in different ratios (1:1, 1:2and, 1:3)and allowed to slug using single station tablet compressing machine under high pressure. The slugs formed were powdered using mortar and pestle and passed through sieve 80#. The solubility of drug in 10ml water was determined.

Solubility studies of cefixime[8]

Solubility measurements of cefixime were performed according to a published method Higuchi and Connors. Samples were mixed with 10 ml of distilled water and shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with distilled water. The diluted solution analyzed for the cefixime in UV 234 nm.

Solubility studies of omeprazole magnesium[8]

Solubility measurements of omeprazole magnesium were performed according to a published method Higuchi and Connors. Samples were mixed with 10 ml of distilled water and shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with distilled water. The diluted solution analyzed for the omeprazole magnesium in UV 302 nm

Evaluation of solid dispersion[10]

Solid dispersions obtained from the above methods were screened for their solubility.

Drug content

The amount of drug present in a 50 mg equivalent amount of solid dispersion and slugging was determined by, dissolving the powder mixture in 10 ml of ethanol and suitably diluted with ethanol and UV absorbance was measured. Drug concentration was determined from standard graph.

Similarly drug dispersion concentrations were calculated in water using ethanol as solvent.

RESULTS AND DISCUSION

Standard graph for Cefixime

Cefixime was found to be soluble in organic solvents such as methanol. A simple reproducible method of estimation was carried out in methanol ranging from 2-26 µ/ml solutions at 234nm in Table No.1-3 against the blank the standard graph obtained was linear was shown in Figure No.1. Cefixime is insoluble in water and having poor bioavailability and coming under the category of class 4 of biopharmaceutical classification (BCS) system

Standard graph for Omeprazole magnesium

Omeprazole magnesium was found to be soluble in organic solvents such as ethanol. A simple reproducible method of estimation was carried out in ethanol ranging from 2-26 µ/ml solutions at 302 nm in Table No.4 against the blank the standard graph obtained was linear was shown in Figure No.2 Omeprazole magnesium is very slightly soluble in water and having poor bioavailability and coming under the category of class 2 of biopharmaceutical classification system.

Saturation solubility

The saturation solubility of cefixime and omeprazole magnesium by solid dispersion and slugging and its solubility of in water are presented in Table No.5-6.

DISCUSSION

The percentage increase in saturation solubility with PVPK-30 and urea was higher than other polymers and techniques. This shows that solid dispersion using solvent evaporation technique gives a better solubity of drug when compared to other techniques. This might be due to the better solubilization effect of drug and polymer with solvent over PEG-6000 and slugging method. Slugging method is next best alternative for increasing solubility of drug.

Table No.1: Physical characteristics and solubility studies of Cefixime

S.No	Drug	Carrier	Ratio	Method of preparation
1	Cefixime	PVP K-30	1:1	Solid Dispersion (Solvent evaporation method)
2	Cefixime	PVP K-30	1:2	Solid Dispersion (Solvent evaporation method)
3	Cefixime	PVP K-30	1:3	Solid Dispersion (Solvent evaporation method)
4	Cefixime	Urea	1:1	Solid Dispersion (Solvent evaporation method)
5	Cefixime	Urea	1:2	Solid Dispersion (Solvent evaporation method)
6	Cefixime	Urea	1:3	Solid Dispersion (Solvent evaporation method)
7	Cefixime	PEG-6000	1:1	Solid Dispersion (Hot melt method)
8	Cefixime	PEG-6000	1:2	Solid Dispersion (Hot melt method)
9	Cefixime	PEG-6000	1:3	Solid Dispersion (Hot melt method)
10	Cefixime	Lactose	1:1	Slugging method

11	Cefixime	Lactose	1:2	Slugging method)
12	Cefixime	Lactose	1:3	Slugging method
13	Cefixime	Sodium chloride	1:1	Slugging method
14	Cefixime	Sodium chloride	1:2	Slugging method
15	Cefixime	Sodium chloride	1:3	Slugging method

Table No.2: Physical characteristics and solubility studies of omeprazole magnesium

S.No	Drug	Carrier	Ratio	Method of preparation
1	Omeprazole magnesium	PVP K-30	1:1	Solid Dispersion (Solvent evaporation method)
2	Omeprazole magnesium	PVP K-30	1:2	Solid Dispersion (Solvent evaporation method)
3	Omeprazole magnesium	PVP K-30	1:3	Solid Dispersion (Solvent evaporation method)
4	Omeprazole magnesium	Urea	1:1	Solid Dispersion (Solvent evaporation method)
5	Omeprazole magnesium	Urea	1:2	Solid Dispersion (Solvent evaporation method)
6	Omeprazole magnesium	Urea	1:3	Solid Dispersion (Solvent evaporation method)
7	Omeprazole magnesium	PEG-6000	1:1	Solid Dispersion (Hot melt method)
8	Omeprazole magnesium	PEG-6000	1:2	Solid Dispersion (Hot melt method)
9	Omeprazole magnesium	PEG-6000	1:3	Solid Dispersion (Hot melt method)
10	Omeprazole magnesium	Lactose	1:1	Slugging method
11	Omeprazole magnesium	Lactose	1:2	Slugging method
12	Omeprazole magnesium	Lactose	1:3	Slugging method
13	Omeprazole magnesium	Sodium chloride	1:1	Slugging method
14	Omeprazole magnesium	Sodium chloride	1:2	Slugging method
15	Omeprazole magnesium	Sodium chloride	1:3	Slugging method

Table No.3: Standard graph of Cefixime

S.No	Concentration (µg / ml)	Absorbance (nm)
1	0	0.0000
2	5	0.106
3	10	0.209
4	15	0.316
5	20	0.423
6	25	0.502

Table No.4: Standard graph of Omeprazole magnesium

S. No	Concentration (µg / ml)	Absorbance (nm)	±SD
1	0	0.0000	0.00
2	2	0.0847	± 0.0613
3	4	0.1750	± 0.0140
4	6	0.2443	± 0.0176
5	8	0.3163	± 0.0146
6	10	0.3940	± 0.0166
7	12	0.4707	± 0.0150
8	14	0.5457	± 0.0255
9	16	0.6527	± 0.0350
10	18	0.7410	± 0.0125
11	20	0.8100	± 0.0234
12	22	0.8870	± 0.0276
13	24	0.9663	± 0.0234
14	26	1.0803	± 0.0155

Table No.5: Solubility of Cefixime in water

S.No	Solid dispersion formulations	Ratio	Absorbance (nm)	Saturation solubility in distilled water (µg/ml)
1.	Cefixime + ethanol		0.876	50.0 (100%)
2.	Cefixime + water		0.197	11.2 (22%)
3.	Cefixime +PVP K-30	1:1	0.778	44.0 (88%)
4.	Cefixime +PVP K-30	1:2	0.860	49.1 (97%)
5.	Cefixime +PVP K-30	1:3	0.875	49.9 (98%)
7	Cefixime +Urea	1:1	0.820	46.8 (93%)
8	Cefixime + Urea	1:2	0.875	37.6 (99%)
9	Cefixime + Urea	1:3	0.875	37.6 (99%)
7.	Cefixime + PEG-6000	1:1	0.542	30.9 (62 %)
8.	Cefixime + PEG -6000	1:2	0.562	32.1 (64 %)
9.	Cefixime + PEG-6000	1:3	0.564	32.2 (64%)
13	Cefixime + lactose	1:1	0.688	43.8 (79%)
14	Cefixime + lactose	1:2	0.702	40.1 (80 %)
15	Cefixime + lactose	1:3	0.702	40.1 (80 %)
16	Cefixime + sodium chloride	1:1	0.684	39.0 (78%)
17	Cefixime + sodium chloride	1:2	0.634	36.2 (81%)
18	Cefixime + sodium chloride	1:3	0.602	34.4 (53%)

Table No.6: Solubility of Omeprazole magnesium in water

S. No	Solid dispersion formulations	Ratio	Absorbance (nm)	Saturation solubility in distilled water (µg/ml)
1.	Omeprazole magnesium + ethanol		0.576	50.0 (100%)
2.	Omeprazole magnesium + water		0.197	17.1 (34%)
3.	Omeprazole magnesium +PVP K-30	1:1	0.496	43.0 (86%)
4.	Omeprazole magnesium +PVP K-30	1:2	0.558	48.4 (97%)
5.	Omeprazole magnesium +PVP K-30	1:3	0.563	48.9 (98%)
6	Omeprazole magnesium +Urea	1:1	0.500	43.0 (86%)
7	Omeprazole magnesium + Urea	1:2	0.545	47.0 (97%)
8	Omeprazole magnesium + Urea	1:3	0.565	49.0 (98%)
9.	Omeprazole magnesium + PEG-6000	1:1	0.274	23.8 (48%)
8.	Omeprazole magnesium + PEG -6000	1:2	0.398	34.5 (69%)
9.	Omeprazole magnesium + PEG-6000	1:3	0.400	34.7 (69%)
10	Omeprazole magnesium + Lactose	1:1	0.380	32.9 (66%)
11	Omeprazole magnesium + Lactose	1:2	0.480	41.7 (83%)
12	Omeprazole magnesium + Lactose	1:3	0.484	41.8 (83%)
13	Omeprazole magnesium + Sodium chloride	1:1	0.440	38.1 (76%)
14	Omeprazole magnesium + Sodium chloride	1:2	0.400	34.7 (69%)
15	Omeprazole magnesium + Sodium chloride	1:3	0.358	31.0 (62%)

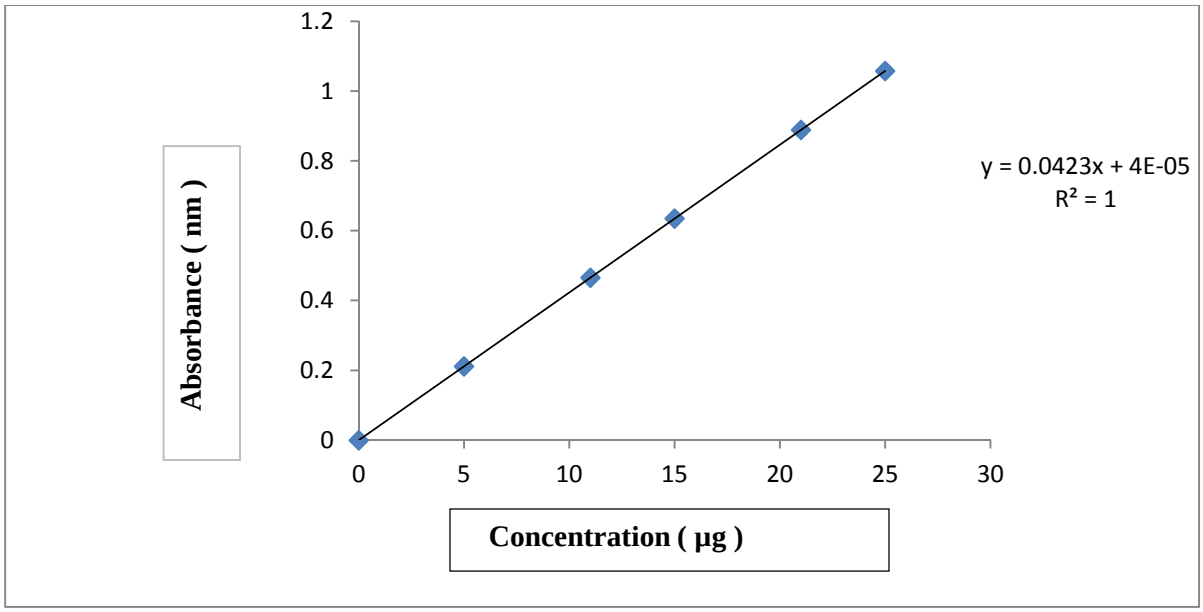

Figure No.1: Standard graph of cefixime

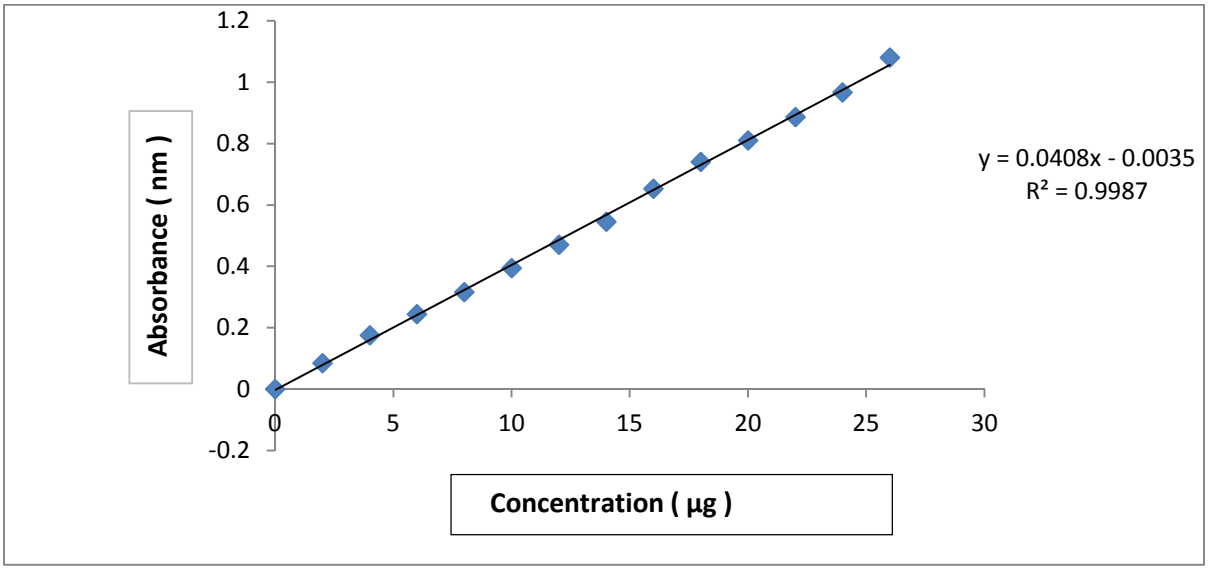

Figure No.2: Standard graph of omeprazole magnesium

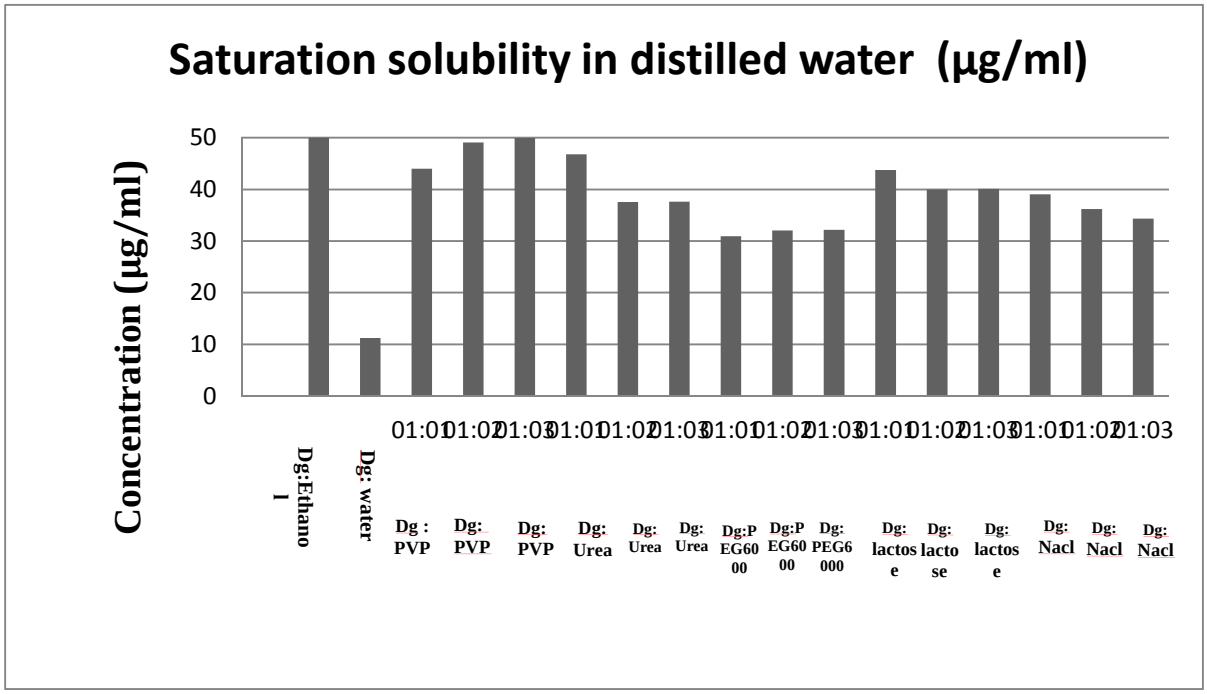

Figure No.3: Saturation Solubility graph of Cefixime in water

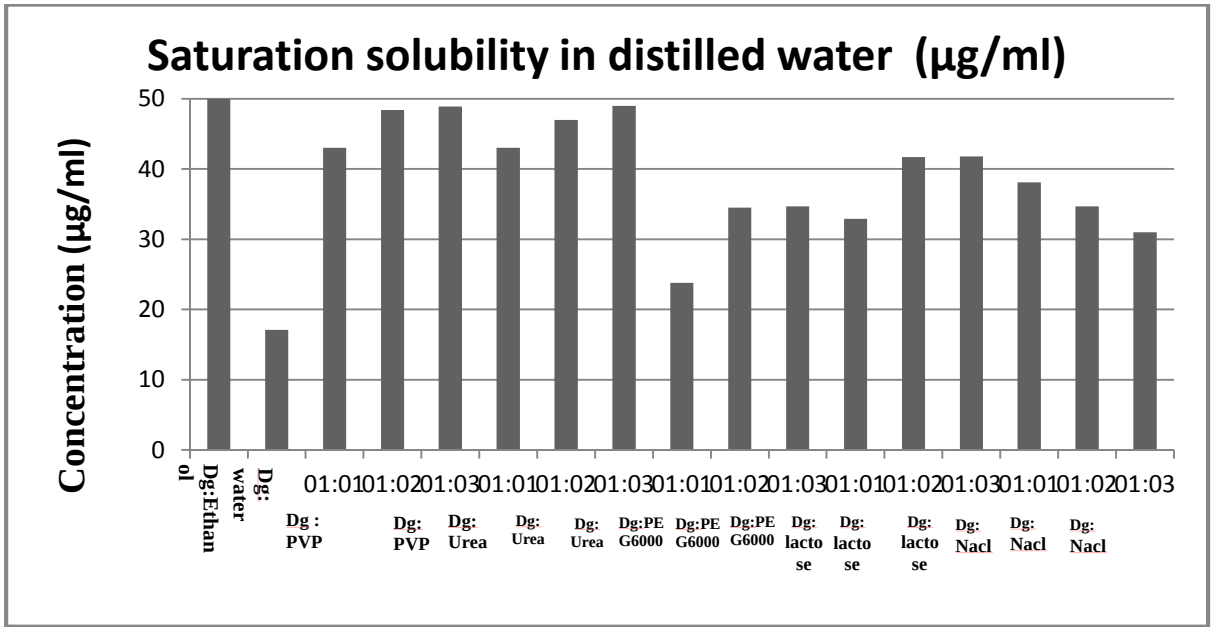

Figure No.4: Saturation Solubility graph of Omeprazole magnesium in water

CONCLUSION

In conclusion, solid dispersion of Cefixime and Omeprazole magnesium with solvent evaporation technique showed higher drug solubility in comparison to other technique like hot melt and slugging method. Hence this solid dispersion technique can be used to improve the dissolution and the bioavailability of given dosage forms.

ACKNOWLEDGEMENT

I am thankful to Seven Hills College of Pharmacy, Tirupati-517561, A.P, India for providing facility to carry out the research work

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Aulton, Aulton's Pharmaceutics. The Design and manufacture of medicine, 3rd edition, 293.
2. Noyes A A, Whitney W R. The rate of solution of solid substances in their own solutions, *J Am Chem Soc*, 19(12), 1897, 930-934.
3. *Nernst W.* Theorieder Reaktions geschwin digkeit in heterogenen systemen, *Zeitschrift Physik Chemie*, 47(1), 1907, 52-55.
4. Galia E, Nicolaides E, Horter D, Lobenberg R, Reppas C, Dressman B. Evaluation of various dissolution media for predicting *in vivo* performance of class I and II drugs, *Pharm Res*, 15(5), 1988, 698-705.
5. Sekiguchi K, Obi N. Studies on absorption of eutectic mixture, I.A comparison of the behavior of eutectic mixture of sulfathiazole and that of ordinary sulfathiazole in man, *Chem Pharm Bull*, 9(11), 1961, 866-867.
6. Craig Q M. The mechanisms of drug release from solid dispersions in water soluble polymers, *Int .J. Pharm*, 231(2), 2001, 131-144.
7. Parakh S R, Gothoskar A V. A review of mouth dissolving tablet technologies, *Pharma Tech*, 27(11), 2003, 92-100.
8. Higuchi T, Connors K. Phase-solubility techniques, *Adv Anal* Chem Instrum, 4, 1965, 117-212.
9. Dhirendra K, Lewis S, Udupa N *et al*. Solid Dispersions: A Review, *Pak. J. Pharm. Sci*, 22(2), 2009, 234-246.
10. Das S K, Saha S K, Das A, Halder A K, Banerjee S N, Chakraborty M. Solid dose, *Journal of the Indian Medical Association*, 106(9), 2008, 589 -590.

Please cite this article in press as: Shahid Mohammed S. *et al.* Compararission of solubility improvement of cefixime and omeprazole magnesium by solid dispersion and slugging method, *International Journal of Research in Pharmaceutical and Nano Sciences*, 3(1), 2014, 50-60.