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RESEARCH ARTICLE

Formulation and Evaluation of Solid Dispersion of Poorly Soluble Drugs

Komal Chandrakant Jadhav[1], Sourabh Sukumar Hegaje[2], Sadhana Uttam Jadhav, Rupesh Sopanrao Vaidhya[3], Mayuresh Ramesh Redkar[4]*
[1]Annasaheb Dange College of Pharmacy, Ashta.
[2]Tatyasaheb Kore College of Pharmacy, Warananagar.
[3]Alard College of Pharmacy, Pune.
[4]Assistant Professor, Department of Pharmaceutics, Yashwantrao Bhonsale College of Pharmacy, Sawantwadi.
*Corresponding Author E-mail: **mayuresh.redkar253@gmail.com**

ABSTRACT:
Solid dispersion is one of the method, which was most widely and successfully applied to improve the solubility, dissolution rates and consequently the bioavailability of poorly soluble drugs. The solid dispersion based on the concept that the drug is dispersed in an inert water- soluble carrier at solid state. Several water-soluble carriers such as methyl cellulose, urea, lactose, citric acid, polyvinyl pyrrolidone and HPMC, cyclodextrin, polyethylene glycols 4000 and 6000 are used as carriers for solid dispersion. In the current research work, the solid dispersion technique can be successfully used for the improvement of dissolution of piperine and sulfamethaoxazole. In this regards, solid dispersions of these drugs were prepared by using HPMC E 100 and 2-Hydroxyproplyl beta cyclodextrin as a carrier in 1:1 ratio by solvent evaporation method. The saturation solubility and in-vitro dissolution studies of prepared solid dispersions were examined against pure piperine and sulfamethaoxazole. Faster dissolution was exhibited by piperine-2 hydroxypropyl beta cyclodextrin solid dispersion containing 1:1 ratio.

KEYWORDS: Piperine, Sulfamethaxazole, Solid Dispersion, Poorly Soluble Drug, Solibility Enhancement etc.

INTRODUCTION:
The enhancement of oral bioavailability of poor water-soluble drugs remains one of the most challenging aspects of drug development. The development of solid dispersions as a practically viable method to enhance bioavailability of poorly water-soluble drugs overcame the limitations of previous approaches such as salt formation, solublization by co solvents, and particle size reduction[1].

The poor solubility and low dissolution rate of poorly water-soluble drugs in the aqueous gastro-intestinal fluids often cause insufficient bioavailability[2]. Lipophilic molecules, especially those belonging to the bio pharmaceutics classification system (BCS) class II and IV, dissolve slowly, poorly and irregularly, and hence pose serious delivery challenges, like in complete release from the dosage form, poor bioavailability, increased food effect, and high inter-patient variability[3].

In 1961, Sekiguchi and Obi 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

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eutectic mixture of drugs with water-soluble carriers by the melting of their physical mixtures[4].

The term solid dispersion refers to a group of solid products consisting of at least two different compounds, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particle (clusters) or in crystalline particles[5].

Solid dispersion can be prepared by various methods such as solvent evaporation and melting method. Solid dispersion technique has been extensively used to increase the solubility of a poorly water-soluble drug. According to this method, a drug is thoroughly dispersed in a water-soluble carrier by suitable method of preparation. The mechanism by which the solubility and the dissolution rate of the drug are increased includes: reduction1 of the particle size of drug to submicron size or to molecular size in the case where solid solution is obtained. The particle size reduction generally increases the rate of secondly, the drug is changed from amorphous to crystalline form, the high energetic state which is highly soluble; finally, the wet ability of the drug particle is improved by the hydrophilic carrier Solid dispersion of drug helps to reduce the particle size of drug due to molecular dispersion[6,7].

Particle size reduction by micronization or nanonization can enhance the dissolution rate; however, the apparent solubility remains unaltered. At the molecular level, polymorphs offer a limited solubility advantage because of a small difference in free energy. In contrast, amorphous systems with excess thermodynamic properties and lower energetic barrier can offer significant solubility benefits[8].

There were several ways in which bioavailability of the drug can be enhanced all of which aimed at increasing the surface area of the drugs which includes. Micronization, use of salt form, use of metastable polymorphs, solvent deposition, selective adsorption on insoluble carriers, solid dispersion, solute solvent complexation, with cyclodextrins[9,10].

MATERIAL AND METHOD:

Material:

For the present research investigation Piperine and Sulfamethaxazole used as active pharmaceutical ingredients obtained as a gift sample from Sigma Aldrich Chemicals Pvt. Ltd. and Triveni Chemicals Pvt. Ltd. respectively. (2-2Hydroxypropyl)-B- Cyclodextrine used as solubility enhancing polymer received from Hi Media Laboratories Pvt. Ltd. HPMC E 100 of analytical grade purchased from VIVA Pharma Pvt. Ltd.

Method:

The solid dispersion was prepared by solvent evaporation method. The drug polymer was mixed separating mixed separately in given ration (table-1). The polymer solutions were prepared by adding given quantity of polymer in methanol. The given quantity of Piperine was added to the polymer solutions and resulting mixture was evaporated at room temperature.

RESULT AND DISCUSSION:

Table 1. Calibration data of Piperine

Sr. No.	Concentration of Piperine (µg/ml)	Absorbance at 331.20 nm
0	0	0
1	1	0.157
2	2	0.328
3	3	0.506
4	4	0.694
5	5	0.889
6	6	1.07

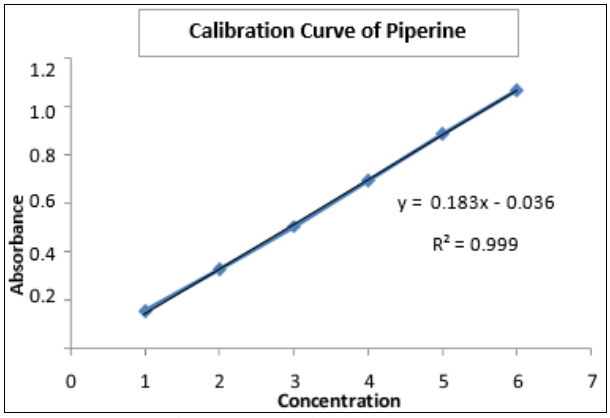

Figure 1. Graph of Calibration of Piperine

Table 2. Saturated Solubility of PD, PH and PC

Sr. No.	Polymer	Ratio	Saturation Solubility [mg/ml]	% Increase in Solubility
1	HPMC E 100	1:1	0.247	15.40
2	2 Hydroxypropyl beta cyclodextrin	1:1	0.726	41.41

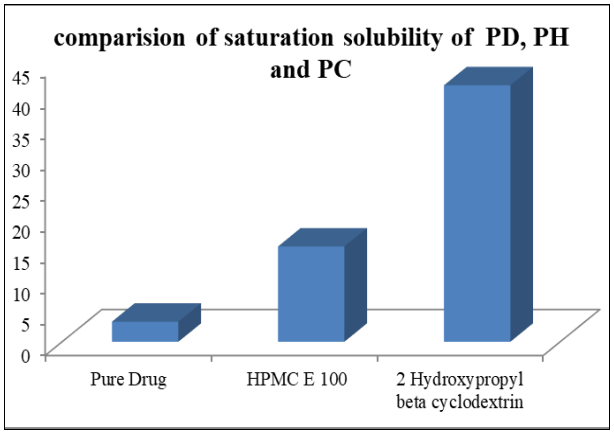

Figure 2. Comparison of saturation solubility of PD, PH and PC

Solid dispersion prepared by solvent evaporation method for 1:1 ratio of 2 Hydroxypropyl beta cyclodextrin showed maximum increasing in saturation solubility as compared to ratio 1:1 of HPMC E100.

In Vitro Dissolution Study in Water:

Table 3. Percentage drug release of solid dispersion of Piperine

Time in min	Pure drug	2 hydroxypropyl beta-cyclodextrin (1:1)	HPMC E 100 (1:1)
15	3.98	64.74	32.6
30	14.39	75.21	58.65
45	17.01	98.21	67.39
60	22.23	105	77.46

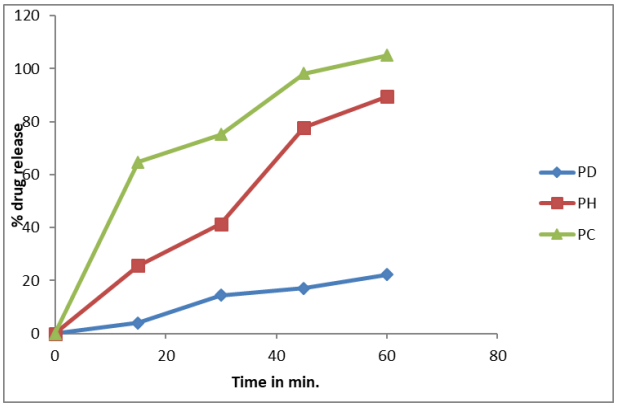

Figure 3. Percentage of drug release of solid dispersion of Piperine

From dissolution studies, it was observed that pure drug shows 22-23 % drug dissolved within 60 min. Which shows strong need to improve the dissolution Solid dispersion prepared by solvent evaporation method for all the four polymers showed marked increase in the dissolution profile of drug release as compared to pure drug. However, solid dispersion with 2 hydroxypropyl beta cyclodextrin showed complete drug dissolution.

Table 4. Calibration curve of Sulfamethaoxazole

Sr. No.	Concentration of Sulfamethaoxazole (µg/ml)	Absorbance at 259.60 nm
0	0	0
1	0.2	0.159
2	0.4	0.305
3	0.6	0.450
4	0.8	0.609
5	1	0.752
6	1.2	0.912

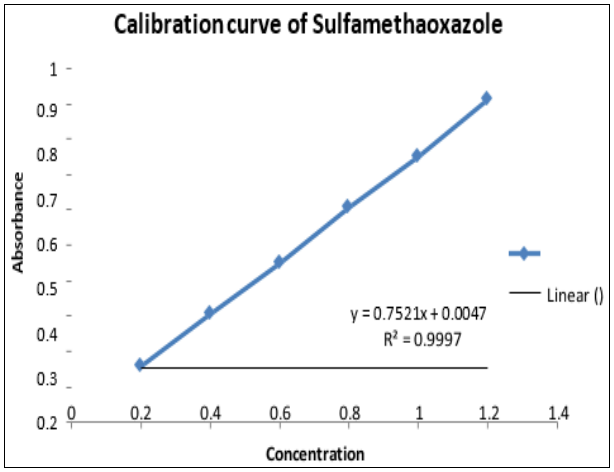

Figure 4. Calibration curve of Sulfamethaoxazole

Table 5. Saturated Solubility of solid dispersion of PD, SH and SC

Sr. No.	Polymer	Ratio	Saturation Solubility [mg/ml]	% Increase in Solubility
1	HPMC E 100	1:1	0.421	553.5
2	2 Hydroxypropyl beta cyclodextrin	1:1	0.221	287.59

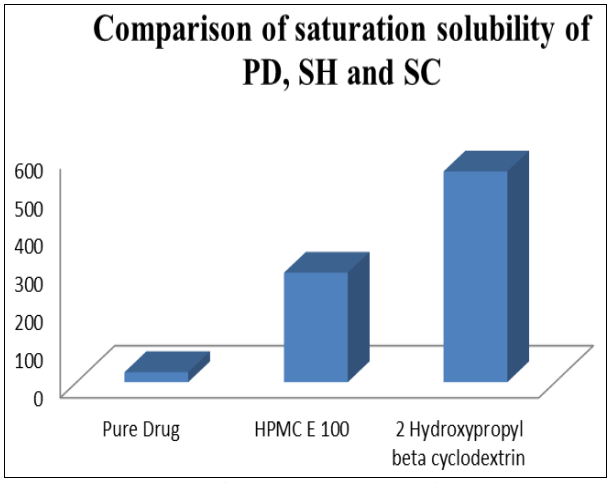

Figure 5. Comparison of saturation solubility of PD, SH and SC

Solid dispersion prepared by solvent evaporation method for 1:1 ratio of 2 Hydroxypropyl beta cyclodextrin showed maximum increasing in saturation solubility as compared to ratio 1:1 of HPMC E100

In Vitro Dissolution Studies in Water:

Table 6. Percentage drug release of solid dispersion of Sulfamethaoxazole

Time in min	Pure drug	2 hydroxypropyl beta cyclodextrin (1:1)	HPMC E 100 (1:1)
0	0	0	0
15	12.76	35.42	44.75
30	14.16	46.39	55.30
45	24.46	86.42	65.31
60	34.94	98.66	76.74

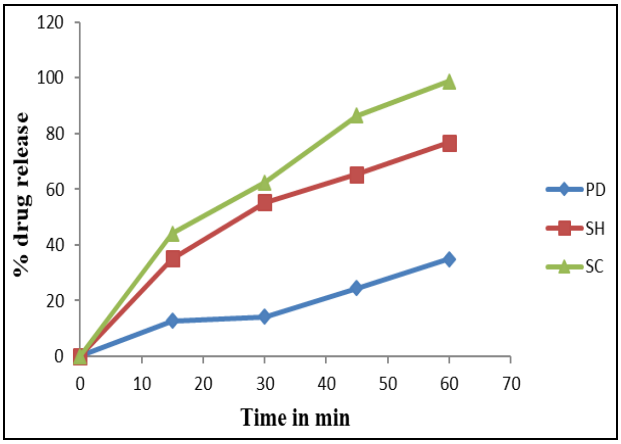

Figure 6. Percentage of drug release of Sulfamethaoxazole

From dissolution studies, it was observed that pure drug shows 22-23% drug dissolved within 60 min, which shows strong need to improve the dissolution. Solid dispersion prepared by solvent evaporation method for both the polymers showed marked increase in the dissolution profile of drug release as compared to pure drug. However, solid dispersion with 2 hydroxypropyl beta cyclodextrin showed complete drug dissolution.

CONCLUSION:

Piperine is an antimicrobial drug having antiproliferative action and Sulfamethaoxazole is antibacterial drug having poor aqueous solubility with high permeability. To improve the dissolution properties, solid dispersion of Piperine and Sulfamethaoxazole were prepared in same ratio with different carrier viz. 2 hydroxypropyl beta cyclodextrin and HPMC E 100 by solvent evaporation method. The prepared solid dispersion was evaluated by saturation solubility study and dissolution studies. From the present investigation it has been concluded that solid dispersion of 2 hydroxypropyl Beta cyclodextrin was found to be more efficient and its superdisintegrant property helps to improve the drug solubility and dissolution rate. In vitro release studies of Piperine and Sulfamethaoxazole indicated complete drug release in 60 min. as compared to pure drug having only 22-23% and 34-35% respectively.

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