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Studies to Enhance Dissolution of Piroxicam

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Piroxicam, a nonsteroidal antiinflammatory agent, is widely used as a first line drug in the symptomatic relief of rheumatoid arthritis and osteoarthritis. One of the major problems with this drug is its very low solubility in biological fluids, which results into poor bioavailability after oral administration. Therefore, solid dispersions of piroxicam with polyethylene glycol 400 and polyvinyl pyrolidone K-30 were prepared to increase its water solubility. Solid dispersions of piroxicam were prepared using polyethylene glycol 400 as a water soluble carrier (1:4, 1:8, 1:12, 1:16, 1:20 by weight) employing solvent evaporation method. The drug release profile was studied according to USP XXIII monograph in simulated gastric fluid. Piroxicam was released at a much higher rate from solid dispersions containing polyethylene glycol 400 and physical mixture as compared to that of pure drug powder. Faster dissolution rate was observed in 1:12 drug:carrier ratio. Physical mixture of piroxicam and polyethylene glycol 400 in a same ratio released the drug at a slower rate as compared to that of solid dispersions. Solid dispersions of piroxicam were also prepared using PVP K-30 as a water-soluble carrier (1:1, 1:2, 1:3, 1:4 and 1:5 by weight) employing solvent evaporation method. Piroxicam was released at a much higher rate from solid dispersion and physical mixture as compared to that of pure drug powder. Faster dissolution was exhibited by solid dispersion containing 1:4 ratio of drug: PVP compared to physical mixture and pure drug. The increase in dissolution rate of the drug may be due to increase of wettability, hydrophilic nature of carrier and also possibly due to reduction in drug crystalinity.

Piroxicam is used as a first line drug in the treatment of rheumatoid arthritis and osteoarthritis and has less incidence of side effects[1]. It is practically insoluble in water and peak blood level reaches between 1-3 h and its bioavailability is between 45-75 % after oral administration[1]. It shows erratic dissolution profile in gastric and intestinal fluid due to its poor water solubility. Piroxicam is available in market as hard gelatin capsules and dispersible tablets. Rate of absorption and/or extent of bioavailability for such insoluble hydrophobic drug is controlled by rate of dissolution in gastro-intestinal fluids. The peak plasma concentration (C_{max}) and the time taken to reach C_{max} (t_{max}) depend upon extent and rate of dissolution of drug respectively. Hence the present work was aimed to increase rate of dissolution of piroxicam and to minimize the erratic dissolution profile of drug. Dissolution of drug can be increased by variety of contemporary approaches like solid dispersions, complexation and by the use of hydrophilic carriers. Solid dispersion can be prepared by various methods such as solvent evaporation and melting method[2,3]. In the present investigation, solvent evaporation method was employed for the preparation of piroxicam solid dispersions. Attempts were made in the present investigation to enhance the dissolution rate of piroxicam using hydrophilic carriers like polyvinyl pyrolidone K-30 (PVP K-30) and polyethylene glycol 400 (PEG 400).

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MATERIALS AND METHODS

Lactose was purchased from Vikas Pharmaceuticals, Mumbai. Microcrystalline cellulose was purchased from

Maruti Chemicals, Ahmedabad. PEG-400 was purchased from Ases Chemical Works, Ahmedabad. Piroxicam USP was obtained as a gift sample from Cadila Healthcare, Ahmedabad. Polyvinyl pyrolidone K-30 was obtained as a gift sample from Helios Pharmaceutical, Ahmedabad. All other materials used were of pharmaceutical grade.

Preparation of solid dispersions of piroxicam containing PEG 400:

Solid dispersions containing piroxicam and PEG 400 in various ratios were prepared. Five hundred milligrams of piroxicam was dissolved in 10 ml chloroform in a beaker and PEG 400 was added and mixed to dissolve. Lactose: MCC (4:1, 10 g) was added to the above solution with Stirring. Chloroform was evaporated at room temperature and the resulting semi-wet mass was passed through 60 #. The granules were dried at room temperature for 1 h and further dried at 65° for 6 h in a hot air oven. The granules were kept at room temperature till further use. The composition of various batches is shown in Table 1.

Preparation of physical mixture of piroxicam containing PEG 400:

Weighed amount of piroxicam and PEG 400 were mixed in a glass mortar for 5 min in the ratio that has resulted in maximum dissolution in solid dispersion formulation (1:12), and mixed with lactose-microcrystalline cellulose (4:1) mixture. This physical mixture (Batch-PP3) was then stored at room temperature.

Preparation of solid dispersions of piroxicam containing PVP K-30:

Solid dispersions containing piroxicam and PVP K-30 in various ratios were prepared by the solvent evaporation method. Five hundred milligrams of piroxicam was dissolved in 10 ml chloroform in a beaker and then PVP K-30 was added and mixed to dissolve. Lactose: MCC (4:1, 10 g) was added to the above solution with Stirring. Chloroform was evaporated at room temperature and resulting mass was passed through # 60. The granules were dried at room temperature for 1 h and then dried at 65° for 6 h in a hot air oven. The dried granules were stored at room temperature. The composition of various batches is shown in the Table 2.

Preparation of physical mixture of piroxicam containing PVP K-30:

Weighed amount of piroxicam and PVP K-30 were mixed in a glass mortar for 5 min in the ratio that has resulted in maximum dissolution in solid dispersion formulation (1:4), and mixed with lactose-microcrystalline cellulose (4:1) mixture. This physical mixture (Batch-PB4) was stored at room temperature.

***In vitro* dissolution study:**

Quantity of granules equivalent to 20 mg of piroxicam was filled in hard gelatin capsule by hand filling method. Dissolution study of capsule was carried out using USP dissolution apparatus I. In a 900 ml of simulated gastric fluid[4] (pH-1.2), maintained at 37±0.5° at a speed of 50 RPM. Five ml of samples were withdrawn at time intervals of 5, 10, 20, 30, 45, 60, 90 and 120 min. The volume of dissolution fluid was adjusted to 900 ml by replacing each 5 ml aliquot withdrawn with 5 ml of simulated gastric fluid, pH 1.2. The concentration of piroxicam in the samples was determined by measuring absorbances at 333 nm. The absorbances were converted to concentration using standard curve equation.

RESULTS AND DISCUSSION

The dissolution rate of pure piroxicam was very poor and during 120 min a maximum of about 38.4% of the drug

TABLE 1: COMPOSITION OF BATCHES CONTAINING PEG 400

Batch	Piroxicam (mg)	PEG 400 (g)	Lactose-MCC [4:1] (g)
P1	500	2	10.0
P2	500	4	10.0
P3	500	6	10.0
P4	500	8	10.0
P5	500	10	10.0

TABLE 2: COMPOSITION OF BATCHES CONTAINING PVP K30

Batch	Piroxicam (mg)	PVP K-30 (g)	Lactose-MCC [4:1] (g)
B1	500	0.5	10.0
B2	500	1.0	10.0
B3	500	1.5	10.0
B4	500	2.0	10.0
B5	500	2.5	10.0

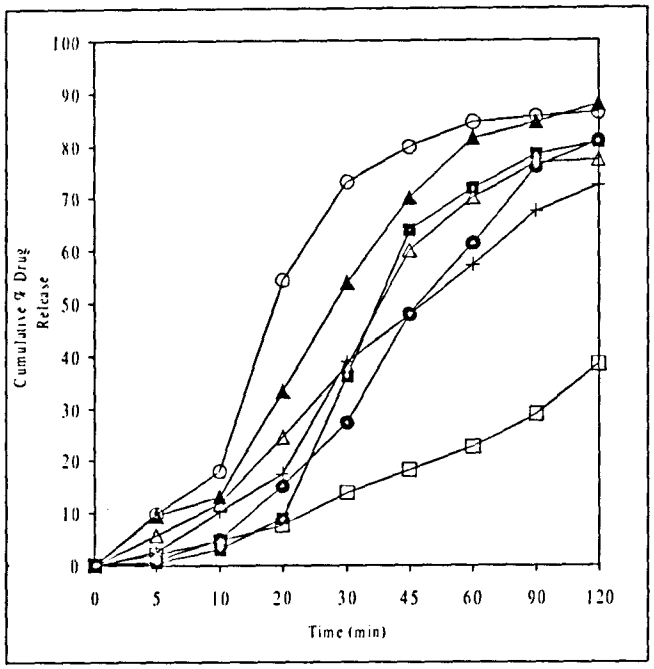

Fig. 1: Comparative *in vitro* release profile of piroxicam from solid dispersions containing PEG 400.

Batch P1 (-▫-), Batch P2 (-▲-), Batch P3 (-○-), Batch P4 (-△-), Batch P5 (-●-), Batch PP3 (-+-) and Piroxicam (-□-).

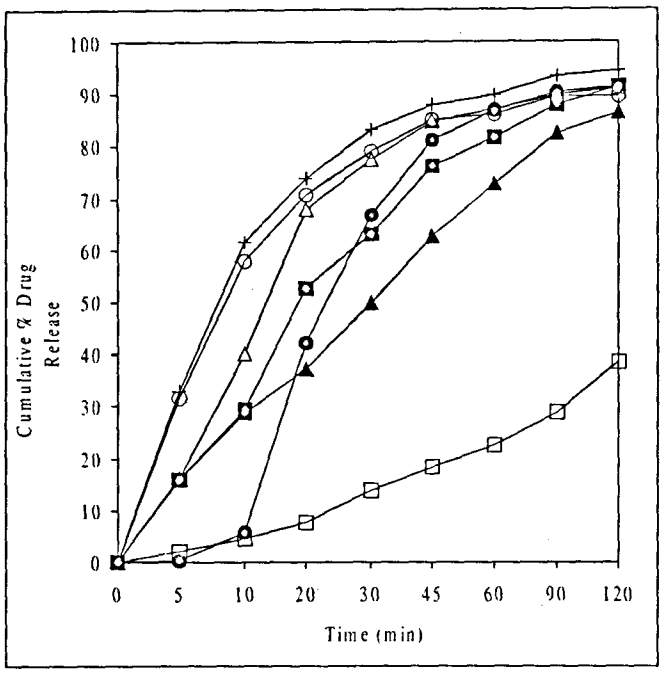

Fig. 2: Comparative *in vitro* release profile of piroxicam from solid dispersions containing PVP K-30.

Batch B1 (-▫-), Batch B2 (-△-), Batch B3 (-○-), Batch B4 (-+-), Batch B5 (-●-), Batch PB4 (-▲-) and Piroxicam (-□-).

was released. The reason for the poor dissolution of pure drug could be poor wettability and/or agglomeration of particles. Fig. 1 shows the comparative release profile of various solid dispersions of piroxicam with PEG 400 having different weight ratios of PEG 400 such as 4, 8, 12, 16, 20 for 1 part of piroxicam, physical mixture (1:12 drug to carrier) and pure drug. From the release profile, it can be seen that dissolution of piroxicam increases with increase in PEG 400 up to 1:12 ratio of drug: PEG 400. This increase in the dissolution rate may be due to improved wettability by the carrier. At higher level (after 1:12 ratio) the change in the dissolution rate may be due to localized solvent effect of PEG 400. It can be concluded that the drug release from the physical mixture is greater than that of pure drug and slower than that of the solid dispersion. From the results, it can be concluded that solid dispersion containing with PEG 400 exhibits improved dissolution of piroxicam.

Fig. 2 shows the comparative release profile of various solid dispersions of piroxicam with PVP K-30 having different weight fractions of PVP K-30 such as 1, 2, 3, 4, 5 for 1 part of piroxicam, physical mixture (1:4 drug to carrier) and pure drug. From the release profile it can be seen that dissolution of piroxicam increases with increase in PVP K-30 up to 1:4 ratio of drug: PVP K-30. This may be attributed to the increase in drug wettability, solubilization of the drug due to hydrophilic carrier. After this particular ratio with further increase in the amount of PVP K-30, the dissolution was decreased. This decrease in dissolution may be due to increased viscosity. It can be concluded that the drug release from the physical mixture is greater than that of the pure drug and is slower than that of the solid dispersion. From the results, it may be concluded that the dissolution rate of piroxicam can be increased by preparing the solid dispersion with PVP K-30.

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REFERENCES

1. Reynolds, J.E.F., Eds., In; Martindale: The Extra Pharmacopoeia, 29th Edn., The Pharmaceutical Press, London, 1989, 32.
2. Vandre, M. K., In; Swarbrich, J., Eds., Encyclopedia of Pharmaceutical Technology, Vol. III, Marcel Dekker, Inc., New York, 1991, 337.

3. Udupa, N., Tatwawadi, S.V., and Code, K.D., **Eastern Pharmacist**, 1985, 28, 45.

4. The United States Pharmacopoeia, XXIII Rev., National Formulary, XVIII, US Pharmacopoeial Convention, Inc., Rockville, MD, 1995, 2053.