



Preparation, Physico Chemical Characterization of Solid Dispersions of Tenoxicam with Poloxamer

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Abstract

The objective of the present study is to improve the dissolution rate of Tenoxicam, a poorly water soluble drug by solid dispersion technique using a water soluble carrier, poloxamer 127(PXM). The solid dispersions are prepared by melting method and the prepared systems showed an enhancement in dissolution. Solid dispersions are characterized with Differential scanning calorimetry, X-ray diffraction revealed that enhanced dissolution of tenoxicam from solid dispersion is due to a decrease in crystallinity of drug and additive and also due to dissolution of tenoxicam in molten form of solid dispersion. In conclusion preparation of tenoxicam dispersion with meltable hydrophilic polymer could be a promising approach to improve the dissolution rate.

Key words: *Poloxamer, Tenoxicam, Solid dispersion, Dissolution.*

INTRODUCTION

Tenoxicam is an oxycam derivative with a potent anti inflammatory activity than other NSAIDs, such as diclofenac, naproxen and piroxicam. It is used in the treatment of ankylosing spondylitis, osteo arthritis and rheumatoid arthritis. Tenoxicam(TEN) is a poorly water soluble drugs and the water insoluble drugs shows poor, erratic dissolution profile in gastrointestinal fluids, which consequently results in low and variable bioavailability. This undesirable property, may also increase the GI damage due to long contact of drug with the mucus of GI tract.(1,4)

To improve the dissolution of poorly water soluble drugs the scientists employed various approaches such as micronization, solubilization, solid dispersions, salt formation, complexation with polymers, alteration of pH, drug derivatization and others. Among all the methods solid dispersion technique has proved to be the most successful, simple, economical method in improving the dissolution and bioavailability of poor water soluble drugs. (2)

Many water soluble carriers have been employed for the preparation of dispersions of poor water soluble drugs. The most commonly used carriers are poly vinyl pyrrolidone, β -cyclodextrin, hydroxyl propyl methyl cellulose, poly ethylene glycols. Recently Pluronic or Poloxamers, a group of block copolymers has been exploited their use in pharmaceutical formulation of poor water soluble drugs.

Poloxamer (PXM) consists of hydrophilic poly oxy ethylene chain, and hydrophobic core (poly propylene) arranged in a tri block structure to give an amphiphilic structure. The hydrophobic drug may be solubilized with in the core of micelle or conjugated to the micelle forming polymer to increase dissolution of poor water soluble drugs. These polymers are widely used as emulsifiers, solubilizing agents, wetting agents and stabilizers in pharmaceutical formulations. (2, 3)

In the present study attempts were made to increase the dissolution of tenoxicam using a solid dispersion technology. Solid dispersions of PXM and TEN were prepared using the melting method and physico chemical characterization of dispersion was performed to evaluate the chemical interaction between the drug and polymer. (6, 7)

MATERIALS AND METHODS

Tenoxicam was a gift sample from Ranbaxy Laboratories, Guargaon, India. poloxamer127 was kindly supplied by DR. Reddy's Laboratory, Hyderabad.

Preparation of Solid Dispersions

The solid dispersions of TEN-PXM were prepared by melting method. PXM was heated at a temperature of 55 °c \pm 5 c using a thermostatically controlled water bath. TEN in 1:1, 1:2, 1:4 and 1:8 drug to polymer ratio was dispersed in melted polymer. The resultant

mixture was cooled using an ice water mixture for a period of 30 min. The solidified mass was then removed allowed to attain room temperature. It was then pulverized, sifted through a #100 sieve, and stored at in type- 1 glass vials at 30 ° c for further work. (1, 2)

Dissolution Studies

In vitro dissolution studies of Tenoxicam and its dispersions were carried out using USP paddle dissolution method. Sample equivalent to 20mg of Tenoxicam was added to 900 ml of 6.8 phosphate buffer at $37 \pm 0.5 \pm ^\circ\text{C}$ and stirred at 50 rpm. An aliquot of 5 ml of sample was withdrawn at different time intervals and filtered. The filtered samples were analyzed at 360 nm using UV spectrophotometer (Systronics)(10)

Differential scanning calorimetry

The thermal analysis of tenoxicam and its dispersions was performed using differential scanning calorimeter (Perkin Elmer). Accurately weighed samples were placed in sealed aluminum pans and heated in a temperature range of 30-300 °c under the nitrogen flow rate of 20ml/min. The diffraction scan of solid dispersion was compared with drug and poloxamer scans for interactions.

X-Ray diffraction

X-ray diffraction pattern of Tenoxicam and its dispersion of poloxamer were obtained using diffractometer (Seifer 3003TT) using cu k α radiation at 30ma and 450kv. Powder X-ray diffraction pattern were traced for tenoxicam, poloxamer and its dispersions. The position and intensities of diffraction peaks were considered for the identification and crystallinity of drug or carrier.

Fourier transform infra red spectroscopy

The FTIR measurements of Tenoxicam and its dispersion were taken in shimadzu 8033 model and the samples were dispersed in KBr powder and pellet was made by applying 6000 kg/cm³. The spectra of solid dispersion were compared with the finger print region of drug and poloxamer.

RESULTS AND DISCUSSIONS

Dissolution studies

In dissolution studies of different proportions of tenoxicam dispersions the presence of poloxamer showed a significant role in the dissolution enhancement (table-1). The drug release profile of dispersion at 6.8 pH showed an enhanced rate of dissolution with the increase in the concentration of poloxamer. Several mechanisms may be responsible for the enhanced drug release of tenoxicam from solid dispersion i.e. the reduction in crystallinity, reduction in particle size to expand the surface area for dissolution enhancement of poloxamer. During the melting process the particles come in contact or adhere to polymer particles, when the particles come in contact with water with water, the polymer get hydrated rapidly in to polymer solution solubilizing the adjacent drug particles and subsequently releasing the drug in to the dissolution medium. (1, 2)

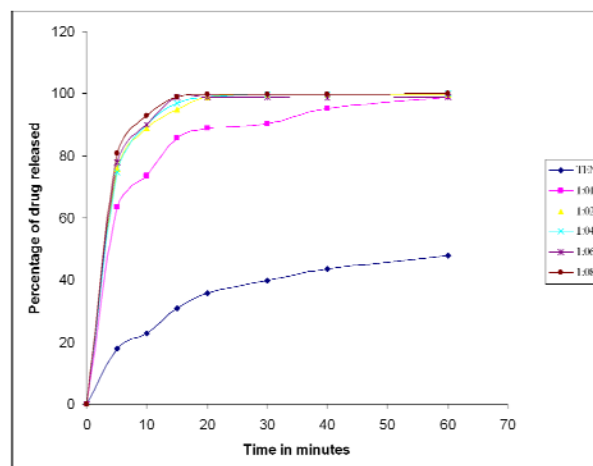


Fig-1: Comparative dissolution profile of tenoxicam poloxamer dispersion

Fourier transform infra red spectroscopy

The fig -2 shows the FTIR spectra of TEN, PXM, physical mixture and solid dispersion systems. The IR spectrum of tenoxicam was characterized by principle absorption peaks at 3429,3119,3092 due to NH OH stretching and 1635,1598,1530 for amide, C=O and C=N groups. The characteristic peaks at 2887, 1343 and 1124 are assigned due to C-H, O-H and C-O groups of poloxamer. The IR spectrum of

poloxamer dispersions showed the characteristics peaks of tenoxicam with decreased intensity and little shifting of peaks. The IR spectrum of dispersion shows shifting of the characteristic peak of N-H from 3429 to 3414 due to hydrogen bonding. However the IR spectrum does not showed any additional peak indicating the absence of any chemical interaction between tenoxicam and poloxamer. From the above data it was assumed that physical interaction of drug with polymer is responsible in dissolution enhancement. (2, 3)

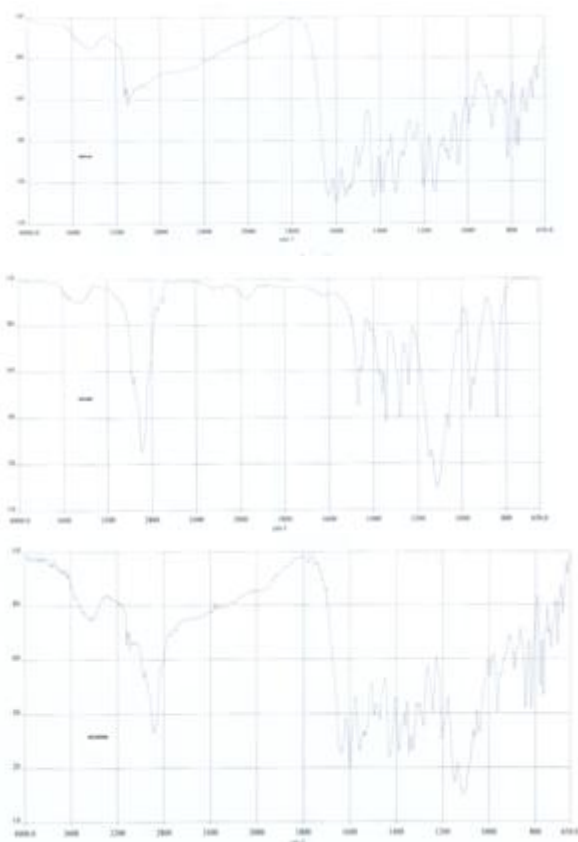


Fig- 2:FTIR spectra of tenoxicam,poloxamer and its dispersion.

X-Ray diffraction analysis

The X- ray diffraction pattern of tenoxicam displayed intense, sharp peaks (fig-3) indicating its crystalline nature. Tenoxicam showed sharp peaks at a diffraction angle of (2 θ)of 11.8°,13.03°,17.23° and 23.45° with high peak intensities while, the solid dispersions showed sharp peak at 24.2 ° with

less intensity .This data reveals that typical drug crystalline peaks were still detectable and the diffraction pattern with reduced intensity and less number indicates reduced crystalline nature of dispersion. The diffraction pattern of TEN, PXM and solid dispersions showed a total of 33, 9 and 26 respectively.

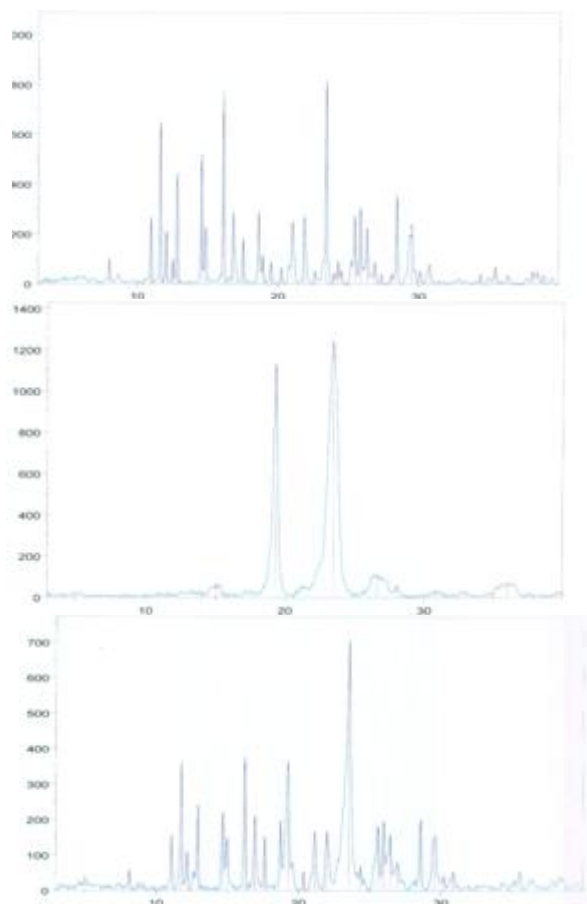


Fig-3: X-Ray diffraction patterns of tenoxicam, poloxamer and its dispersions

The X ray diffraction pattern of solid dispersion exhibits 15 peaks less than the sum of number of peaks of TEN and PXM in their pure forms. This confirms that crystalline character of drug and polymer is reduced in solid dispersion form. Decrease in crystallinity of the drug and polymer in dispersion may contribute to the enhancement of dissolution of the drug. (2, 6)

Differential scanning calorimetry

The thermograms of tenoxicam, poloxamer and its dispersions are illustrated in fig-4.

Tenoxicam is showing high melting point at 215.41°C due to large crystalline lattice energy. In case of poloxamer a peak at 54.70 °C indicate the melting of poloxamer. The endothermic scan of solid dispersion shows less intense poloxamer peak at 47.97°C and a tenoxicam peak with marked decrease in sharpness, intensity and broadness. It suggests the formation of different crystalline form, which might be responsible in the formation of dissolution enhancement. (8, 12)

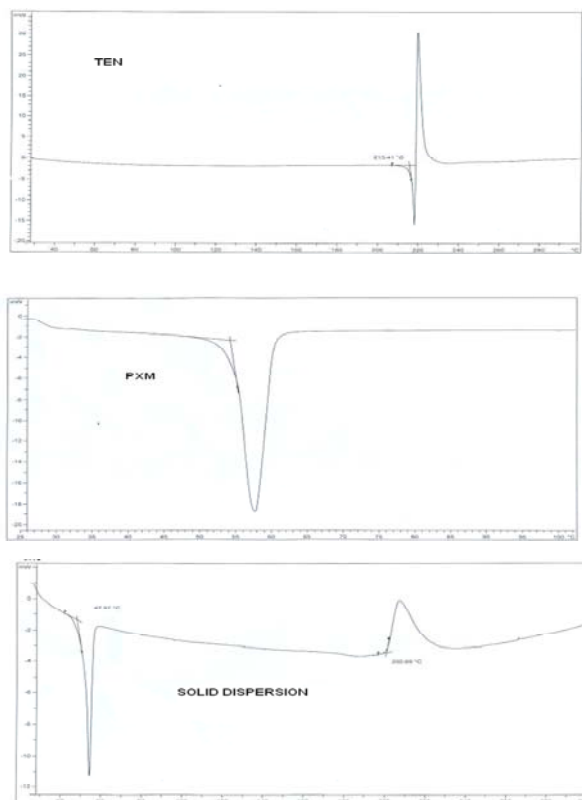


Fig-4: Differential scan of tenoxicam solid dispersion with poloxamer

CONCLUSION

The results of the above study confirm that the poloxamer solid dispersions has greater influence on the rate of dissolution. Characterization studies revealed that solid dispersions showed the enhancement due to conversion of tenoxicam in to less crystalline form. Based on the above results it can be concluded that solid dosage form of tenoxicam can be formulated with high dissolution rate,

faster onset of action and improved bioavailability.

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