ENHANCEING SOLUBILITY OF POORLY SOLUBLE DRUG ETORICOXIB BY SOLID DISPERSIONS METHOD

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ABSTRACT

This search based on solid dispersion method use of drug Etoricoxib a new cox-2 inhibitor used in rheumatoid arthritis, osteoarthritis, and acute gouty arthritis, It is practically insoluble in water and in aqueous fluids both acidic and basic. Because of limited solubility it exhibits poor soluble characteristics. The dissolution characteristics of poorly soluble drugs are improved by commonly used long chain polymers like polyethylene glycol and polyvinyl pyrrolidone. PEG is used as a dissolution enhancer for poorly water soluble drugs by solvent evaporation and melting methods. it was thought to prepare solid dispersions using different PEG polymers. The higher solubility and dissolution rate may possibly due to particle size reduction, improved wet ability of the hydrophobic drug particle by the presence of water soluble carrier, solubilising effect of the carrier and the possible conversion of crystalline form of drug to amorphous form.

KEYWORD: Polyethylene Glycol, Etoricoxib, Cox -2inhibiter, Solid Dispersion

Etoricoxib a new cox-2 inhibitor used in osteoarthritis, rheumatoid arthritis and acute gouty arthritis It is practically insoluble in water and in aqueous fluids both acidic and alkaline. Because of limited solubility it exhibits poor dissolution characteristics. The dissolution characteristics of poorly soluble drugs are improved by commonly used long chain polymers like polyethylene glycol and polyvinyl pyrrolidone5. Literature reported that the PEG is used as a dissolution enhancer for poorly water soluble drugs by solvent evaporation and melting methods6' 13. The melting method was not suitable for compounds which are thermo-labile in nature. Therefore solvent evaporation method is commonly used for preparation of solid dispersions. Thus, it was thought to prepare solid dispersions using different PEG polymers.

MATERIALS AND METHODS

Drug Etoricoxib used as a standard and drug sample got from ziess Pharmaceutical industries Ltd baddi. Polyethylene glycols, sodium hydroxide, potassium dihydrogen ortho phosphate and ortho phosphoric acid, were used for all experiments. Acetonitrile, Methanol &triple distilled water was use in the examination .

Preparation of Physical Mixture

Physical mixtures of ET and PEG were weighed parfect in the ratio of 1:5, mixed thoroughly by trituration and transfer through mesh #60. The physical mixture was stored in dessicator until used in further study.

Preparation of Solid Dispersions

Solid dispersions of ET and PEG were prepared in 1:1, 1:2, 1:3, 1:4 and 1: 5 w/w ratios by solvent evaporation method. ET was solution in minimum quantity of isopropyl alcohol to get a transperent solution. Polymer PEG was diffuse as fine Particles in to the solvent was removed by drying on water bath at 60°C. The dried mass was stored in dessicator for 72 hr, pulverized and sifted through mesh # 60. Solid dispersions were stored in dessicator until used in repit study.

Efficiency Solid dispersions and physical mixture (100 mg) was take in 100 ml volumetric flasks. Solvent Methanol (30 ml) was added, Informality thorough and syndicated for 30 min. The volume was made up to mark with solvent methanol. The mobile phase was formulate to mixing methanol , acetonitrile and 10 mm potassium dihydrogen phosphate (pH 3.0 adjust with 1% v/v ort/zo-phosphoric acid) in the ratio of 35:35:30 v/v. The flow rate, run time and volume of injection loop were set at l ml/min, 8.0 min and 20 Pi, respectively. injection of the drug solutions, the column was equilibrated for at least 30 min with the mobile phase flowing through the systems. Validate at 234.0 nm and the data were acquired, stored and analyzed with the software Class CR-10 series version

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(Shimadzu). Etoricoxib content was calculated from the calibration curve. Inclusion efficiency was calculated using the formula, Inclusion efficiency = (estimated % drug content /theoretical % drug content) x 100

Solubility Study

An excess amount of ET, physical mixture and solid dispersions were added to glass test tubes containing water (5 ml). The tubes were sonicated for 45 min, vortexed for 10 min (each) and kept aside for 24 hr for equilibrium at room temperature. The solutions was filter through Whatman filter paper nd filtrates was collect in a containers. The solutions were suitably diluted and assayed for ET at 284.0 nm against blanks prepared in the same concentration of PEG in water.1

Dissolution Study

Dissolution rate of ET, physical mixture and solid dispersions were studied in phosphate buffer pH 6.8 (900 ml) employing an USP XXIII dissolution apparatus with a paddle stirrer15. ET (60 mg), physical mixture and solid dispersion equivalent to 60 mg of ET, a speed of 50 rpm and a temperature of 37 ± 0.2 °C were employed in each test. Samples of dissolution medium was taken in (5 ml) solution and filter and Etoricoxib-PEG Solid Dispersions different time intervals (5, 10, 15, 30, 45, 60, 90 and 120 min.) suitably diluted and assayed for ET at 284.0 nm. Dissolution experiments were conducted in triplicate. Khan16 suggested Dissolution Efficiency (DE) as a suitable parameter for the evaluation of in vitro dissolution data. DE is defined as the area under dissolution curve up to a certain time 't' expressed as percentage of the area of the rectangle described by 1 0 0% dissolution in the same time.

RESULTS AND DISCUSSION

Solid dispersions were prepared using PEG 600, PEG 1000, PEG 2000, PEG 3000, PEG 4000 and PEG 6000. PEG 4000 gave higher solubility and dissolution profile compared to other polymers of PEG. Solid dispersions were prepared principally by two methods: melting and solvent evaporation. Higher solubility profile was achieved in solvent evaporation method as compared to melting method. Thus, solid dispersions of ET in 1:1, 1:2, 1:3, 1:4 and 1:5 w/w ratios were prepared by solvent evaporation method by using PEG 4000. Prepared solid dispersions was found to be fine and free flowing powders (by measuring the angle of repose method).

CONCLUSION

The higher solubility and dissolution rate may possibly due to particle size reduction, improved wet ability of the hydrophobic drug particle by the presence of water soluble carrier, solubilising effect of the carrier and the possible conversion of crystalline form of drug to amorphous form. One or more of the above reasons may be responsible for the higher dissolution rate observed with the solid dispersions. Thus both solubility and dissolution rate of ET were markedly enhanced by solid dispersion with PEG.

REFERENCES

Maheshwari Rk, Padiyar A, Putliwala M ;2015, Utilization Of Mixed-Solvency Technique In Spectrophotometric Analysis Of Cefixime Trihydrate Tablets. International Journal of Pharmaceutical Research & Analysis . Vol 5 Issue 1 (1)-3.

Shashanka Venkata, Dinesh Kumar P; 2015,Enhancement of Solubility of Poorly Soluble Drugs by Using Solid Dispersion Technique International Journal of Pharma And Chemical Research I Volume 1 I Issue 1 (1):1

Reddy T A, Srinivasan S, Kavitha K, Kumar R; 2013, Review on: better solubility enhancement of poorly water soluble drugs. International Journal of Inventions in Pharmaceutical Sciences, 1(4): 267.

Bindu Madhavi. B, Kusum. B, Ramalingam. R, Ravinder Nath.A, Zulkar Nain K, Arjun. G and David. B., Preparation, characterization, and tableting of a solid dispersion of Simvastatin with super disintegrants, Journal of Pharmacy Research., 3, 2568-2570, 2010.