HYGEIA

HYGEIA
Vol.1, No.1
March-Aug, 09

Solid Dispersion of Nabumetone in Ethyl Cellulose an Approach to Enhance the Solubility and Dissolution Rate

Prasobh GR*, Mohammed Sabir AS, Sameera FA, Nooruddeen K, Jyothi B Nair, Soumya R V

Crescent College of Pharmaceutical Sciences, Payangadi, Kannur, Kerala, India

Abstract

The solubility characteristics of drugs remain the most challenging aspect in the formulation development. With the advent of combinatorial chemistry and high throughput screening the number of poorly soluble compounds has dramatically increased. The dissolution rate of drug from its dosage form is considered as an important parameter in the absorption. Dissolution is the rate-limiting step in the absorption of drugs from solid dosage form especially when the drug is poorly water soluble[1]. Poor wettability of drugs leads to the decrease in their bioavailability. Increasing the surface area of the drug particle may curb out this problem. For drugs whose GI absorption is rate limited by dissolution, reduction of particle size increases the rate of absorption and total bioavailability. This is common with drugs of poor water solubility. Solid dispersion of Nabumetone is already carried with methyl cellulose. The main perspective of this study aims at overcoming these problems by solid dispersion technology using carriers like ethyl cellulose as well as other natural, semi synthetic and synthetic carriers with a view to develop fast release formulation of Nabumetone improving its dissolution characteristics. Nabumetone is an effective NSAID, it is practically insoluble in water, where the dissolution is rate limiting. The dissolution of Nabumetone from the tablet formulation containing the solid dispersion was found to be fast and rapid when compared with marketed formulation

Keywords: Solid Dispersion, Ethyl cellulose, Nabumetone

Introduction

Bioavailability can be defined as the rate and extent at which the drug is delivered to the general circulation from dosage form and reach the site of action to produce the desired effect. New drugs with aqueous solubility less than 0.01 mg/ml are very likely to cause bioavailability problems and hence affect the therapeutic efficacy of new drugs[1]. The term solid dispersion was defined by Chiou and Riegelmann *et.al* [2] as the dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by melting, solvent or melting-solvent method the aqueous solubility of a drug is increased, the disintegration and dissolution properties can be easily altered; as a result an increase in bioavailability can be easily achieved. The term solid dispersion was defined as the dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by melting, solvent or melting-solvent method[3]. Solid dispersions are stable mixtures of finely suspended solids in a liquid with other functional ingredients including stabilizers and dispersing agents. Solid dispersions made using water-insoluble carriers loaded with hydrophilic drugs lead to delivery systems aimed at optimizing the pharmacokinetics and reducing drug side effects[1].

Materials and Methods

Materials

Nabumetone was received as a gift sample fom Micro labs laboratoies, Bangaluru. Ethyl Cellulose was obtained from Loba Chemie, Mumbai. Method: Solvent Evaporation method[3]. In this method, methanol is used as a solvent and drug: carrier (1:1) was used to prepare the solid dispersion of Nabumetone. The desired amount of carrier was dissolved in stated volume of methanol (25ml) taken in a conical flask. A magnetic stirrer can be used to get a clear polymer solution. The weighed amount of Nabumetone was added to this solution carefully with constant stirring. Stirring was continued until the drug was completely

incorporated into the solvent. The solvent was then removed by evaporation at 40°C using a thermostatically regulated water bath for about four hours. The mass obtained was further dried in a desiccators overnight, crushed, pulverized and sifted through sieve no. 80.

Physical mixture:

Drug: carrier (1:1) was used to prepare the physical mixture (1000mg of drug and 1000mg of carrier). The drug and carrier thoroughly mixed in a mortar; the mixing was done

*For Correspondence: prasobhgr@yahoo.com

in geometric dilution technique so as to ensure homogenous distribution.

Evaluation:

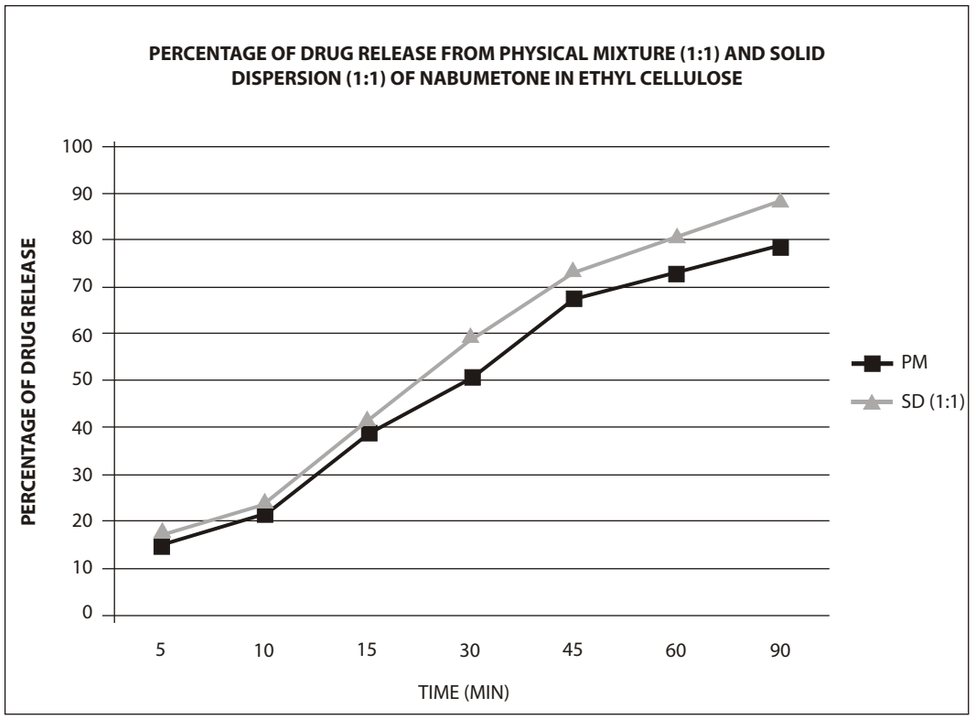
Dissolution rate studies[3]:

The dissolution studies form the most important part of the evaluation of a solid dispersion, where the dissolution of pure drug and solid dispersion is carried out. Dissolution rate studies of the prepared solid dispersion was carried out in 0.2M, pH 7.8 phosphate buffer using USP XXII dissolution rate apparatus (Electrolab).

900ml of 0.2M, pH 7.8 phosphate buffer was used as dissolution medium. Solid dispersions equivalent to 50mg of Nabumetone was taken in a hard gelatin capsule; a stainless steel wire was wound around the capsules as a sink. The basket type stirrer was adjusted to 75rpm. The temperature was maintained at 37±1°C. 5ml aliquot dissolution media was withdrawn at different intervals and volumes withdrawn were replaced with fresh quantity of dissolution media.

The samples were analyzed for Nabumetone after suitable dilution measuring absorbance at 226nm using SL164 UV-visible spectrophotometer. 0.2M, pH 7.8 phosphate buffer used as a blank[3]. The percentage of Nabumetone dissolved at various time intervals was calculated and plotted against time values were calculated from the dissolution curves.

Time (min)	Percentage of Drug release	
	PM	SD
5	5	18
10	22	24
15	39	42
30	51	60
45	68	74
60	73	81
90	79	89



Results and Discussion

Dissolution rate of Nabumetone from the solid dispersion was found to be increased when compared to the physical mixture of Nabumetone with the carrier. The reduction in aggregation and agglomeration and increased wettability from the drug particulars are responsible for observed increased in solid dispersion.

Dissolution of Nabumetone formulation in tablets was studied in USP dissolution rate apparatus (Electrolab). 900ml of 0.2M pH 7.8 phosphate buffers was used as dissolution medium. The paddle type stirrer was adjusted to 75 rpm. The temperature was maintained at 37°C±1°C. 5ml of aliquot dissolution media was withdrawn at different time intervals and volumes withdrawn were replaced with fresh quantity of dissolution media.

The samples were analyzed after suitable dilution measuring the absorbance at 226nm for Nabumetone using Elico UV visible spectrophotometer using 0.2M pH 7.8 buffer as the blank. The percentage of drug dissolved from each preparation at various time intervals was calculated and plotted against time. The marketed product of drug Nabumetone was also subjected to dissolution study and the results were compared.

The tablets prepared were studied for the drug release characteristics. The dissolution of Nabumetone from the tablet formulation containing the solid dispersion was found to be fast and rapid when compared with marketed formulation. The additives do not hinder the dissolution of Nabumetone from the solid dispersion. Hence, the solid dispersion can be mixed with various other additives required in the tablet formulation without losing their rapid dissolution properties. The formulation product showed rapid release rate when compared to pure Nabumetone marketed product.

Hence this formulation can be regarded as a fast release dosage form of Nabumetone. Studies were undertaken on the preparation and evaluation of solid dispersion of Nabumetone with a view to develop rapid release formulation of Nabumetone. In the preparation of solid dispersion the cellulose derivative Ethyl Cellulose was used. The solid dispersion for this study was prepared by the solvent evaporation method. Nabumetone solid dispersion in ethyl cellulose prepared at a drug: carrier ratio of 1:1 was formulated into tablet with usual additives and the tablets were evaluated for dissolution characteristics. The dissolution of Nabumetone from the tablet formulation based on the prepared solid dispersion was found to be rapid compared to the marketed formulation, containing the pure drug.

The additives added have not hindered the dissolution of Nabumetone from the solid dispersions. Hence the tablet formulation based on solid dispersion can be considered as a fast release dosage form of Nabumetone.

References

1. Aulton ME, Pharmaceutics: The science of dosage form design, 2nd ed.; Harcourt Publishers Limited, 2002; 15-32.
2. Tripathi KD, Essentials of Medical Pharmacology; 6th ed.; Jaypee Brothers Private Ltd, 2008; 184-188.
3. Rao SY, Chowdary KPR., Calorimetric Assay Method for Nabumetone, *Ind. J. Pharm. Sci*., 2003; 3:206-207.
4. Liebermann, Lachmann., Schwartz., Pharmaceutical Dosage Forms,Tablets: Vol.2; Marcel Dekker Inc. 1990; 378-386.
5. Ansel HC, Pharmaceutical Dosage forms and Drug Delivery Systems; 7th ed., 199-205.
6. Notari RE, Biopharmaceutics and Pharmacokinetics, 4th ed., Marcel Dekker Inc, 2005; 22-37.
7. Martin's Physical Pharmacy and Pharmaceutical Sciences, 5th ed.; Lippincott Williams and Wilkins, 2006; 301-330.
8. Remington, The Science and Practice of Pharmacy, 20th ed., Lippincott Williams and Wilkins, 2002; 995-1002.
9. Martin A, Physical Pharmacy, 4th ed., Lippincott Williams and Wilkins, 2002; 113-157.