Dissolution Profile of Ibuprofen Solid Dispersion Prepared with Cellulosic Polymers and Sugar by Fusion Method

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ABSTRACT

The purpose of this study was to prepare and characterize solid dispersions of the NSAID Ibuprofen with HPMC, HPC, icing sugar, dextrose, mannitol and lactose with the intention of improving its dissolution properties. The solid dispersions were prepared by the fusion method. Evaluation of the properties of the dispersions was performed using dissolution studies. The results obtained showed that the rate of dissolution of Ibuprofen was considerably improved when formulated in solid dispersions with HPMC and HPC. Solid dispersions with icing sugar, dextrose, mannitol and lactose showed drug retarding capability which may trigger more research in the intention of exploiting this feature to prepare sustained release dosage form.

Key words: Ibuprofen, Solid dispersion, Fusion method, Dissolution rate.

INTRODUCTION

Among all non-steroidal anti-inflammatory drugs (NSAID), Ibuprofen can be well-mentioned for its wide usage in the treatment of mild to moderate pain and fever (Moore, 2003). For any drug to exhibit its prompt pharmacologic action, its serum concentration has to reach optimum level within a short period of time (Buxton, 2006). Thus rapid ibuprofen absorption could be a prerequisite for the quick onset of its action (Rainsford, 2003). Because of its high membrane permeability characteristic, extent of ibuprofen absorption approaches up to 100% (Martinez et al., 2002). Therefore, dissolution becomes the rate limiting step for absorption and the quick release of ibuprofen in the gastrointestinal tract following oral administration is desirable (Nowa et al., 2008, Levis et al., 2003; Matthias et al., 2005). Enhancing solubility and dissolution rate of poorly water-soluble drugs like ibuprofen is one of the striking areas of research in pharmaceutical field (Dhirendra et al., 2009). To overcome the problems associated with oral absorption and bioavailability issue, various strategies have been utilized including prodrug formation (Murtha and Ando, 1994), complexation (Ghorab and Adeyeye, 2001), microcapsulation (Adeyeye et al., 1994), the use of surfactants, lipids, permeation enhancers, micronization, salt formation, cyclodextrines, nanoparticles, solid dispersions, self emulsifying drug delivery system (Shakhtshneider et al., 1996; Craig, 2002; Gao and Morozowich, 2006; Rane et al., 2007; Tang et al., 2007) etc. However ahead of all, solid dispersion is the most promising method to the scientists due to the ease of preparation, ease of optimization and reproducibility of the manufacturing method.

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(Chiou and Reigelman, 1971; Ford, 1986; Law et al., 1991; Leuner and Dressman, 2000).

Many methods like spray drying, co-precipitation, co-evaporation and freeze drying are used for solid dispersion manufacturing; however, costly equipments are required along with complicated procedures. Apart from these techniques, fusion method is a method of choice because it is environmentally friendly, cost effective, represents no stability nor toxicity problems and can be easily scaled up for commercial purpose (Bhandari et al., 2007).

The aim of this study was to prepare different solid dispersions of Ibuprofen by fusion method with two cellulosic polymers, named Hydroxy Propyl Methyl Cellulose (HPMC) & Hydroxy Propyl Cellulose (HPC) and four sugars, named icing sugar, dextrose, mannitol and lactose. The aim of the study was also to characterize them by dissolution studies to evaluate the effect of these carriers on solubility profile of Ibuprofen.

MATERIALS AND METHODS

Experimental material: Ibuprofen RS was gift sample from Orobinder, India. HPMC 6 cps and HPC were obtained from Samsung, Korea. Icing sugar, Dextrose Lactose and Mannitol were purchased from BDH.

Reagent: Di-sodium hydrogen phosphate and Sodium di-hydrogen phosphate (Merck, Germany); all other ingredients were of analytical grade.

Equipment: USP dissolution tester-Apparatus-II (VEEGO, India); UV Spectrophometer (UV mini-1204, SHIMADZU CORP., Kyoto, Japan); Digital pH meter (pH 211 Microprocessor pH Meter, HANNA Instruments, Romania); Electronic balance (AY 120, SHIMADZU CORP., Kyoto, Japan); Sieve (Endecott’s Test Sieve, Endecotts Limited, England); glass vials, water bath, dessicator etc.

Preparation of the solid dispersion

Fusion method was used for the preparation of solid dispersions of ibuprofen (Dhirendra et al., 2009; Vasconcelos et al., 2007). Required amount of drug, polymer and sugar is shown in Table 1 and 2. Ibuprofen was taken in a previously washed and cleaned moisture free glass vial and was heated in a water bath at a temperature range of 80°C-90°C until a clear solution was obtained. Polymer or Sugar was added to the clear solution and heating was continued till a homogeneous mixture was obtained. Continuous stirring of the drug and polymer was ensured using a glass rod to prevent the separation of the constituents. As homogeneous mixture achieved, the vial was taken out of the water bath. Stirring was continued and solid mass was obtained. The solid mass in the vial was kept in a dessicator. After complete removal of moisture the solidified formulation was crushed in a mortar and pestle, size reduced and sieved through a 150 micron sieve. All glass vials were labeled with care and kept in dessicator. Samples for dissolution studies were taken from the vials.

Preparation of phosphate buffer pH 7.2

7.34gm di-sodium hydrogen phosphate and 1gm sodium hydroxide were weighed out and dissolved in small amount of distilled water, volume was adjusted to 1 liter with the same solvent to prepare 1 liter phosphate buffer. The pH of the buffer solution was adjusted using a pH meter.

In vitro dissolution Study

These studies were conducted at 37±0.5°C on an USP specification dissolution rate test type II apparatus (Paddle apparatus) with six sections assembly according to the USP 30 procedure (USP 30 and NF 25, 2007). For in vitro dissolution studies, phosphate buffer pH 7.2 was used as dissolution media. Water-bath temperature was fixed & confirmed to be 37±0.5°C before starting the experiment. The medium was preheated to 37°C and then a quantity of 900 ml was added to each vessel. The apparatus was then assembled and paddle rotation was started and adjusted at 100 rpm and the system was allowed to equilibrate for 15 minutes.

After that the paddle rotation was stopped and fixed amounts of solid dispersion containing 50mg equivalent ibuprofen from each batch were placed in the vessels. The apparatus was immediately operated at 100rpm. Each vessel, vessel position and corresponding sample result
were assigned the same code. The duration of the experiment was 60 minutes for each set of sample.

10ml of sample was withdrawn from the media at pre-determined intervals of 5, 10, 15, 20, 30, 45, 60 minutes. Each and every time 10ml of dissolution sample was compensated by adding 10ml fresh phosphate buffer. The sample solutions were diluted and analyzed at 221nm for ibuprofen by UV spectrophotometer. The amount of drug present in the samples was calculated from calibration curve constructed from the standard solution of USP reference standard test drug.

**RESULT AND DISCUSSION**

Effects of cellulosic polymers (HPMC and HPC) on solid dispersion of Ibuprofen are shown in Figure 1 and 2.

### Effect of HPMC

Using HPMC as polymer gave 100% release of ibuprofen from solid dispersions within 15 minutes when drug to polymer ratio were 1:4 and 1:2. Drug to polymer ratio of 1:1, 2:1 and 4:1 gave 100% release of drug from the formulations in a time frame of 30 minutes, 45 minutes and 60 minutes respectively.

### Effect of HPC

Data showed that 100% release of ibuprofen was attained within 15 minutes when ibuprofen to HPC ratio was 1:4 which is significantly faster than compared to ibuprofen-HPC ratio of 1:2 (it took 30 minutes to release ibuprofen by 100%) and 1:1 (it took 45 minutes to release ibuprofen by 100%). 2:1 and 4:1 ibuprofen to HPC ratio solid dispersions failed to release 100% drug within 60 minutes and released 99.96% and 91.16% of drug, respectively.

Effects of sugars (icing sugar, dextrose, mannitol and lactose) on solid dispersion of Ibuprofen are shown in Figure 3 to 6.

### Effect of icing sugar

Incorporation of icing sugar in the formulation improved release of drug. But no formulation was able to release 100% ibuprofen within 60 minutes time frame. As the amount of sugar was increased % release of ibuprofen improved but the increment was insignificant.

### Effect of dextrose

Dextrose based formulations showed improved drug release from the solid dispersions. But even drug to sugar ratio of 1:4 did not give 100% release of ibuprofen within 60 minutes. Increasing polymer percentage improved drug release rate but in an insignificant way.

### Effects of Mannitol

Mannitol based solid dispersions also failed to release 100% drug within 60 minutes. When the drug to sugar ratio was 1:4, 90.84% of drug released from the solid dispersions. At drug to sugar ratio of 4:1 the release within 60 minutes was 74.53%.

### Effects of lactose

Lactose based formulations showed very poor drug release. 4:1, 2:1, 1:1, 1:2 and 4:1 drug to sugar ratio released drug by 64.64%, 67.22%, 71.94%, 75.37% and 77.51% respectively within 60 minutes.

Among HPC and HPMC based solid dispersions of ibuprofen, HPMC based solid dispersions gave faster dissolution profile in comparison to HPC based solid dispersions. At higher

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**Table 1. Different ratios of Ibuprofen with HPMC and HPC.**

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Table 2. Different ratios of Ibuprofen with icing sugar, dextrose, mannitol and lactose.

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Figure 1. Percent release of ibuprofen from solid dispersions prepared in different polymer ratios of HPMC.

Figure 2. Percent release of ibuprofen from solid dispersions prepared in different polymer ratios of HPC.
Figure 3. Percent release of ibuprofen from solid dispersions prepared in different polymer ratios of icing sugar.

Figure 4. Percent release of ibuprofen from solid dispersions prepared in different polymer ratios of dextrose.

Figure 5. Percent release of ibuprofen from solid dispersions prepared in different polymer ratios of mannitol.

Figure 6. Percent release of ibuprofen from solid dispersions prepared in different polymer ratios of lactose.
concentration of HPC and HPMC (1:4) the release rate was almost same; 100% release of drug within 15 minutes. When the polymer percentage was in between 65-80%, both HPC and HPMC showed nearly same dissolution profile.

Whereas, none of the four sugar based solid dispersion formulations was able to release drug by 100% within 60 minutes dissolution time. Drug release rate of dextrose and icing sugar was similar. Highest drug release was found with solid dispersions prepared using icing sugar (97.23% release of ibuprofen within 60 minutes when drug to sugar ratio was 1:4; at the same ratio dextrose based formulations released 96.78% of drug).

CONCLUSION

Solid dispersions are of immense importance now-a-days in the development of poorly water soluble drugs in oral solid dosage forms with enhanced dissolution rate and thus improved oral bioavailability (Huda et al., 2010; Uddin et al., 2010). In our experimental protocol we used fusion method to prepare solid dispersions of ibuprofen. Cellulosic polymers (HPMC and HPC) and four sugars (icing sugar, dextrose, mannitol and lactose) were used in the work. It is clear from the data obtained that a higher polymer concentration gave faster drug release. Again, from the discussion it can be concluded that solid dispersion systems have a potential usage as controlled release drug delivery system with careful use of different polymers along with sugars. It will be interesting to observe the outcome of such experiments.

REFERENCES


Murtha JL, Ando HY (1994). Synthesis of the cholesteryl ester prodrugs cholesteryl ibuprofen and...


