Development and formulation of itraconazole capsule by using reliable dispersion technique for solubility enhancement

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ABSTRACT

Solid dispersions enhance the bioavailability and dissolution rate of the drugs by increasing the solubility of low soluble drugs. Different methods are employed in the preparation of Solid Dispersions such as kneading technique, co-precipitation technique, hot-melt extrusion technique, fusion technique, solvent technique, etc. Solid Dispersions has used various types of carriers to enhance the solubility of low soluble drugs. In this paper to overcome the drawback of adaptive solid diffusion methods and also to recover the bioavailability of itraconazole without crystalline change, we have used the following itraconazole, poloxamer, Sporanox, citric acid and PVP to prepare the solid dispersions. Itraconazole, poloxamer, Sporanox chemical are supplied by the various chemical supplier like Hemmi Pharma, BASF Chemical, Korea-Hanssen Pharm respectively. Solid diffusion the properties of carriers on the solubility of itraconazole has experimented. Also, the dissolution and stability have been investigated and evaluated with commercial chemicals such as Sporanox which consist of 100 mg itraconazole. Hence it is crucial to show the changes in a crystalline form of the drug for a minimum of 6 months to shows the stability of the presented dispersion approach. Thus, developed formulation shows the importance of solubility without crystalline change by improving the bioavailability and increased the solubility of the drug.

INTRODUCTION

The motivation to develop more strategies in the pharmaceutical industry is because of high cost and also to increase the improvement of drug release into market in less time and fewer costs (Engers et al., 2010). Itraconazole is an antifungal representative with a wide band action against mycotic contaminations. Itraconazole is represented as ICZ. ICZ is usually weak but high hydrophobic. This chemical is marked in category 'B' drug with bad solubility and low dissolution, which causes poor bioavailability. These drawbacks made a way to form a new material for solid dispersions. In recent years, researchers have used numerous methods to improve solubility (Jung et al., 1999). ICZ represented in contradiction of blastomycosis, histoplasmosis, and onychomycosis. The manner of the act of pharmacological is shown in vitro that will azole the nitrogen interacts of cytochrome (Six et al., 2005). ICZ required better metabolism makes hydroxyl-itraconazole mainly active because of metabolite in humans. The Serum meditations of hydroxyl-itraconazole are two to three times
sophisticated than the corresponding parent drug stages (Karanth et al., 2006).

The advancement of solid diffusion is practically equipped technique to enhance the bioavailability of solid diffusion because of the limitation as mentioned. (Zhang et al., 2013). Solid diffusions have been defined as “the dispersion of one or more active ingredients in an inert excipient or matrix” where the active ingredients could exist infinitely crystalline, solubilised or amorphous states (Park et al., 2010). The remaining of the paper is organised, such as section 2 delivers the survey of existing research, section 3 analyse the materials and methods. Section 4 discusses the results, and section 5 concludes the work.

**Literature Survey**

Gudikandula et al. (2013) have presented a study to improve the dissolution profile accuracy and the drug Ezetimibe for bioavailability of water using the liquid-solid compact method. They have developed a formula using PEG-400 as a non-volatile liquid vehicle with a carter-based material such as silica gel was used for coating the materials.

Srikanth (2013) have presented an approach to maximise the dissolution range of water-soluble drug using povidone K30 and magnesium aluminium silicate have been used as enhancers. The lipids of bicalutamide have been equipped using wet lipid method using K30 and aluminium silicate at various combinations. Hence the carter range of 3:1 of magnesium aluminium silicate and povidone K30 was investigated to be high dissolution rate.

Suryavanshi et al. (2012) have presented the study to maximise the solubility of cyproheptadine into water. The solid diffusions like glycol 6000, poloxamer 188 and poloxamer 407 equipped by a different method such as Melt, Spray drying and freeze-drying. The solubility and dissolution rates of cyproheptadine were maximised using solid diffusion, and the improvement of stability is not better compared to other methods.

Dharmalingam et al. (2013) have investigated an approach for solid dispersion using PEG 6000 as carter in different ranges of Aceclofenac using melting approach. The percentage of the release of drugs of Aceclofenac from solid diffusion was 98.3% within 180min.

Rao et al. (2011) have presented Mefenamic acid soluble in water polymer, and crospovidone was prepared using the standard solvent approach. The solid diffusions of mfenamic acid are defined using dissolution range and accuracy. The sorting range of dissolution range has been observed to be the maximisation of crospovidone range.

**Development and Formulation**

In this paper to overcome the drawback of adaptive solid diffusion methods and also to recover the bioavailability of itraconazole without crystalline change, we have used the following itraconazole, poloxamer, Sporanox, citric acid and PVP to prepare the solid diffusions. The properties of carters on the solubility of itraconazole has experimented. Also, the dissolution and stability have been investigated and evaluated with commercial chemicals such as Sporanox which consist of 100 mg itraconazole.

**MATERIALS**

To develop an itraconazole based solid diffusion by improving the bioavailability is prepared using itraconazole, poloxamer, Sporanox, citric acid and PVP. In this section, we have discussed the list of materials used and the supplier from where we collected the chemicals. The Table 1 shows the list of materials and suppliers used.

**Itraconazole Capsules**

This capsule is a wide range of antifungal representative which fits in triazole band used for the treatment of fungal contaminations. Itraconazole is represented as ICZ. ICZ is usually weak but high hydrophobic. This chemical is marked in category ‘B’ drug with bad solubility and low dissolution, which causes poor bioavailability. These drawbacks made a way to form a new material for solid diffusions. Figure 1 shows the chemical structure of itraconazole capsules.

**Preparation**

For the preparation of itraconazole based solid dispersion, various materials/chemicals have been used as the exact combination are as follows;

1. At first, a Buchi 190 nozzle kind of small spray dryer has been used for the preparation of itraconazole based solid diffusions.

2. At the second stage, the Poloxamer, PVP and Citric acid are liquefied in water.

3. Third, the flow range of air was preserved to set at 10, where the weight of the aspirator filter container is defined as -25mbar.

**Solubility**

To experiment with the properties of carters on the solubility of itraconazole in solid diffusions where 30mg of solid diffusions are further mixed to 10mL of pH 1.2 gastric fluids. Then this mixture will be
Table 1: List of materials and supplier

<table>
<thead>
<tr>
<th>Materials/Chemicals</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itraconazole</td>
<td>Hanmi Pharm.</td>
</tr>
<tr>
<td>Poloxamer</td>
<td>BASF Chemical</td>
</tr>
<tr>
<td>Sporanox</td>
<td>Korea-Hanssen Pharm.</td>
</tr>
</tbody>
</table>

Table 2: Structure of itraconazole based solid diffusions

<table>
<thead>
<tr>
<th>Ingredients (g)</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itraconazole</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>PVP</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Poloxamer</td>
<td>0.25</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 1: Itraconazole Chemical Structure

Figure 2: Properties on solubility of itraconazole

shaken well for seven days in a water bath at 25°C for 10 min, and membrane filter is used for the filtering process.

Dissolution

ICZ dust of 10mg with ICZ based slid diffusions are added into the pack which is placed for testing of dissolution. This testing equipment was placed outside the water bath to maintain the consistent temperature and for sink condition. This test of dissolution has been achieved at 37 + 0.5°C using basket technique at 100rpm with 900mL pH 1.2 simulated fluids as an average of dissolution.

RESULTS AND DISCUSSION

The presented solid diffusion method is equipped with a spray drying method using water, surfactant and polymer. Hence Poloxamer and PVP have been used as surfactant and polymer correspondingly. The outcome results by providing itraconazole based solid diffusions.

To evaluate the formulation of itraconazole based solid diffusion, which minimises the number of carters with exact PVP and poloxamer range on solubility was examined. Table 2 shows the composition of itraconazole based solid diffusions. The properties of solubility of itraconazole are shown in Figure 2.

In this, we have performed dissolution test using commercial products and powder of itraconazole which is shown in Figure 3. The rate of diffusion from solid diffusion is high comparing powder. From the outcome, it is clear that the presented solid diffusion approach has obtained better dissolution.
rate comparing to commercial products.

**CONCLUSION**

This paper solves the drawback of adaptive solid diffusion methods equipped with water, poloxamer, and PVP delivers less range of carter to the drug. Hence this is processed without a crystalline form of drug and by avoiding the pollutions. The properties of carters on the solubility of itraconazole with dissolution and stability have evaluated with commercial chemicals such as Sporanox which consist of 100 mg itraconazole. Hence outcome shows the crystalline form of drug been tested for a minimum of 6 by analysing the stability and improved the bioavailability.

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**Conflict of Interest**

The authors declare that they have no conflict of interest for this study.

**REFERENCES**


