Comparative Dissolution Study of Telmisartan Tablets

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ABSTRACT SUMMARY

The wet granulation method was successfully used to manufacture amorphous telmisartan tablets (YSU) for comparison with the spray-drying method, used for Pritor™. Drug crystallinity in the tablet was characterized using differential scanning calorimetry and powder X-ray diffraction, and pharmaceutical properties of the tablets such as hardness, friability, water absorption, and in vitro dissolution in pH 1.2, 4.0, 6.8 and 7.5 were characterized. Especially with regard to the water absorption feature, the YSU tablets showed better performance by maintaining their original structures. Since both Pritor™ and YSU tablets had similar physical properties of crystallinity, hardness, friability, and > 50% f2 value in an in vitro dissolution study, the bioequivalence of YSU tablets should be analyzed in a future in vivo study. Therefore, telmisartan tablets can be produced using a more economical and easier method than that used to produce Pritor™ tablets.

INTRODUCTION

Telmisartan is a class II drug with a logP value of 7.23 and poor water solubility; however, it is freely soluble in highly alkalized solution [1].

Due to the solubility, alkalizing agents, such as sodium hydroxide (NaOH) and meglumine are necessary for manufacturing product, such as Pritor™. Since a large amount of water is used in the manufacturing processes of these products, the spray-drying technique is necessary to obtain drug particles. This spray-drying technique requires expensive facilities and involves more steps in tablet preparation than does the wet granulation method, causing it to be an uneconomical method of manufacture. Furthermore, it has been reported that sorbitol is used as a water soluble diluent in the preparation of Pritor™, occupying the most of the portion in the tablet. Since sorbitol absorbs water easily, Pritor™ is not stable once that is exposed to the air.

In this study, we prepared YSU tablets using a simple conventional wet granulation method to overcome the drawbacks of the spray-drying process and compared the tablets with the marketed product Pritor™ that was prepared using the spray-drying method.

EXPERIMENTAL METHODS

YSU tablets were prepared using the conventional wet granulation method and content of formulation is summarized in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Formulation of YSU tablet</th>
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<tbody>
<tr>
<td>Telmisartan</td>
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<tr>
<td>Content (mg)</td>
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<tr>
<td>Meglumine</td>
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<td>Content (mg)</td>
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YSU tablets were evaluated for DSC, PXRD, hardness, friability, water absorption, and in vitro dissolution. In vitro dissolution studies were performed according to the USP XXXIII paddle method using UDT-804. The 900 mL dissolution medium was used at a temperature of 37 ± 0.1°C; the stirring speeds were 75 rpm and 50 rpm for pH 7.5 phosphate buffer solution (KP IX) and pH 1.2, 4.0 and 6.8 (KP IX), respectively.

RESULTS AND DISCUSSION

The crystalline form of telmisartan has an endothermic peak at 268.44°C, the melting point of telmisartan, as determined by DSC (Fig. 1). The physical mixture of YSU had three hump like peaks around 100, 130 and 260°C which are glass transition temperature of PVP (Tg: 110-180°C), melting point of meglumine (Tm: 128-132°C) and telmisartan (Tm: 268.44°C), respectively. However, Pritor™ had an endothermic peak at 99.46°C, the melting point of sorbitol, and no endothermic peak at 268.44°C. In addition, no endothermic peak was observed in YSU.

The PXRD pattern of telmisartan (Fig. 2) had three characteristic peaks of high intensity at 6.8, 14.2, and 22.3°, similar to those reported in the literature [1]. However, there were no such peaks in YSU or Pritor™; this difference was attributed to sorbitol. We assumed that the manufacturing process of Pritor™ resulted in the formation of a solid dispersion system with the drug being molecularly dispersed as microspheres in amorphous...
forms. In addition, in YSU, telmisartan existed in amorphous microcapsule forms.

According to the results of DSC and PXRD, the crystalline form of telmisartan was transformed into amorphous forms in both of YSU and Pritor™. Therefore, the drug solubility was increased not only by the alkalizing agents, but also by the changes in crystalline form [2].

The YSU tablet was sufficiently hard (18 ± 0.5/14 ± 0.5 kPa). Generally, a marketable tablet needs to exist within the friability range of 0.8 to 1%, and YSU tablets satisfy this condition by having a friability of 0.01% (Table 2).

The water absorption test was performed at 40°C and 75% RH in open conditions. As mentioned above, sorbitol was used as filler for Pritor™ and MCC was used as filler for YSU. One week into the experiment, Pritor™ had absorbed about 40% water, and most of the tablet was dissolved and liquefied. However, YSU had only 15% water absorption and, due to the capabilities of ADS and MCC, it maintained its original structure. Based on the results of the water absorption study, YSU was more able to withstand the humidity.

The similarity factor, f2 value between 50 and 100 suggests that the two dissolution profiles are similar. The dissolution profiles of Pritor™ and YSU are shown in Fig. 3.

CONCLUSION

A simple and economical wet granulation method was successfully used to manufacture YSU tablet instead of the spray-drying method. In YSU tablets, crystalline telmisartan was transformed into an amorphous form, as in Pritor™. As a result of the water absorption study, YSU tablets showed better performance by maintaining their original structures and absorbing less water. The f2 values at pH 1.2, 4.0, 6.8 and 7.5 were 61.55, 93.19, 58.74 and 60.46, respectively, which are all between 50 and 100. Therefore, marginal differences observed in the comparison of the dissolution data between Pritor™ and YSU.

REFERENCES


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