Solid Dispersions Obtained Using Fusion Method Increases Solubility of Praziquantel

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ABSTRACT SUMMARY

The effect of fusion method in the solid dispersions containing praziquantel was studied by solubility assays. The results showed that this methodology is important for increase the solubility of insoluble drugs.

INTRODUCTION

The praziquantel (PZQ) is known worldwide as the drug of first choice for the treatment of the most common forms of schistosomiasis and cysticercosis¹. It also is classified as a Class II drug, in other words, poorly soluble in water, but high permeability². This drug is administered by humans only by the oral route. Although it is well absorbed, has variability in bioavailability³ due to its low solubility (0.4 mg mL⁻¹). Therefore, high doses are required to compensate for the low bioavailability⁴. The literature describes several methods to overcome this problem: solid dispersions, complexation and Zydis technology⁵.

The term Solid Dispersion (SD) is used to describe a solid system in which the drug is dispersed in a biologically innocuous hydrophilic carrier¹. There are several hydrophilic carrier, such as, polyethylene glycol⁶, polyvinylpyrrolidone⁷, mannitol⁸, urea⁵ and poloxylglyceride (Gelucire)⁹. The solid state forms (i.e., crystalline polymorphs, solvates, amorphous solids) of a drug substance can have a significant impact on the drug’s solubility, dissolution rate, activity and bioavailability. The mechanism by which and solubility and dissolution rate of the drug are increased includes: reduction of the particle size of the drug to a submicron size or to a molecular size in a case where solid solution is obtained⁵. The aim of SD in pharmaceutical manufacture is to alter the solid state properties of the candidate pharmaceutical, thereby increasing dispersion rate, improving the solubility coefficient as well as raising stability¹.

In this work PZQ/Gelucire(50/13), PZQ/Mannitol and PZQ/G+M solid dispersions were prepared only in ratio 1:1, because the aim was to test different carriers by fusion method and compared with the pure drug and physical mixtures to available the influence, in vitro, of these preparations of PZQ on solubility. The SD were characterized by X-ray powder diffractometry and compared as pure PZQ, Gelucire, mannitol and physical mixtures.

EXPERIMENTAL METHODS

Physical Mixtures (PM)
The drug and polymers were taken in ratio 1:1 and were mixed homogeneously in mortar and pestle.

Solid Dispersions (SD)
Solid dispersions in ration 1:1 by the fusion method were prepared by melting the substance with the highest melting point and this was added other substances and the whole was kept under vigorous stirring until cool. The final solid mass was crushed, pulverized and sieved (0.05 mm).

Solubility assays
To solubility determination a charge of 12.0 mg of PZQ (control) and 24.0 mg of PM and SD were dissolved in 10 mL of distilled water and 10 mL buffered phosphate solution 0.2 N (pH=6.8) at T=23±0.5°C. The solutions were stirred using a magnetic stirrer for a period of 24 h, and then filtered through a 0.45µm filter. The filtered solutions were then assayed using liquid chromatograph system equipped with UV/Vis
detector (wavelength 210 nm). All samples were analyzed on Luna C-18 column (250 mm x 4.6 mm i.d, 5 μm particle size) and pre column Phenomenex (4 mm x 30 mm i.d). The mobile phase—acetonitrile (40:60, v/v) under isocratic condition at a flow rate of 1.5 mL min⁻¹ (USP XXX) to determine the drug concentration. All the determinations were made in triplicate.

**X-ray powder diffraction**

The powder X-ray diffraction was performed by SIEMENS D 5000 using CuKα radiation, a voltage 40KV and a current of 20 mA.

**RESULTS AND DISCUSSION**

The solubility of PZQ (control), PZQ in the PM (control) and SD are showed in the Figure 1 (distilled water) and Figure 2 (buffered phosphate solution). These results show that SD (PZQ/G) in the two conditions there was an increase of solubility do PZQ. So, the fusion method using Gelucire as carrier is a promising approach for to increase solubility this drug.

![Figure 1. Solubility in distilled water of PZQ pure, PZQ in PM and SD.](image)

![Figure 2. Solubility in buffered phosphate of PZQ pure, PZQ in PM and SD.](image)

The diffraction spectra are showed in the Figure 3. The spectra show numerous distinct peaks indicating crystalline state to all substances. It was observed that there was a change of the crystalline structure of solid dispersions when compared to physical mixtures. This change can be one of the factors yielded the increased solubility of the SD.

![Figure 3. XRD spectra of PZQ pure, PZQ in PM and SD.](image)

**CONCLUSION**

The SD technique employing fusion method is important for increase the solubility of insoluble drugs.

**REFERENCES**


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