Digest Journal of Nanomaterials and Biostructures Vol. 7, No. 3, July - September 2012, p. 1015 - 1020

# PREPARATION AND EVALUATION OF SOLID DISPERSION OF ASIATIC ACID WITH PVPK30

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Solid dispersions of Asiatic acid with a hydrophilic polymer, namely, polyvinyl pyrrolidone (PVP) was prepared by the solvent evaporation method. The effect of Asiatic acid: PVPk30 feed ratio by weight on the aqueous solubility was investigated, the aqueous solubility of Asiatic acid reached 2043μg/ml when the weight ratio of Asiatic acid to PVPk30 was 1:5. The aqueous solubility of Asiatic acid was increased by 20-fold in Asiatic acid/ PVPk30 solid dispersions. The Asiatic acid/ PVPk30 solid dispersions system was characterized by Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC) and Scanning Electron Microscopy (SEM). The FTIR spectra of Asiatic acid/ PVPk30 solid dispersions showed that the presence of strong interactions between Asiatic acid and PVPk30. The SEM and DSC spectrum of Asiatic acid/ PVPk30 solid dispersions indicated Asiatic acid existed in amorphous state, this could be explained the fact that the aqueous solubility of Asiatic acid was increased.

(Received April 10, 2012; Accepted July 18, 2012)

*Keywords:* Asiatic acid; PVP; Solid dispersions; Solvent evaporation method

## 1. Introduction

Asiatic acid is one of the component of the titrated extract of Centella asiatica (TECA) [1-2]. Asiatic acid (figure 1) is known to be clinically effective on systemic scleroderma, abnormal scar formation, and keloids [3-5]. The Asiatic acid is practically insoluble in water (100mg/ml) [6]. The poor solubility and wettability of Asiatic acid leads to poor dissolution and hence, variations in bioavailability. Thus, increasing the aqueous solubility and dissolution of Asiatic acid is of therapeutic importance.

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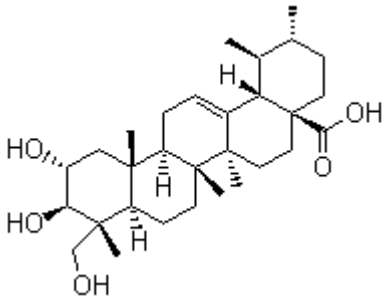


*Fig. 1. Structure of Asiatic acid.*

A variety of ways have been used over the years to enhance the water solubility and the dissolution of the drugs. The solid dispersion method is one of the effective approaches to achieve this ideal therapy particularly for drugs with poor aqueous solubility by incorporating them into a water-soluble polymer matrix [7-10]. Polyvinylpyrrolidone (PVP) which has good water solubility and can improve the wettability of the dispersed compound in many cases has been used as carrier for solid dispersions [11-13]. Due to its good solubility in a wide variety of organic solvents, it is particularly suitable for the preparation of solid dispersions by the solvent method [14]. Several attempts have been made to increase the solubility of Asiatic acid[15-16]. However, no study to date has used PVP by solid dispersions to improve the solubility of Asiatic acid in the distilled water. In this study, it is pursued to increase the solubility of Asiatic acid in the distilled water by solid dispersions with PVP. XRD, FTIR, DSC and SEM were used to characterize the properties of Asiatic acid/PVP solid dispersions systems.

## 2. Materials and methods

### 2.1 Material and chemicals

Reference Asiatic acid (purity 95%) and pharmaceutical grade asiatic acid were purchased from guangxi changzhou natural pharmaceutical co.,Ltd (Guangxi,China). Polyvinylpyrrolidonek30 (PVPk30) was purchased from Beijing Fengli Jingqiu Commerce and Trade co.,Ltd.(Beijing, china) Water was purified using a Milli-Q system (Millipore, Bedford, MA, USA). Chromatographic Grade Acetonitrile was purchased from concord technology co., Ltd (Tianjin, China). Analytical grade ethanol was purchased from concord technology co., Ltd (Tianjin, China).

### 2.2 Phase solubility studies

Solubility studies were performed according to the method described by Higuchi and Connors[17]. Excess of pure drug and inclusion complex were added to 20 ml of distilled water taken in stoppered conical flasks and shaken for 24 hrs in rotary flask shaker at room temperature. After shaking to achieve equilibrium, appropriate aliquots were withdrawn and filtered through whatman filter paper no.41. The filtrate so obtained was analysed by HPLC at 205nm.

### 2.3 Preparation of solid dispersions and physical mixture

Solid dispersions of Asiatic acid were prepared by solvent evaporation method using PVP k30 as polymers in the different weight ratios of 1:1 to 1:10 of drug: carrier polymers. Accurately weighed quantities polymer (PVPk30) were added to the solutions of Asiatic acid in ethanol. The solutions were stirred at room temperature and the solvents were allowed to evaporate. Solid dispersions thus formed, were then dried in vacuum oven for 24 hours at room temperature, pulverized and sieved. After the preparation of solid dispersions, the powdered samples were stored in a closed container away from light and humidity until use [18]. Physical mixtures were prepared by mixing the appropriate amounts of Asiatic acid and polymer (PVPK30) in mortal. The resulting mixtures were sieved, collected and stored in closed container away from light and humidity until use.

**2.4 Fourier Transform Infrared Spectroscopy (FTIR)**

Fourier Transform Infrared spectra of the samples were obtained in the range of 400 to 4000cm$^{-1}$ using a Jasco-FTIR spectrophotometer (Jasco, Essex, UK) by the KBr disc method.

**2.5 Differential Scanning Calorimetry (DSC)**

The DSC thermograms of samples (prue drug, PVP K30, physical mixture of Asiatic acid and PVP K30 and solid dispersions of Asiatic acid and PVP K30) were record on a DSC. The sample were heated in hermeticlly sealed aluminium pans over a temperature range of 25℃ to 350℃ at a constant rate of 10℃/min under nitrogen purge (20ml/min).

**2.6 Scanning Electron Microscopy (SEM)**

Samples were mounted on brass stubs using double-sided tape and vacuum-coated with a thin layer of gold.

## 3. Results and discussion

### 3.1 Solubility studies

The systems of Asiatic acid with PVPk30 showed enhancement in the solubility as compared to pure drug alone (Table 1). As the ratio of PVP k30 was decreased from 2:1 to 1:5, the solubility of Asiatic acid was increased from 776±21.53μg/ml to 2043±41.25μg/ml. On further decreasing the PVPk30 concentration to Asiatic acid: PVPk30 of 1:10, there was a slight decrease in the water solubility of Asiatic acid. This result was in accordance with the studies conducted by Najib N M [19]. The enhancement in aqueous solubility of Asiatic acid could be explained in terms of the improved wetting of Asiatic acid in the presence of PVPk30 probably due to formation of intermolecular hydrogen bonding between the carbonyl group of PVP k30 and the hydrogen atom in the OH group and the molecular interaction based solubilization of the amorphous form of the drug and interactions in the solution state between the components of amorphous molecular dispersions.

*Table1. Solubility study of Asiatic acid with PVPk30 in water*

| System | Solubility in water at 25℃ μg/ml* (Mean±S.D.) | S.E.M |
|---|---|---|
| Asiatic acid | 117.5±10.91 | 6.30 |
| 2:1 KN | 776±21.53 | 12.43 |
| 1:1KN | 1021±35.67 | 20.59 |
| 1:2KN | 1989±44.13 | 25.48 |
| 1:3KN | 2004±43.45 | 26.09 |
| 1:5KN | 2043±41.25 | 23.82 |
| 1:8KN | 1998±46.25 | 26.70 |
| 1:10KN | 1996±48.31 | 27.90 |

*Indicates mean of three readings; S.D.: standard deviation; S.E.M: Standard error of mean; KN: Kneaded product (complex); The ratio represents the molar ratio of Asiatic acid to PVPk30 which is shown in the Table 1.

### 3.2 Fourier transform infrared spectroscopy studies

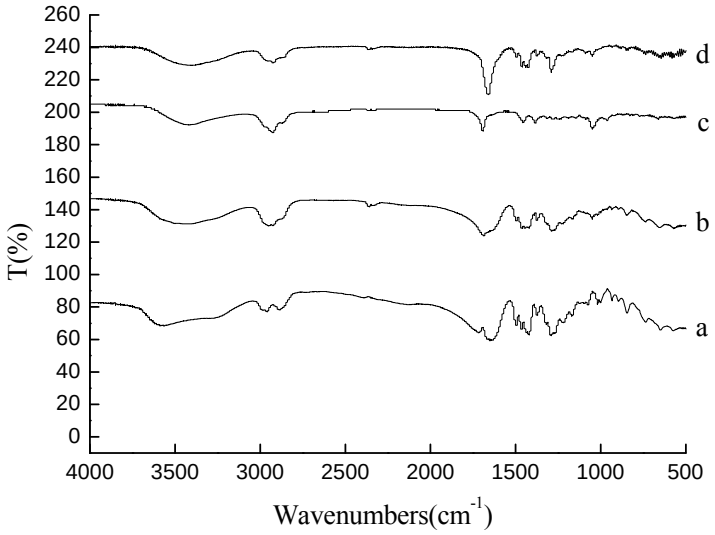


*Fig.2 FTIR spectrum of Asiatic acid- PVP systems (a) PVP k30; (b) physical mixture ; (c) Asiatic acid ; (d) solid dispersion.*

IR spectrum of Asiatic acid (c) was characterized by principal absorption peaks at 2926.14 $cm^{-1}$ (C-H aliphatic asymmetric), 2869.57$cm^{-1}$ (C-H aliphatic symmetric), 1694.12$cm^{-1}$(C=O stretching), 3404.61$cm^{-1}$(O-H), 1049.28$cm^{-1}$ (C-O). The spectrum of PVP K30 (a) showed important bands at 2960.59cm-1 (C-H stretch) and 1651.52 cm-1 (C=O). A very broad band was also visible at 3564.92 $cm^{-1}$, which was attributed to the presence of water confirming the broad endotherm detected in the DSC experiment. From the spectra (b) of physical mixture of drug with PVP k30, it was observed that the peak at 2869.57$cm^{-1}$ was not visible whereas the peak at 2926.14 $cm^{-1}$, 1694.12$cm^{-1}$, 3404.61$cm^{-1}$ and 1049.28$cm^{-1}$ was shifted to 2949.81$cm^{-1}$, 1685.88$cm^{-1}$, 3432.15$cm^{-1}$ and 1049.46$cm^{-1}$ respectively, which indicated the presence of H-bonding between the drug and the polymer. In the spectra obtained for the solid dispersions of drug with PVP k30 (d), the characteristic bands of drug gets shifted from 2926.14 cm-1 to 2923.04 cm-1 and the absorption bands of polymer shifted from 1651.52 cm-1 to 1659.66 cm-1. This data depicted the presence of H- bonding between the -OH group of drug and C=O group of the polymer which shifted the absorption spectra. From the above data obtained, the interaction was expected between Asiatic acid and PVP k30 in the solid state, it should reasonably involve the –OH group of Asiatic acid and the carbonyl group in PVP K30.

### 3.3 DSC studies

DSC technique draws attention to the interaction between the drug and excipients in its formulation. When guest molecules are included in host molecules, their melting, boiling and sublimation points shift to different temperature or disappear [20]. DSC thermograms of Asiatic acid, PVP k30, physical mixture and solid dispersion are presented in Fig.3. The crystalline Asiatic acid displayed a single strong exothermic peak at 241.37℃ and two endothermic peaks at 236.73 and 334.32℃ respectively. In the case of PVP k30, a peak at 100℃ was assignable to water evaporation. Thermograms of physical mixture and solid dispersion systems was similar to that of PVPk30, This may be attributed to the transformation of drug particles from crystalline to amorphous form.

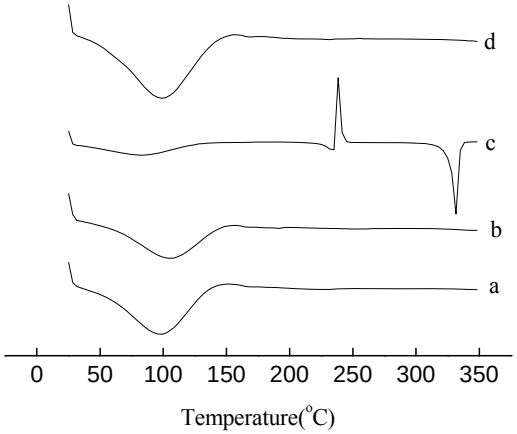


*Fig.3 DSC spectrum of Asiatic acid- PVP k30 systems (a) PVP K30; (b)Physical mixture; (c) Asiatic acid ; (d) solid dispersion.*

### 3.4 SEM studies

The photomicrographs of the samples obtained by scanning electron microscopy (SEM) are shown in the Fig. 4. The PVPk30 powders (a) presented a spherical shape, whereas Asiatic acid (c) presented rod-shape crystals. The physical mixture (b) also presented spherical shape. The Asiatic acid- PVPk30 solid complex presented amorphous particles (d), which employed DSC to demonstrate that Asiatic acid/PVPk30 solid dispersions existed in amorphous state. This result was also in agreement with our previous findings [16].

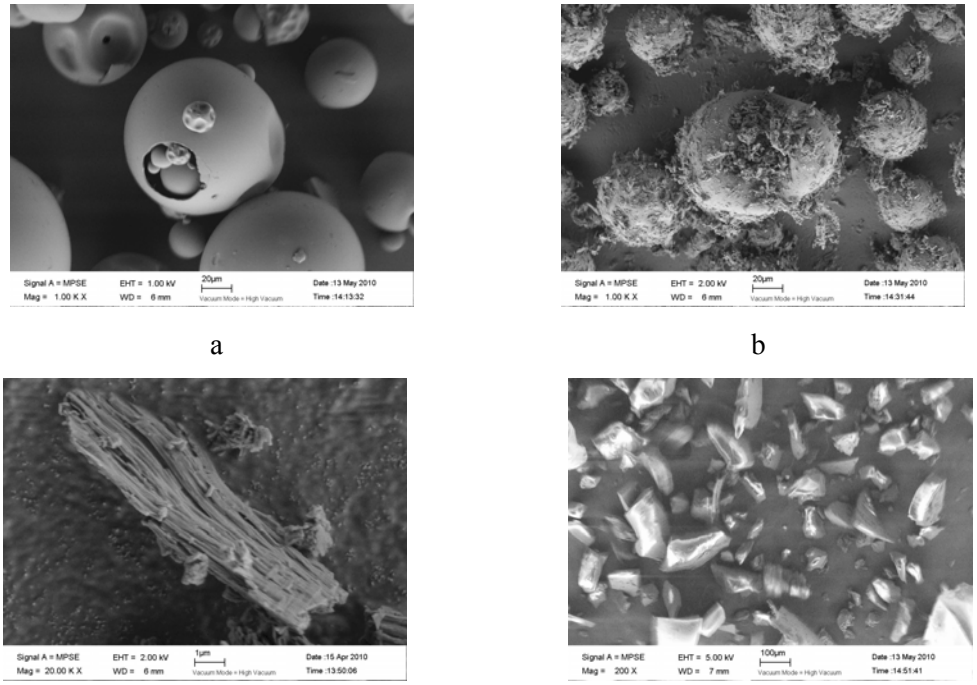


*Fig.4 SEM spectrum of Asiatic acid- PVPk30 systems (a) PVPk30; (b)physical mixture; (c) Asiatic acid; (d) solid dispersion.*

## 4. Conclusions

This study has demonstrated the possibility of improving the water solubility of Asiatic acid by its solid dispersions with PVPk30 using the solvent evaporation method. PVPk30 showed a more pronounced effect on the enhancement of aqueous solubility. The FTIR spectra of Asiatic acid/ PVPk30 solid dispersions showed that the presence of strong interactions between Asiatic acid and PVPk30. The SEM and DSC spectrum of Asiatic acid/ PVPk30 solid dispersions indicated Asiatic acid existed in amorphous state, this could be explained the fact that the aqueous solubility of Asiatic acid was increased. Therefore, the presence of PVPk30 in the solid dispersions can be a good strategy toward improving the aqueous solubility of insoluble drug in pharmaceutical formulations.

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