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Note

Characterization of curcumin–PVP solid dispersion obtained by spray drying

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Abstract

Curcumin, a naturally occurring highly lipophilic molecule has wide range of pharmacological activities. However, its limited aqueous solubility and degradation at alkaline pH restricts its bioavailability. Solid dispersions of curcumin in different ratios with PVP were prepared by spray drying. Physical characterization by SEM, IR, DSC, and XRPD studies, in comparison with corresponding physical mixtures revealed the changes in solid state during the formation of dispersion and justified the formation of high-energy amorphous phase. Dissolution studies of curcumin and its physical mixtures in 0.1N HCl showed negligible release even after 90 min. Whereas, solid dispersions showed complete dissolution within 30 min. This may aid in improving bioavailability and dose reduction of the drug.

Keywords: Curcumin; PVP; Spray drying; Solid dispersion; Dissolution enhancement

Curcumin, obtained from the rhizomes of *Curcuma longa* L., Zingiberaceae (turmeric), is the most widely used phytoconstituent in food industry. Indian and Chinese traditional systems of medicine have reported the use of turmeric for wound healing, anti-inflammatory, and other pharmacological activities (Kirtikar and Basu, 1987; Srimal, 1997). Following oral administration (upto 8 g per day) (Cheng et al., 2001), it is poorly absorbed (Ravindranath and Chandrasekhara, 1980) and only the traces of compound appear in blood. Curcumin is practically insoluble at acidic pH. At alkaline pH although soluble, it undergoes rapid hydrolytic degradation (Tonnesen and Karlsen, 1985; Wang et al., 1997).

Few attempts have been made to improve solubility of curcumin by its chemical derivatisation (Maing and Miller, 1981; Hergenhahn et al., 2003), complexation or interaction with macromolecules, e.g. gelatin (Schranz, 1986), polysaccharides and protein (Todd, 1991), and cyclodextrin (Tonnesen et al., 2002). But slow process of complexation, high molecular weight of cyclodextrins and pH of the processing medium may limit their practical utility.

In the present study we employed solid dispersion technique to improve dissolution of curcumin in acidic medium. Curcumin–PVP K30 (PVP) solid dispersions (SDs) in different ratios (1:1, 1:3, 1:5, 1:7, and 1:10) were obtained by Spray Dryer (Jay Instruments and Systems Pvt. Ltd., India). The operating parameters were: inlet temperature, 60 °C; outlet temperature, 45 °C; feed rate, 4–6 ml/min; atomization air pressure, 2 kg/cm^2 and aspiration, −280 mmWC.

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Physical mixtures (PMs) in the same ratios were also prepared. Physical characterization and dissolution studies of SDs and PMs were performed in comparison with pure drug.

Drug content of SDs was analyzed by HPLC (JASCO, Japan) (Tonnesen and Karlsen, 1983). Surface topography was studied by Scanning Electron Microscope (Stereoscan S120, UK). Thermal changes

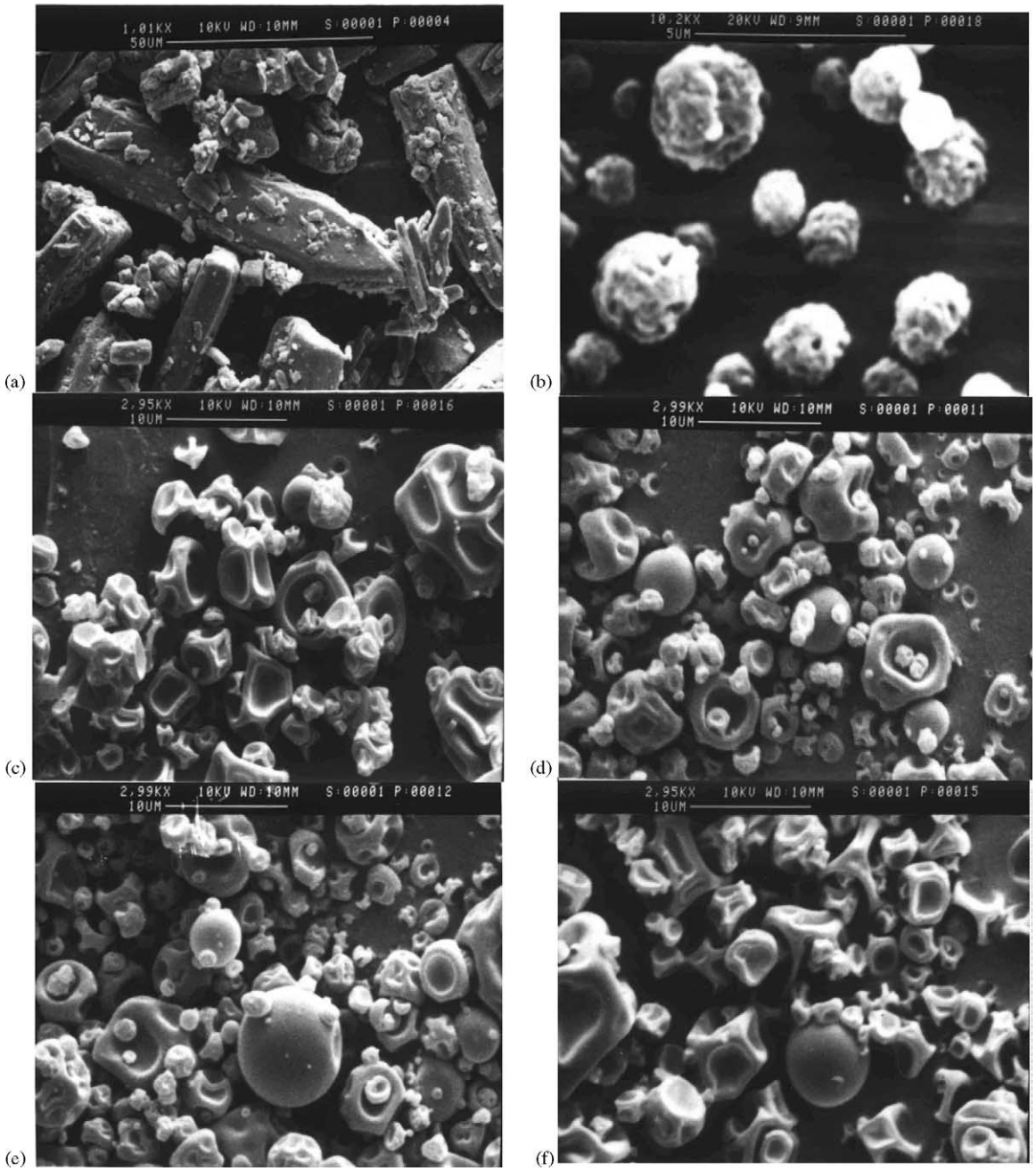

Fig. 1. SEM of pure curcumin (a), SDs of curcumin:PVP in the ratio of 1:1 (b), 1:3 (c), 1:5 (d), 1:7 (e), and 1:10 (f).

during formation of SDs were recorded by Differential Scanning Calorimeter (Mettler-Toledo DSC 821^e, Switzerland). Heating rate was 10 °C/min over a range of 30–220 °C under nitrogen purging. XRPD patterns were recorded on X-ray diffractometer (PW 1729, Philips, Netherlands) over the range 2–50° 2θ. IR spectra were scanned by FT-IR (V5300, JASCO) over wave number range of 4000–400 cm^{-1}. Dissolution studies in 0.1N HCl (pH 1.2) were performed using USP 24 type I dissolution test apparatus (Electrolab TDT-06P, India). The data was analyzed by dissolution software (PCP-Disso v3, India).

SEM of curcumin exhibited flat broken needles of different sizes, with well-developed edges (Fig. 1a). SDs showed spherical particles (Fig. 1b–f). With lower proportions of PVP (1:1–1:3) the sphere surface was rough with pinholes, whereas in higher proportions (1:5–1:10) smooth surface with concave depressions was observed.

All DSC thermograms (Fig. 2) except that of curcumin showed an endothermic peak around 90–100 °C, indicating presence of residual moisture in PVP. The endotherm at 180 °C (ΔH_f 120.8 J/g) may be attributed to melting of curcumin. In case of PMs this endotherm broadened and was shifted slightly to lower temperature (174 °C). Enthalpy of melting also decreased gradually from 57.8 to 9.03 J/g with increasing proportions of PVP (1:1–1:10). This may be due to solvent effect of molten polymer. No peak

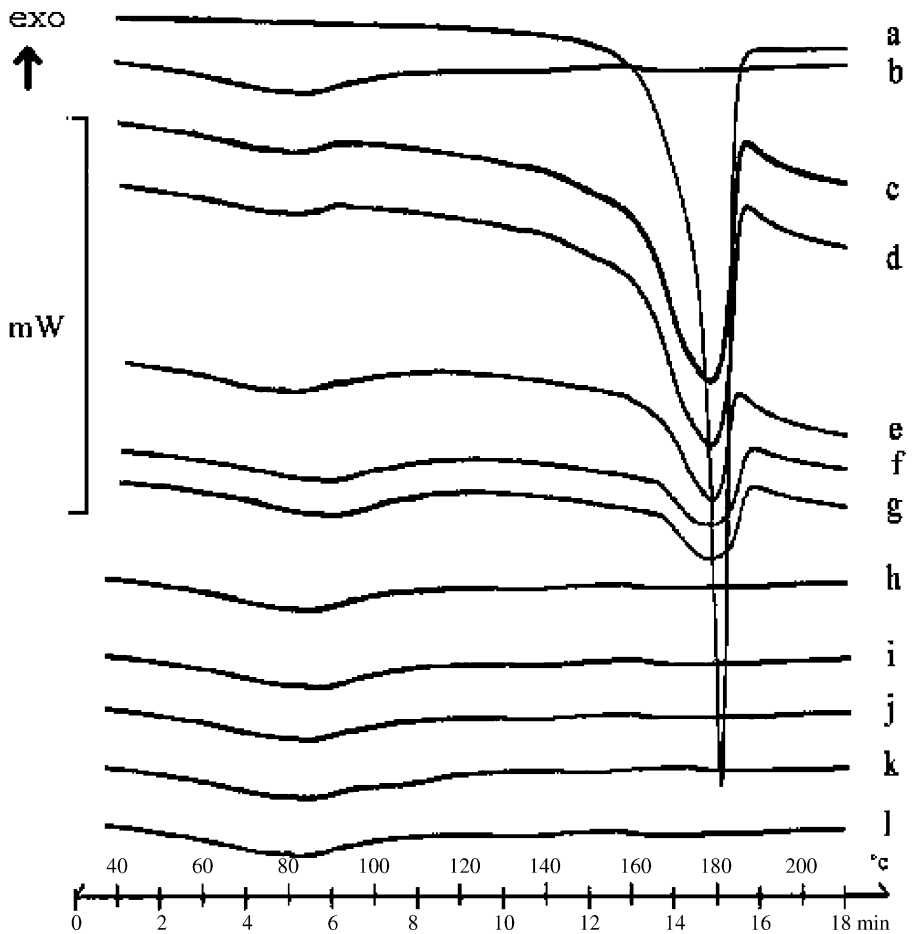

Fig. 2. DSC data for curcumin (a), PVP (b), PMs of curcumin:PVP in the ratio of 1:1 (c), 1:3 (d), 1:5 (e), 1:7 (f), 1:10 (g), and SDs in the ratio of 1:1 (h), 1:3 (i), 1:5 (j), 1:7 (k), and 1:10 (l).

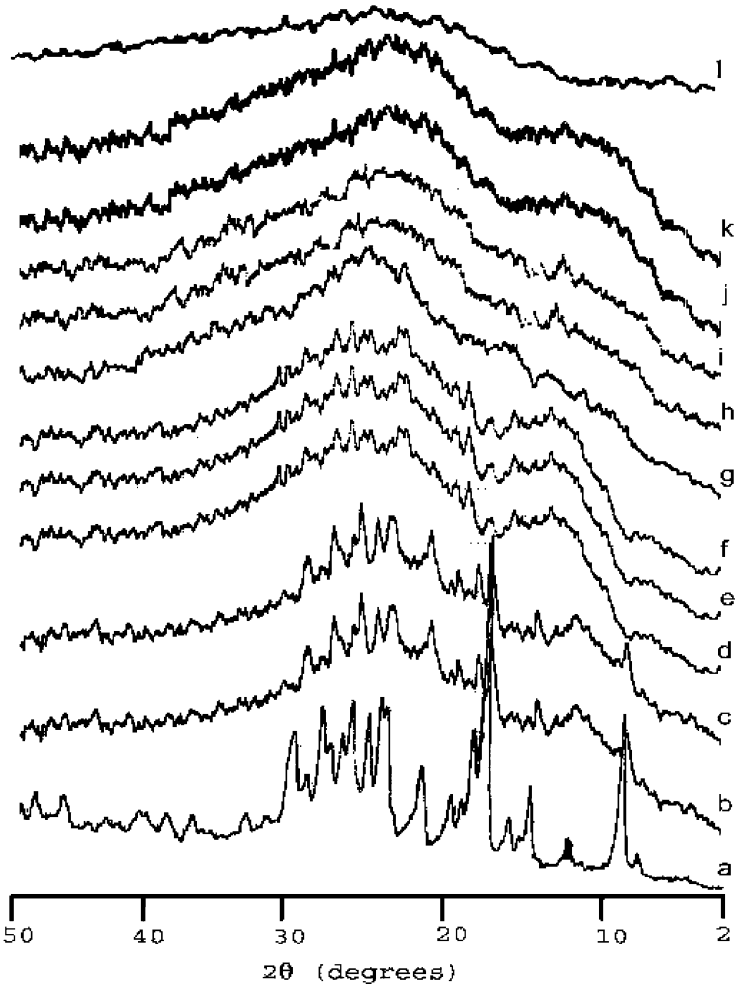

Fig. 3. XRPD data for curcumin (a), PMs of curcumin:PVP in the ratio of 1:1 (b), 1:3 (c), 1:5 (d), 1:7 (e), 1:10 (f), and SDs in the ratio of 1:1 (g), 1:3 (h), 1:5 (i), 1:7 (j), 1:10 (k), and PVP (l).

was observed in the thermograms of SDs indicating amorphous form.

XRPD (Fig. 3) of pure curcumin showed sharp peaks between 7 and 27° 2θ. In PMs, the carrier appeared as an elevated baseline and the drug produced characteristic diffraction peaks. In SDs the characteristic peaks of drug disappeared with significant elevation of the diffractogram in lower ratios (1:1 and 1:3). But at higher proportions of PVP, characteristic hump of amorphous form was observed.

FT-IR analysis (Fig. 4) revealed that stretching vibrations of C=O group (1640–1750 cm^{-1}) in curcumin appeared at lower wave number 1593 cm^{-1}. SDs showed significant broadening of peaks in the region 3600–3400 cm^{-1}. It may be attributed to intermolecular hydrogen bonding.

During dissolution study, pure curcumin and its PMs showed negligible release even after 90 min (Fig. 5). Whereas, SDs showed drastic increase in dissolution rate with increasing concentrations of PVP (Fig. 6). The medium in the dissolution flask was yellow indicating the presence of stable neutral form (H_3A) (Tonnesen and Karlsen, 1985). Increase in dissolution rate of SDs as compared with corresponding PMs was attributed to changes in the solid state during the formation of dispersion. It might be

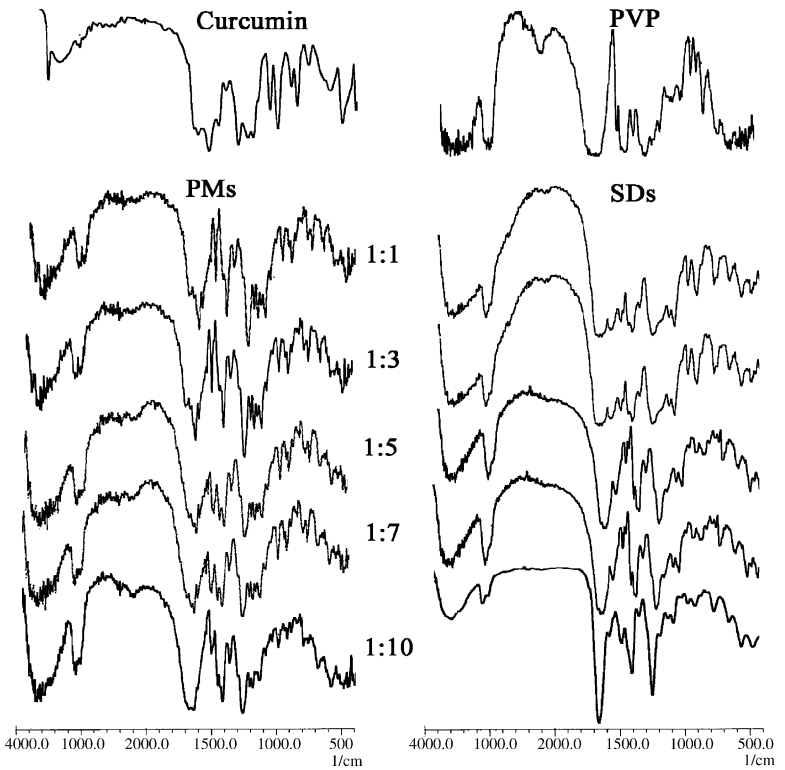

Fig. 4. FT-IR spectra of curcumin, PVP, and their PMs and SDs.

owing to the formation of high-energy amorphous phase as supported by XRPD and DSC data.

Thus, curcumin can be co-spray dried with PVP to obtain SDs containing amorphous form of curcumin. Due to anti-plasticizing activity of PVP, viscosity of the binary system increases, which thereby decreases the diffusion of drug molecules necessary to form crystal lattice (Mooter et al., 2001). PMs with PVP did not affect the physical state of drug and hence no improvement in dissolution characteristics was observed.

Curcumin, a naturally occurring molecule has a wide spectrum of pharmacological activities and medicinal properties. However, its limited aqueous solubility and degradation at alkaline pH restricts

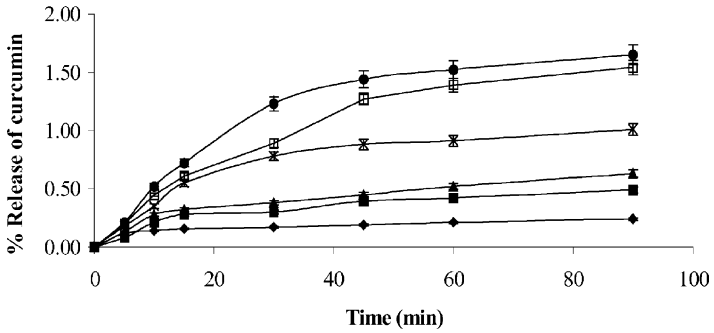

Fig. 5. Dissolution comparison of curcumin (◆) and its physical mixtures with PVP in the ratio of 1:1 (■), 1:3 (▲), 1:5 (×), 1:7 (□), and 1:10 (●).

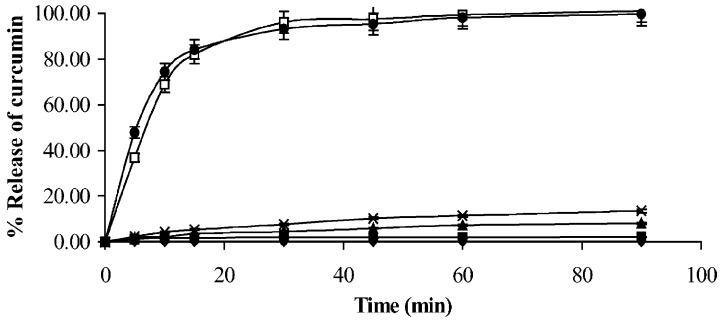

Fig. 6. Dissolution comparison of curcumin (◆) and its solid dispersions with PVP in the ratio of 1:1 (■), 1:3 (▲), 1:5 (×), 1:7 (□), and 1:10 (●).

its bioavailability. The molecule therefore presents a challenge to the formulation scientists. One of the attempts to improve its bioavailability is to maximize its absorption in the pre-intestinal region leading to reduction in dose of the drug.

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