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Ibuprofen–polyvinylpyrrolidone dispersions. Proton nuclear magnetic resonance and infrared studies

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The enhancement of drug dissolution through dispersing it in a water-soluble polymer matrix such as polyvinylpyrrolidone (PVP) is well established, (Chiou and Riegelman, 1971; Shefter and Bates, 1979; Goldberg et al., 1965; Oth and Moes, 1985). This enhancement in release however has been attributed to different mechanisms. Simonelli et al. (1969, 1976) and Corrigan et al. (1980), have suggested that the formation of a high-energy complex between sulphathiazole and PVP is responsible for the increase of the drug dissolution. Chiou and Riegelman (1971) have suggested that the molecular dispersion of the drug in the polymer matrix results in an increase in drug release. Shefter and Cheng (1980) have studied the interaction of a number of drugs with PVP and suggested that the increase in release is related to the ability of the drug to form hydrogen bonding with the pyrrolidone moiety of the polymer. Sekikawa et al. (1979) attributed the increase in release to coacervate formation with the polymer. In order to probe the nature of the interaction between the ibuprofen and PVP, the ibuprofen–PVP system was studied using proton nuclear magnetic resonance (^{1}H-NMR) and infrared (IR) spectroscopy.

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PVP–drug dispersions (1 : 1 w/w) were prepared by dissolving the required amounts of the drug and the polymer which was dried under vacuum in a minimum volume of chloroform previously dried over P_2O_5. The solvent was then removed under vacuum. The resulted mass was left under vacuum for 3 days and then removed, size-reduced and kept under nitrogen. The ^{1}H-NMR spectra were recorded on Bruker WP 80 SY spectrometer with TMS as internal standard. About 0.15 g of the solid dispersion was dissolved in $CDCl_3$ in an NMR tube under nitrogen. Solution of the dry polymer or the drug were also prepared in the same way. The IR spectra were recorded on a Pye-Unicam SP3-100 spectrometer using KBr disks.

The ^{1}H-NMR spectrum of ibuprofen is shown in Fig. 1A. All resonance peaks are assigned to their protons. The carboxylic proton appears at chemical shift $\delta = 11.34$ ppm, which is a typical shift for free carboxylic acid. Fig. 1B shows the ^{1}H-NMR spectrum of the polymer. Two complex multiplets appear in the spectrum in the range $\delta = 1$–2.5 ppm and 2.8–4.0 ppm which are attributed to the polymer chain protons ($\sim CH_2$–$CH_2 \sim$) and the pyrrolidone ring proton respectively. The spectrum of the solid dispersion is shown in Fig. 1C. The important feature in the spectrum is

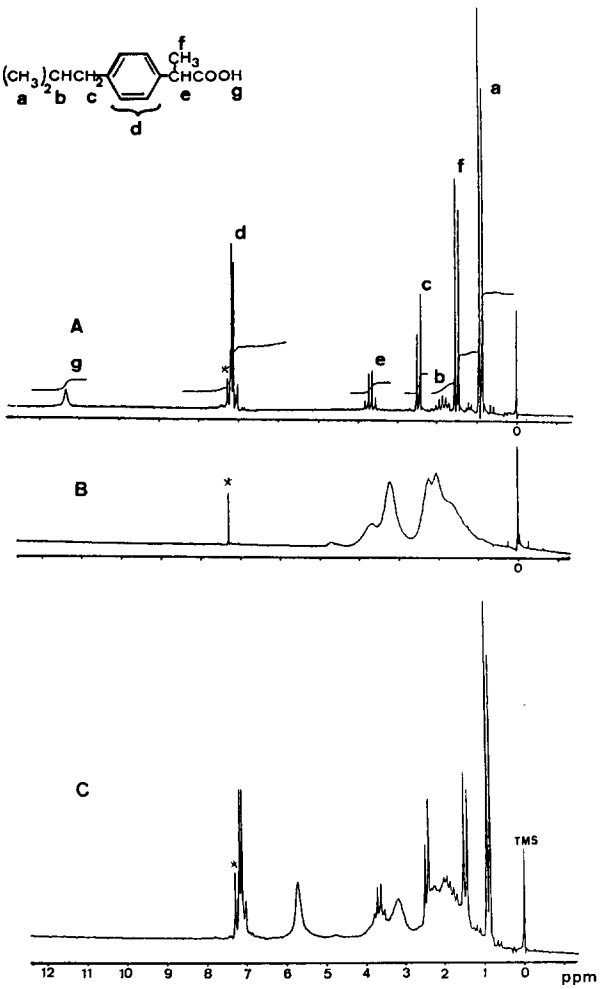
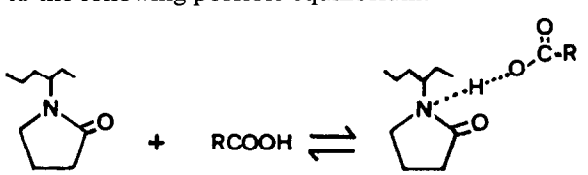


Fig. 1. Proton NMRs of A: ibuprofen; B: PVP; C: solid dispersion. *, $CDCl_3$ peak.

that the carboxylic proton peak appeared in the free acid at $\delta = 11.34$ ppm has disappeared in the dispersion and a new peak at $\delta = 5.71$ ppm is observed. These results very likely suggest that the carboxylic group of the drug has interacted with the polymer through hydrogen bonding according to the following possible equilibrium:



The broadening of the new peak at $\delta = 5.71$ ppm might also indicate that the nitrogen of pyrrolidone ring is involved in the hydrogen bonding.

The IR spectra of the drug, the polymer, the drug –PVP (1 : 1 w/w) physical mixture and the solid dispersion (1 : 1 w/w drug: polymer) are shown in Fig. 2. In the region 4000–2000 cm^{-1} the drug exhibits a broad band at about 2800–3200 cm^{-1} due to the stretching of the carboxylic O–H group which is subjected to intermolecular hydrogen bonding. The aromatic C–H stretch is interferred in the O–H range. A broad multiplet at about 2600–2800 cm^{-1} which is attributed to the aliphatic C–H stretch is observed. In the same region (4000–2000 cm^{-1}), the polymer shows a broad band centered at 3500 cm^{-1} due to the O–H stretch from the absorbed moisture. The other broad band at about 2800 cm^{-1} is attributed to the aliphatic C–H stretch. In the dispersion, the bands due to moisture O–H, carboxylic O–H and C–H stretches are well defined. It was found that the solid dispersion was very sensitive to moisture. Although the KBr pellet was prepared using dry dispersion, but the O–H stretching band due to moisture appeared in the spectrum. In the carbonyl frequency region, the drug shows a strong band at 1740 cm^{-1} due to the CO stretch in the carboxylic group. The polymer gives a broad strong band at about 1660 cm^{-1} due to

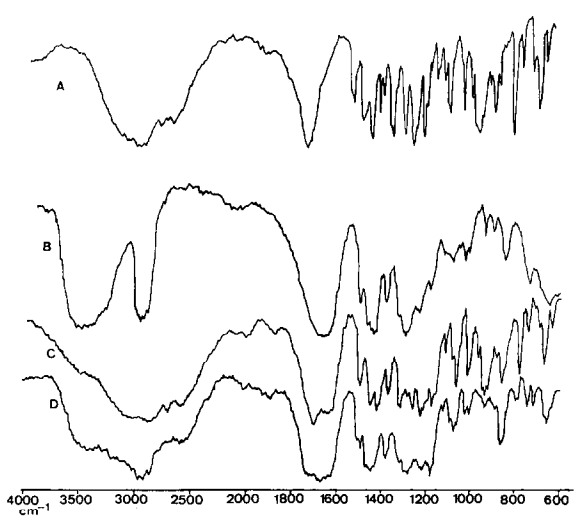


Fig. 2. IR spectra of A: ibuprofen; B: PVP; C: physical mixture; D: solid dispersion.

the CO stretch in the cyclic amide. The dispersion shows a broad band at about 1660 cm^{-1} and another broad shoulder at about 1735 cm^{-1}. In the physical mixture, Figure 2C, the CO stretch of the drug appears as narrow and separated band from the broad CO stretch of the polymer. The broadening of the CO band of the drug in the dispersion might be due to the presence of hydrogen bonding which does not exist in the physical mixture. In the low frequency region 600–1600 cm^{-1} the bands observed in the dispersion are both for the polymer and the drug, but some bands for the drug have either disappeared or are significantly reduced in intensity. For example, the strong band at 780 cm^{-1} in the pure drug has disappeared in the dispersion. The spectrum of the physical mixture shows identical spectra of both polymer and pure drug. These results might indicate that in the solid dispersion a significant change in the total symmetry of the drug molecule in the solid polymer matrix has occurred.

From the above spectroscopic studies it can be concluded that ibuprofen interacts with PVP mainly through hydrogen bonding between the carboxylic acid group and the nitrogen of the pyrrolidone ring of the polymer. This interaction exists in the solid dispersion system and in solution of inert solvent matrix.

References

Chiou, W.L. and Riegelman, S., Pharmaceutical applications of solid dispersion systems. *J. Pharm. Sci.*, 60 (1971) 1281–1303.

Corrigan, O.I., Farvar, M.A. and Higuchi, W.I., Drug membrane transport enhancement using high energy drug polyvinylpyrrolidone coprecipitates. *Int. J. Pharm.*, 5 (1980) 229–238.

Goldberg, A.H., Gibaldi, M. and Kanig, J.L., Increasing dissolution rates and gastrointestinal absorption of drugs via solid solutions and eutectic mixtures I: Theoretical considerations and discussions of the literature. *J. Pharm. Sci.*, 54 (1965) 1145–1148.

Oth, M.P. and Moes, A.J., Enhanced In vitro release of indomethacin from non-aqueous suspensions using indomethacin polyvinylpyrrolidone coprecipitates. *Int. J. Pharm.*, 24 (1985) 275–286.

Sekikawa, H., Fujiwara, J., Nagamma, T., Nakano, M. and Arita, T., Dissolution behaviours and gastrointestinal absorption of phenytoin in phenytoin–polyvinylpyrrolidone coprecipitate, *Chem. Pharm. Bull.*, 27 (1979) 1223–1230.

Shefter, E. and Bates, T.R., Dissolution behaviour of 17β-estradiol (E_2) from povidone coprecipitates. Comparison with microcrystalline and microcrystalline E_2. *Int. J. Pharm.*, 2 (1979) 113–123.

Shefter, E. and Cheng, K.C., Drug–polyvinylpyrrolidone dispersions. A differential scanning calorimetric study. *Int. J. Pharm.*, 6 (1980) 179–182.

Simonelli, A.P., Mehta, S.C. and Higuchi, W.I., Dissolution rates of high energy polyvinylpyrrolidone-sulphathiazole coprecipitates. *J. Pharm. Sci.*, 58 (1969) 538–549.

Simonelli, A.P., Mehta, S.C. and Higuchi, W.I., Dissolution rates of high energy sulphathiazole povidone coprecipitates II: Characteristics of form of drug controlling its dissolution rate via solubility studies. *J. Pharm. Sci.*, 65 (1976) 355–361.