

Note

Preparation and Evaluation of Solvent Deposited Systems of Felodipine

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Solvent deposited (SD) systems of felodipine were prepared with biologically inactive carriers like microcrystalline cellulose (MCC), lactose, potato starch (PS), and aerosil in different ratios. These systems were evaluated for drug content uniformity, drug carrier interactions, and drug release profiles. Drug-carrier interactions were evaluated by using Differential Scanning Calorimetry (DSC), IR, and TLC. The results of drug-carrier interaction studies indicated that there was no interaction between the drug and the carrier. Release of drug from SD system was markedly increased than that of the corresponding physical mixture. The increase in the order of dissolution rate of felodipine from SD systems was: MCC > aerosil > PS > lactose.

Introduction

Felodipine (FP) is a vasoselective calcium antagonist of the dihydropyridine type, specially developed for the treatment of hypertension¹. It is practically insoluble in water². Solvent deposition technique is widely used to improve dissolution rate by depositing the poorly soluble drug on the surface of an inert carrier. Improvement of dissolution rate by this technique is due to an increase in surface area and wettability of the drug^{3,4}. In the present study, solvent deposited systems of FP have been prepared with inert carriers such as microcrystalline cellulose, lactose, potato starch, and aerosil and evaluated for

the possible drug-carrier interactions, drug content uniformity, and drug release profiles.

Materials and Methods

Materials

Felodipine BP was obtained from sample from Cipla Ltd, Bangalore. Microcrystalline cellulose, lactose, potato starch and aerosil were purchased from BDH, Ltd. All other chemicals used were of analytical reagent grade.

Methods

The SD systems of FP with MCC, lactose, PS and aerosil were prepared in the drug to carrier ratios of 1: 1, 1: 2, 1: 3, 1: 4 and 1: 9 by solvent evaporation method. Physical mixtures having the same weight ratios were prepared by thoroughly mixing the appropriate amounts of FP and carrier in a mortar using geometric dilution technique.

The FP content of all SD systems was estimated using spectrophotometer (Systronics model 118, Ahmedabad) at 241.5 nm. Drug-carrier interactions were studied by DSC (Seiko, Japan, DSC 220C), IR (Perkin-Elmer 725, KBr pellet method), and TLC (40:60 ratio of ethyl acetate : cyclohexane as eluting mixture). Dissolution rates of FP from pure drug, physical mixtures, and different SD systems were determined using USP XXIII, dissolution test apparatus 2 (Paddle method) in 900 ml of pH 1.2 medium containing 0.2 per cent w/v SLS at 37°C and a rotation speed of 50 rpm. The samples were withdrawn at different durations and assayed spectrophotometrically at 241.5nm. Dissolution efficiency (DE) of the dissolution data was calculated by the method proposed by Khan⁵.

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Table I—DE₆₀ values of the prepared physical mixtures and solvent deposited systems

Ratio of FP:car rier	Per cent of carrier	Physical mixtures				Solvent deposited systems			
		Lactose	PS	Aerosil	MCC	Lactose	PS	Aerosil	MCC
1:0	0	9.34	9.34	9.34	9.34	9.34	9.34	9.34	9.34
1:1	50	10.65	13.85	18.1	18.4	30.89	40.36	41.65	42.9
1:2	66.7	13.42	16.79	20.84	23.26	47.31	48.07	56.32	59.75
1:3	75.0	19.32	19.25	23.53	27.46	71.85	72.25	63.25	66.46
1:4	80.0	21.66	20.91	28.48	30.25	76.78	75.25	78.1	79.08
1:5	90.0	24.91	25.16	30.16	32.25	79.91	81.66	81.16	82.08

Results and Discussion

The FP contents of all the SD systems were found to be within ± 5 per cent range of the expected percentage of drug content values and the low values of standard deviation values ensured the drug content uniformity of the SD systems. Consistency in mean per cent drug content of batches prepared was also ensured by low coefficient of variation values.

The DSC thermograms of FP and SD systems (1:1 weight ratio) prepared with various carriers are shown in Figure 1. DSC curve of pure drug exhibited a sharp peaks at 147.2°C, which is corresponding to its melting point. The SD systems prepared with MCC, aerosil, PS, and lactose have shown the sharp endothermic peak at 144.2, 140.8, 145.9, and 148.4°C, respectively, almost coinciding with the melting point of FP. These results showed no evidence of interaction between the drug and the used carriers. This is further confirmed by the results of IR studies and TLC studies.

The results of DE₆₀ values are given in Table 1. The DE₆₀ values of all the physical mixtures prepared with the carriers increased in dissolution rate of FP when compared to pure drug and increased with increase in weight fraction of the carrier. This may be due to solubilizing effect of the carriers used in the study of the drug. The DE₆₀ values of all the physical mixtures containing lactose are found to be highest than that of the physical mixtures containing other carriers. This is because of complete solubility of lactose in aqueous fluids, which facili-

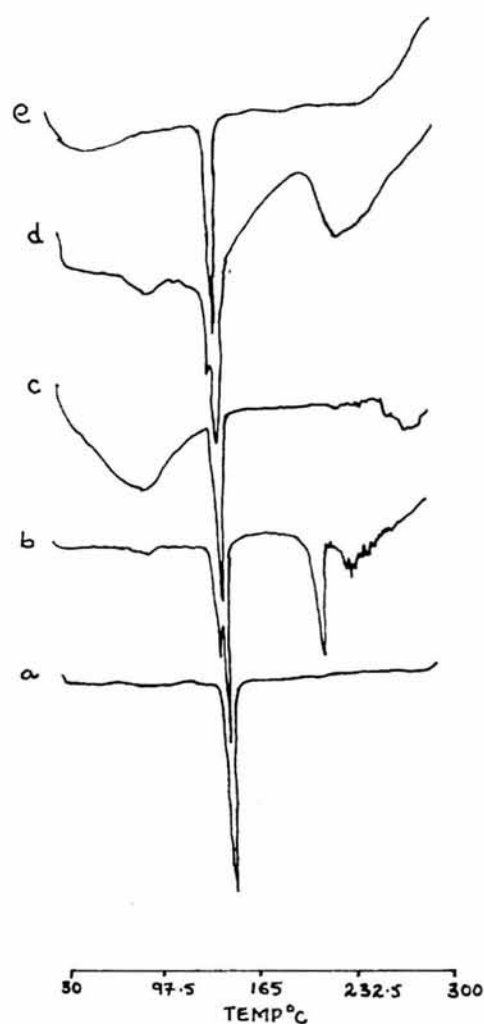


Figure 1—DSC thermograms of felodipine and prepared SD systems: (a) Pure drug, (b) P:Lactose (1:1), (c) FP:PS (1:1), (d) FP:Aerosil (1:1), and (e) FP:MCC (1:1)

tates the dissolution rate. The SD systems of all the carriers showed marked improvement in dissolution profile compared to corresponding physical mixtures. It is observed that the rate of dissolution is dependent on drug to carrier ratio. In the solvent deposited systems the coating of the drug on the surface of the carrier resulted in an increase in effective surface area of the drug particles leading to faster dissolution^{3,4}. The values of DE_{60} indicated that the 1:3 drug to carrier ratio is considered optimum for enhancing the dissolution rate of FP.

Among the four carriers used in the study, SD systems prepared with MCC gave the highest dissolution rate of FP and the order of effectiveness of carriers in increasing the dissolution rate is: MCC>aerosil>PS>lactose. The faster dissolution rate by MCC-FP SD system can be attributed to swelling ability of the carrier which further increases the effective surface area of the surface deposited drug⁶. Though physical mixtures containing lactose gave faster dissolution rate when compared to that of physical mixtures containing other carrier the SD systems containing lactose was found to be least in an increasing order of dissolution rate. This may be

due to less surface area available for the deposition of the drug on the surface of the lactose compared with MCC.

Hence, from the studies carried out, it can be concluded that the improvement in the dissolution profile of the FP is achieved through solvent deposited systems. The SD system utilizing MCC, as carrier in 1:3 ratio, shows promising results in improving the dissolution rate of FP.

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