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Dissolution Characteristics of Biphenyl Dimethyl Dicarboxylate from Solid Dispersions with Copolyvidone

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Solid dispersions were used to increase the dissolution rate of biphenyl dimethyl dicarboxylate (DDB) in water, with the ultimate goal of optimizing its bioavailability when incoporated into pharmaceuticals.

Carriers used were Kollidon 30, Kollidon VA 64, 2-hydroxypropyl-ß-cyclodextrin (HPCD), sodium salicylate or sodium benzoate. DDB solid dispersions were prepared at drug to carrier proportions ranging from 1 : 5 to 1 : 20 (w/w) by solvent evaporation method. DDB tablets (7.5 mg) were prepared by compressing the powder mixture composed of solid dispersions, lactose, corn starch, crospovidone and magnesium stearate using a single-punch press. DDB capsules (7.5 mg) were prepared by filling the mixture into empty hard gelatin capsules (size #1). Dissolution studies of DDB from powdered solid dispersions, tablets and capsules were performed in 900 ml of water at 100 rpm and 37°C by the paddle method. The dissolved amount was assayed by HPLC and expressed as the mean (%) of three determinations.

Dissolution rates after 10 min were found to be 23.5, 22.8, 82.5 and 11.8% for DDB solid dispersions in sodium benzoate, sodium salicylate, and Kollidon VA 64 (drug : carrier = 1:10) and drug alone, respectively. For the solid dispersions in Kollidon VA 64, dissolution rates of DDB after 30 min at the drug : carrier proportions of 1 : 10 and 1 : 20 were 80.5 and 95.0%, respectively. For the DDB tablets prepared using solid dispersions (1 : 20), the initial dissolution rate was dependent on carrier material, and was fast in the rank order of Kollidon 30 << Kollidon VA 64 < HPCD. For the HPCD solid dispersion tablets, dissolution rate reached 97.4% after 15 min, but thereafter slowly decreased to 80.7% after 2 hr due to the precipitation of DDB. However, in the case of Kollidon VA 64 solid dispersion tablets, dissolution increased linearly and reached 93.4% after 2 hr. Contrarily, the reference tablets made of physical mixture of the same composition resulted in low dissolution (16.1% after 2 hr). Reducing the volume of test medium from 900 to 300 ml markedly decreased the dissolution rate from the tablets containing 1 : 20 HPCD solid dispersions and 1 : 10 Kollidon VA 64 solid dispersion (11.0 and 27.5% after 2 hr, respectively). But for 1 : 20 Kollidon VA 64 solid dispersion tablets, there was no significant change in DDB dissolution up to 1 hr with different volume of test medium. On the other hand, preparation of the Kollidon VA 64 solid dispersion (1 : 20) in capsule form markedly delayed the dissolution unexepectedly (31.2% after 2 hr).

From these findings, it was concluded that formulations of DDB in Kollidon VA 64 solid dispersions remarkably improved the dissolution rate of the drug, both in powdered form and in tablets, and the most efficient release occurred at a proportion of drug to Kollidon VA 64 of 1:20.