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Chemical stability of acetylsalicylic acid in tablets prepared with different particle size fractions of a commercial brand of dicalcium phosphate dihydrate

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Abstract

The proportion of acetylsalicylic acid degraded to salicylic acid in tablets prepared with different particle size fractions of a single brand of dicalcium phosphate dihydrate (DCPD), and then stored for 6 months at 35° C and 82.9% relative humidity, was linearly correlated ($r = -0.9937$) with the mean particle size of the excipient. Mean particle size may therefore be a useful predictor of the chemical stability of easily hydrolysed active principles in tablets prepared with a given brand of DCPD.

Keywords: Dicalcium phosphate dihydrate; Acetylsalicylic acid; Tablets; Mean particle size; Chemical stability

Landín et al. (1994) have recently described the effects of switching brands of dicalcium phosphate dihydrate (DCPD) on the chemical stability of DCPD tablets containing acetylsalicylic acid (ASA). The significant between-brand variation of ASA stability was attributed to differences in the micromeritic properties and in the particle sizes of the excipients, an assertion supported by a close correlation between the amount of ASA degraded and the excipient's specific surface, which itself is a reflection of the intraparticle porosity and mean particle size of the DCPD. On the basis of the above observations, we evaluated mean particle size – which is more easily determined than specific surface – as a parameter for prediction of the chemical stability of the active principle in tablets prepared using a single brand of DCPD. In this situation, the intraparticle porosity of the excipient should scarcely vary with particle size, which will therefore be proportional to specific surface. Four particle size fractions of DCPD (Kyowa, Japan) were prepared using an Alpine Multiplex Zig-Zag A 100 MZR particle sizer fitted with meshes of 5, 15, 25, 35 and 45 μm; fractions retained between successive meshes were assigned a mean particle size corresponding to the mean aperture of those meshes (10, 20, 30

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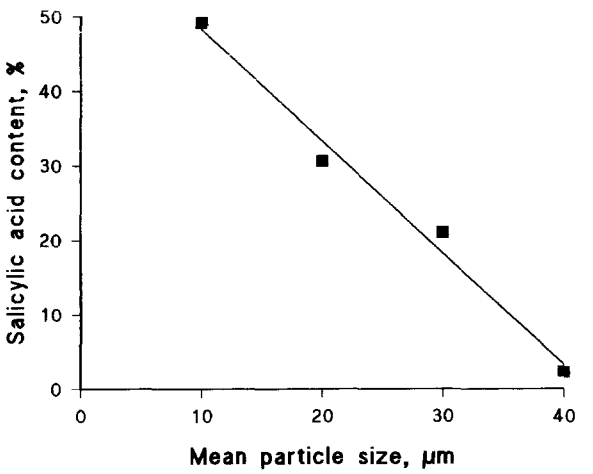

Fig. 1. Correlation of salicylic acid content (as a percentage of initial ASA content) of tablets stored for 6 months at 35° C and 82.9% relative humidity, with the mean particle size of the dicalcium phosphate dihydrate used to prepare them ($r = -0.9937$).

and 40 μm). Each of the four DCPD fractions was mixed (Turbula T2C, 30 rpm for 5 min) with acetylsalicylic acid in the ratio 9:1 (w/w), and used to make 350 mg tablets by direct compression in a Korsch EKO excentric press equipped with pressure transducers and 9 mm diameter flat-faced punches applying compression forces of up to 10.7 kN. The tablets were stored at 35° C and relative humidity 82.9% (maintained using an aqueous solution of KCl (Lausier et al., 1977; Rabach and Mielck, 1981; Vila-Jato et al., 1985). After 6 months, the salicylic acid (SA) content of the tablets was determined by the spectrophotometric method reported by Gore et al. (1968). Fig. 1 shows the linear correlation ($r = -0.9937$) between the SA content (as a percentage of initial ASA content) of the tablets after 6 months and the mean particle size of the DCPD excipient. This correlation was not discernible in the study of Landín et al. (1994) because of the widely differing intraparticle porosities of the various brands of DCPD they employed. In this work, the observed correlation confirms the predicted correlation between the mean particle size and specific surface of DCPDs of similar intraparticle porosities, and indicates that when, as is usual, different batches of a single brand of DCPD are employed for tablet preparation, mean particle size is a good predictor of the stability of easily hydrolysed active principles such as acetylsalicylic acid.

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