THE EFFECT OF PARTICLE SIZE, COMPRESSION PRESSURE AND CRYSTAL FORM ON THE DISSOLUTION RATE OF DISINTEGRATED TABLETS OF PHENYLBUTAZONE

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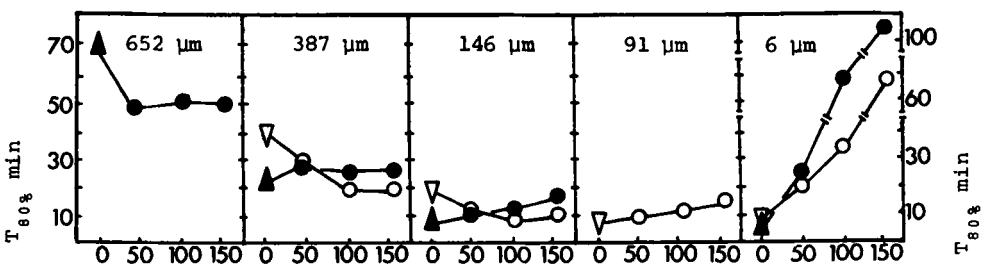
Carless and Sheak (1976) showed that during compression of powders of different particle size there was a critical size where the phenomena of bonding and cleavage of particles within the tablet balanced each other. Kitamori and Makino (1979) showed that comparative measurement of dissolution of disintegrated tablets with that of granules can be used to elucidate whether particle bonding or cleavage occurs within the tablet during compression.

The dissolution rates of tablets of phenylbutazone crystal Form A (m.pt.105^{0}C) and Form B (m.pt.103^{0}C) of various particle sizes were studied before and after compression. In order to eliminate variations due to differing tablet disintegration rates, the tablets were disintegrated in 3ml. of dissolution medium prior to the dissolution test. Size fractions of both crystal forms were prepared by grinding compacts of the crystals and separating different particle fractions. Tablets containing drug (10% or 60%), Avicel PH 102/Lactose EF crystals (80% or 30%) and STA-Rx 1500 (10%) were prepared by direct compression in a single punch machine (unlubricated die) at three compression levels - 48.1, 102.9 and 157.7 MN m^{-2}. No change in crystal form occurred on compression or grinding. The dissolution rates of the disintegrated tablets were measured by a modification of the U.S.P. paddle method.

The graphs show the change in the dissolution rate of disintegrated tablets of phenylbutazone with original particle size of the drug, compression pressure and crystal form using 60% drug, 30% Avicel, 10% STA-Rx.



Tablets: ○ Form A ● Form B

Uncompressed powder: ▽ Form A ▲ Form B

When the excipient was Avicel, the critical particle size of Form A was approximately 90 µm but this value was increased when Avicel was replaced by lactose. The critical particle size for Form B was approximately 600 µm when either lactose or Avicel was used. The results in this work show that the relationship between compression pressure and dissolution rate of these formulations was dependent upon the crystal form of the drug, the drug content and the nature of the excipient.

Carless, J.E. & Sheak, A. (1976) J.Pharm.Pharmac. 28, 17-22.

Kitamori, N. & Makino, T. (1979) J.Pharm.Pharmac. 31, 501-504, 505-507.

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