effects of baclofen did not seem GABA mediated which is in support of several reports questioning the specificity of baclofen as a GABA agonist (for ref. see Mao & Costa 1978).

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LETTER TO THE EDITOR

A cautionary note on the use of ordered powder mixtures in pharmaceutical dosage forms

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Ordered powder mixtures (Hersey 1975) have become an acceptable method of preparing a highly homogenous powder mixture (Yip & Hersey 1976, 1977; Crooks & Ho 1976; Rees 1975; Yeung & Hersey 1979). Such mixtures appear to have wide application in the preparation of dosage forms containing relatively small doses of highly potent drugs. In this situation, the drug particles would be finely divided and highly cohesive, allowing them to adhere to a more coarse carrier particle.

We wish to caution those pharmaceutical formulators, who having prepared a highly homogenous ordered powder mixture, wish to use this mixture in the development of a dosage form. The addition of a third component may, if it preferentially adheres to the carrier particles, displace the original drug particles from their adhesion sites. The situation is exactly anomalous to that occurring at adsorption sites or in protein-binding problems, where a third component is preferentially absorbed.

An alternative explanation is that the third component may interfere with the adhesion of the drug onto the carrier particles, effectively stripping them from that substrate. In this case the third component itself is not bound to the carrier articles and does not replace the drug particles it has stripped from the carrier.

An ordered powder mixture containing 0·2% salicylic acid of particle size 3·4 μm onto carrier particles of 425–620 μm sucrose particles was produced after 5 h in the Revolvo-cube mixer.

The cohesiveness of the salicylic acid is demonstrated by the fact that the mix was sifted at 106 μm for 120 min, during which period only 0·45% of the salicylic acid passed through the screen.

Subsequently 4% of the magnesium stearate was added to the cube mixer and mixed for a further 5 h. Again the mix was sifted at 106 μm for 120 min. Under these conditions, 7·09% of the salicylic acid passed through the screen. This figure was further increased to 10·89% after a further 3 h sifting, indicating that the magnesium stearate is seriously affecting the adhesion of salicylic acid particles to the sucrose carrier. Since magnesium stearate itself is also being removed from the mix through the screen to the extent of 26·8% after 5 h sifting, it would appear that the magnesium stearate is stripping the salicylic acid particles from the sucrose carrier rather than replacing it as a preferential adhesive.

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