THE EFFECT OF FORMULATION AND MANUFACTURING PROCESSES ON THE CHARACTERISTICS OF DIRECT COMPRESSION TABLETS

by

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Contents

Page Number

ABSTRACT

Two model direct compression tablet formulations have been examined by means of factorially designed experiments. The formulations were based on a direct compression vehicle (Avicel) containing 25%w/w of either paracetamol or aspirin. A disintegrant (maize starch), a lubricant (magnesium stearate) and a glidant (Aerosil) were also included. The influence of changes in mixing time and compaction pressure were used to represent changes in the manufacturing process. Alterations to the starch concentration and the drug particle size were chosen to reflect formulation changes. The coefficient of weight variation, porosity, tensile fracture stress, friability, the time for 50% liquid saturation of the tablets, and 90% of drug dissolution were used to monitor the effects of the changes.

The lubricant distribution, as determined by the mixing time, was found to control the tablet strength to a greater extent than the other factors. With the paracetamol formulations, where the particle size was similar to the bulk of the excipients, the particle size also had an appreciable effect on the tablet strength. The compaction pressure was the least effective factor.

A novel method of measuring liquid uptake into tablets based on gamma scintigraphy showed that the penetration into aspirin tablets was largely determined by the tablet strength. The uptake into paracetamol tablets was controlled by the drug particle size and the mixing time.

Increasing the starch concentration increased the dissolution rate, but this has been postulated to be due to an interaction of the starch with the drug surface rather than any disintegrant action. The drug particle size had a significant effect on the dissolution of the paracetamol tablets where the larger size dissolved more rapidly. There was little effect on the aspirin tablets where the drug size was greater than that of the other excipients.

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List of Figures and Plates

List of Tables