

## RELATIONSHIP BETWEEN GRANULE STRUCTURE, PROCESS OF MANUFACTURE AND TABLETING PROPERTIES

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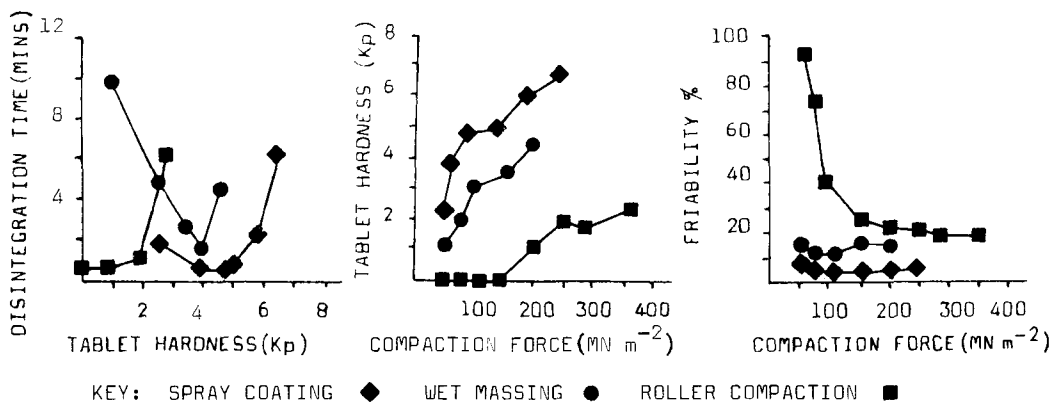
Granules can be made by precompression, wet massing and spray coating techniques. We have found that each method gives a product with a different granule structure e.g.

Granulation Method	State of Binder within Granule	Possible Bonding Mechanisms within Granule	Concentrations of Binder at Granule Surface	Tabletting Properties
Precompression	Whole or disintegrated particles	Asperity melting, Brittle fracture, plastic deformation	Low	Poor
Wet massing	Internal film matrix	Binder cohesion, salt bridging	Moderate	Good
Spray coating	Surface shell	Binder cohesion, salt bridging	High	Very good

We have studied the properties of paracetamol granules prepared by the three manufacturing methods and have compared the structure of the granules with their tableting properties.

The granules contained between 1% and 7% of a hydrolysed gelatin (Protein S) as the binder. They were manufactured using a roller compactor plus a mill, a planetary mixer plus a mill and dryer and a large scale industrial spray dryer. The following properties were examined: size, shape, flow, bulk density, drug content, moisture content and dissolution rate. The granule structure was elucidated by drug solvent extraction and scanning electron microscopy.

The granules were mixed with 1% magnesium stearate, 10% Avicel and 1% Explotab and were compressed into tablets over a range of pressures, using an instrumented F3 tableting machine. Measurements of weight uniformity, drug content uniformity,



compact volume, pore size distribution, friability, crushing strength, work of failure, diametral deformation, moisture content, disintegration time and dissolution rate showed that the tablet quality varied (see graphs for tablets with 3% Binder) and was governed by the position of the granule binder (see table).