THE INFLUENCE OF BINDING AGENT ON THE DRUG RELEASE RATE OF GRANULES AND TABLETS

X.L. Wang, S.B. Tan and D. Ganderton, Department of Pharmacy, King's College London, Manresa Road, London SW3 6LX

The merits of both single and multi-unit sustained release systems may be realized by a tablet which rapidly breaks up after ingestion into a number of coherent granules with controlled release properties. This report assesses the drug release rate before and after compression of granules made using either an acrylic polymer solution (Eudragit RS100 dissolved in acetone/isopropyl alcohol) or an aqueous dispersion (Eudragit NE40D) as the binding agent.

250 g of calcium phosphate and 50 g of theophylline were massed for 10 min with 130 ml of the binding agent. The wet mass was screened, dried and classified. The granules of 1.4-2.0 mm size were compressed at pressures of 64 or 255 MPa using 10% of Ac-Di-Sol as a disintegrant. The time for 50% drug release (T_{50}) from the granules and tablets and the granule size distribution before and after compression were measured as before (Wang et al 1990). Free films of Eudragit RS100 and NE40D were made by casting the solution or dispersion on a mercury surface and their mechanical properties were assessed using a tensile strength tester.

From Table 1, granules made with polymer solution (OG) released drug much more slowly than granules made with the aqueous dispersion (AG). The electron microscope revealed that the surface of OG was covered by a continuous polymer film, whereas the surface of AG showed discontinuity with much drug and filler exposed. We can infer that the organic solution spreads more of the polymer over the substrate than the aqueous dispersion. After compression, granules were regenerated by the disintegration of the tablets. Granule size measurement (Fig.1) revealed a significant size reduction of OG whereas most AG maintained their integrity. This is explained by the brittle and tough properties of RS100 and NE40D films respectively (Table 2). Under pressure, fracture of the brittle OG resulted in an increased dissolution rate. T_{50} changed from 80 min (granules) to 38 and 30 min (tablets of 64 and 255 MPa). The consolidation of the tough AG, however, depressed the drug release rate. T_{50} increased from 8 min (granules) to 18 and 20 min (tablets of 64 and 255 MPa). These effects were complete at lower pressure (64 MPa). Further compression caused little change in the dissolution rate of the systems.

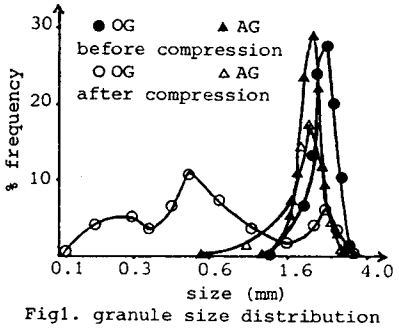

Fig1. granule size distribution

Table 1. T_{50} of OG and AG

System	Pressure (MPa)	T_{50} (min)
OG	0	80
	64	38
	255	30
AG	0	8
	64	18
	255	20

Table 2. Properties of Eudragit Films

Film	Elongation ratio at break	Ultimate tensile strength (MN/m^2)	Young's modulus (MN/m^2)
RS100	1.64	1.12	22.0
NE40D	4.76	5.07	15.5

Wang, X.L., Tan,S.B., Ganderton, D. (1990) Proceedings of The 9th Pharmaceutical Technology Conference, Veldhoven, Holland. 3:4-16.