A comparison of the pore structure of tablets prepared from force screened and comminuted granules

Granules of lactose B.P. (Whey Products Ltd., Crewe) were prepared by the wet massing and screening technique described by Ganderton & Selkirk (1970).

Further batches of granules were prepared in an analogous manner except that the wet mass was subdivided by passing it through a comminutor, (Fitzmill Model D, Manesty Machines, Liverpool). Subdivision was achieved by knife edge blades rotating at 1350 rev min^{-1} above a number three mesh.

The two sets of granules thus differed only in the manner of subdivision of the wet mass.

A more uniform shape was found with the comminuted granules. They were approximately spherical and had comparatively smooth surfaces. The granules prepared by forced screening however were 'flaky', and much more irregular in shape. The more regular shape of the comminuted granules resulted in their packing more closely, (Table 1). The lower tap porosities found with the comminuted granules were not due to shape factors alone. The intragranular porosity of the comminuted granules was found by Dr. B. M. Hunter (personal communication) to be less than that of the equivalent force screened granules. The force screening process, by virtue of its rubbing action appeared to open up the wet mass, to produce porous granules, whereas comminution did not.

These initial differences in porosity quickly disappeared on compression. Tablets made from granules, produced by both methods, had similar porosities at compression pressures greater than 30 MN m^{-2}, (Table 2).

Further investigations by permeametry, and mercury porosimetry, revealed that tablets, made from granules prepared by both methods had an identical pore structure.

The effect of porosity on the permeability of lactose tablets made from − 8 + 16 mesh granules prepared by force screening and comminution showed that for both kinds of granules at 34·0, 28·0 and 19·0% porosity the 13% massing water concen-

Table 1. *A comparison of the tap porosities of lactose granules prepared by force screening and comminution.*

Granule size (mesh fraction)	Force screened		Comminuted	
	Massing water concentration		Massing water concentration	
	13%	25%	13%	25%
−8 + 16	71·3	62·8	67·3	60·9
−60 + 85	69·7	62·1	66·3	60·0

Table 2. *The effect of compression pressure on the porosity of lactose tablets made from force screened and comminuted granules.*

Compression pressure MN m^{-2}	Porosity	
	Force screened	Comminuted
50	23·9	23·8
75	19·6	19·6
100	16·6	16·7

tration values for permeability were (m^2): $2{\cdot}2 \times 10^{-13}$, $8{\cdot}5 \times 10^{-14}$ and $1{\cdot}0 \times 10^{14}$ respectively; for 25% massing water concentration the respective values were: $1{\cdot}0 \times 10^{-12}$, $1{\cdot}0 \times 10^{-13}$ and $1{\cdot}0 \times 10^{-14}$. The cumulative % oversize distribution of pores in lactose tablets of 26·5% porosity made from $-8+16$ mesh granules prepared by forced screening and comminution was 1·8, 1·7, 63·0, 63·0; 98·4, 98·6 respectively for each kind of granule for pore diameters of 20·00, 0·20, 0·02 μm.

Thus although the method of subdivision of a wet mass, to produce granules would appear to affect the packing characteristics of the granules, it does not effect tablet pore structure.

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REFERENCE

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The influence of synthetic "Substance P" on tremor caused by LSD in mice

Stern and Hadzović (1973) have recently shown that synthetic "Substance P" (SSP) (Tregear, Niall & Potts, 1971) passes through the blood-brain barrier, reduces aggressivity in mice and antagonizes abstinence symptoms in morphinized mice. Earlier it had been shown that impure "Substance P" (SP) potentiated the effect of lysergic acid diethylamide (LSD) upon the isolated ileum of a guinea-pig (Krivoy, 1957) and that it also acted centrally by enhancing electric potentials of dorsal roots of the spinal cord in the cat (Krivoy & Kroeger, 1963). I have examined the effect of SSP on static tremor caused by LSD (Ahmed & Taylor, 1959) and excitement caused by amphetamine. Tremor was induced not only by LSD, but also by oxotremorine and harmine, both causing the static type of tremor, and also by guanethidine, which causes intentional tremor (Stern, Milenković & Cetinić, 1970).

Mice of either sex, (Pasteur institute, Novi Sad) 20 ± 2 g were used. SSP was dissolved in 0·1 N acetic acid and administered at a dose of 0·5 mg kg^{-1} (i.m.) Controls were given the solvent. I also examined the effect of SSP on the concentration of acetylcholine in mouse brain (MacIntosh & Perry, 1950). This was considered necessary because the quantity of acetylcholine in the cns is of great importance for understanding the origins of tremor.

All the substances examined were administered 15 min after SSP, SSP doses smaller than 500 μg kg^{-1} i.m. could not cure either static or intentional tremor in mice. SSP does not cause tremor alone, even in doses between 100 and 2000 μg (i.m.)

The intensity of both static and intentional tremors was observed independently by 2 persons, neither of whom knew which group of animals was experimental and which was control.

Table 1 shows that SSP potentiates oxotremorine and LSD tremor. Tremor caused by oxotremorine can be abolished by atropine whilst tremor caused by LSD is unmodified.

As shown previously for SP (Zetler, 1956), SSP abolishes harmine induced tremor. The same effect was observed in animals that were excited by amphetamine. SSP has no effect on the intentional tremor caused by guanethidine.

SSP raises acetylcholine in mouse brain significantly 60 min after SSP has been administered (control value (μg g^{-1} fresh tissue): $2{\cdot}35 \pm 0{\cdot}2$ n = 5; animals injected