We thank Dr. E. L. May, National Institutes of Health, Bethesda, Maryland, for the pharmacological results.

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February 12, 1974

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The effect of massing time on drug concentration in different sized granules

Lachman & Sylwestrowicz (1964) have shown that granules of different size fractions may have different drug concentrations. Their results were obtained using a poorly soluble drug, massed for a given length of time. The results presented below show the effect of varying the massing time on the distribution of borax within a batch of granules.

Borax, of mean particle size 3·6 μm (Analar grade, BDH Chemicals, Poole), and lactose B.P., of mean particle size 2·5 μm (Hopkins and Williams, Essex), were mixed together in a Z blade mixer (Morton Machines Ltd., Wishaw, Scotland), for 2 min. The overall concentration of borax in the mixer was 2·0%. The contents of the mix were emptied onto a tile and subdivided into ten portions. Each of these portions was assayed for its borax content by titration with 0·01N HCl and the results are in Table 1.

Similar proportions of lactose and borax were placed in a Z blade mixer, mixed for 2 min and then massed with water. The mass was forced through a twelve mesh

Table 1. *The distribution of borax in lactose in a Z blade mixer after 2 min mixing (each portion is the mean of twenty analyses).*

Portion number	Mean % borax	Standard deviation
1	2·04	0·079
2	2·01	0·071
3	1·95	0·072
4	1·98	0·071
5	2·00	0·076
6	1·98	0·079
7	2·00	0·077
8	2·02	0·077
9	2·01	0·079
10	1·99	0·071

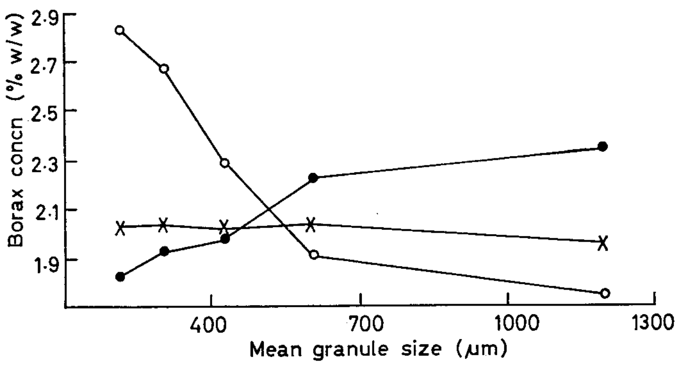

FIG. 1. The effect of massing time on the distribution of 2% borax in lactose. Massing time: ○ 0·5 min; × 2·0 min; ● 10·0 min.

screen, and resultant granules were dried to a constant weight at 70° and rescreened. The massing water concentration was 16% v/w of the dry powder. Three batches of granules were prepared with massing times of 0·5, 2 and 10 min respectively. The granules were sieved and the resulting sieve fractions assayed for their borax content by the method described above. The results (Fig. 1) are the average values of twenty assays.

The results obtained for the lactose/borax dry mix (Table 1) show that the borax is evenly dispersed throughout the lactose.

A wide variation of borax distribution was found throughout the various size fractions with the shortest massing time. The borax was concentrated in the smaller granules. This was probably due to the water having insufficient time to distribute itself evenly throughout the mass. In the regions of high water concentration, the lactose, by virtue of its greater solubility, will tend to go into solution first and subsequently form crystalline bridges between the primary particles, on drying. Thus excess borax will be left as a fine powder.

Massing for 2 min produced an even distribution of borax throughout the granules. The longest massing time (10 min) resulted in the larger granules containing a high concentration of borax with a subsequent loss of borax in the finer granules. This result is similar to that obtained by Lachman & Sylwestrowicz (1964), indicating that the rationale proposed by these authors may also be applied to the above system. Since lactose has a greater solubility in water than borax, addition of water to the mix, followed by massing for 10 min, will result in much more lactose going into solution than borax, which in turn may result in the borax becoming encapsulated by the lactose. Any mechanical disruption of a granule, formed in this way, e.g. by the "rubbing" action of the granulator, will remove lactose particles rather than borax particles from the granules. This will lead to a higher concentration of borax in the larger granules and excess lactose in the fine particles.

Therefore it would appear, for the above system, that massing time has a significant effect on the distribution of borax throughout a batch of granules.

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November 30, 1973

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