LETTERS TO THE EDITOR

The intraparticulate structure of calcium phosphate

It is well known that calcium phosphate B.P.C. requires more granulating fluid to produce a coherent mass during wet granulation than other tablet diluents such as lactose or starch.

Recently Ganderton & Hunter (1971) reported that calcium phosphate showed uncontrollable ball growth during pan granulation at moisture contents in excess of 191% v/v and rapid ball growth above 174% v/v. Furthermore in granulation by massing and screening, suitable granules were prepared only over a narrow range of lower moisture contents (117–157% v/v). Assuming the particle density of calcium phosphate to be approximately 3·0 g cm^{-3} and allowing for the 10% w/v dextrose monohydrate dissolved in the granulating fluid (Ganderton & Hunter, 1971) these ranges of liquid content are equivalent to moisture contents of between 40 and 60% w/w dry basis. This agrees well with work in these laboratories which has shown that calcium phosphate shows no measurable change in tensile strength at liquid concentrations up to 45–50% by weight of the dry mass (Eaves & Jones, 1971, 1972a, b).

This has been attributed to the porous nature of the individual particles of calcium phosphate, a phenomenon inferred from the gross difference in the surface areas obtained firstly by Nitrogen adsorption and secondly by calculation from the size distribution data assuming the particles to be non-porous spheres of equivalent volume (Eaves & Jones, 1972a).

It is assumed that the intraparticulate porosity is such that at low moisture contents the liquid becomes located within the particles thus preventing the formation of pendular liquid bridges between adjacent particles. Once the intraparticle voids are saturated, the moisture can exert an influence at the surface of the particle by increasing tensile strength or, as in Ganderton and Hunter's work, by assisting aggregation and densification.

This is in agreement with the suggestion of Glushkov, Karnaushenko & Platanov (1969) that the internal friction of materials composed of porous particles increased only after saturation of the internal structure.

Fig. 1A and B are scanning electron micrographs obtained from a 'Stereoscan' Mark

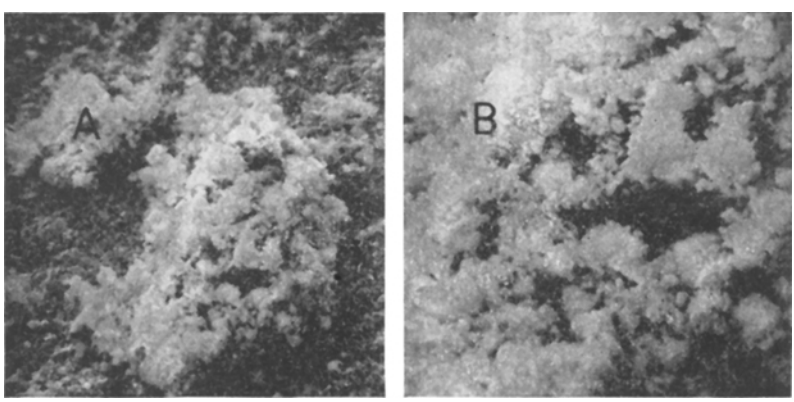

FIG. 1A. Scanning electron micrograph of calcium phosphate. Magnification 270×. B. Detail of intraparticulate structure, Magnification 750×.

2A (Cambridge Scientific Instruments Ltd.) of a representative particle of calcium phosphate at high magnifications (270 × 750 ×). The specimen was prepared by painting the surface of an Aluminium stub with Dag 915 (Acheson Colloids Co., Plymouth, Devon) and allowing a small amount of sample to fall from a 150 μm sieve onto the surface. Excess material was removed after 5 min by a blast of air. The sample was coated in a vacuum on two occasions to allow penetration into the intraparticular voids.

The high intraparticle porosity can clearly be seen both on the single particle (Fig. 1A) and on an area of the same particle at higher magnification (Fig. 1B).

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Microphotographic study of lyophilization of oil-in-water emulsions

A technique for drying oil-in-water emulsions by lyophilization and the use of several materials that act as supports in the process were described by Lladser, Medrano & Arancibia (1968). The dried emulsion could be reconstituted by adding water. The reconstituted emulsion showed a slow increase in the mean diameter of the dispersed globules, along with an increase in creaming rate.

A microscopic study now complements the previous information. The emulsions examined had the following composition: Liquid Petrolatum (U.S.P. XVIII), 10%; polysorbate 80 (HLB 15), 1·25%; sorbitan mono-oleate (HLB 4·3) 0·75%; support 13·3%; distilled water to make 100 g. D-(−)-Mannitol, urea and glycine were used as supports.

Lyophilization was effected using an Edwards model L 5 "Speedivac" Centrifugal Freezedryer using 2–3 drops of emulsion.

To observe the process, two procedures were followed:

(a) The emulsions were placed on a microslide and processed in the freezedryer for 2 h. Once lyophilization was completed, a coverglass was placed over the product and the edges sealed with melted beeswax.