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.

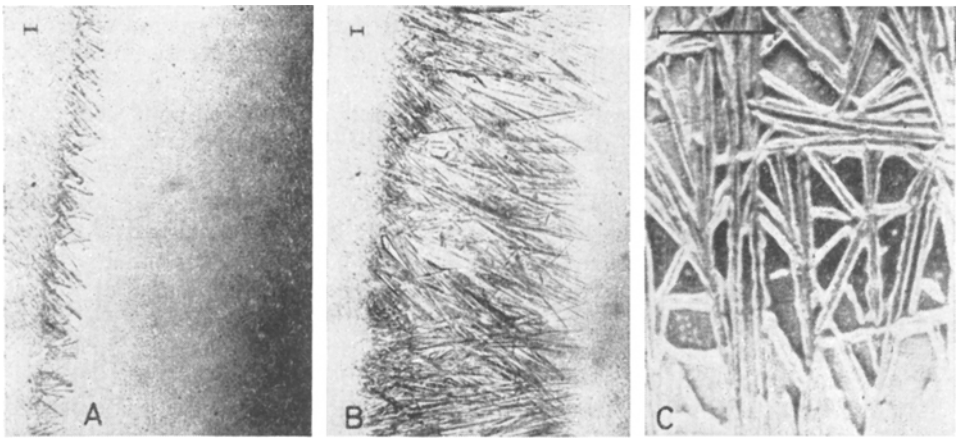

FIG. 1. Microphotophotographs of the lyophilization process using urea as support. A and B. Stage in the crystallization process of the emulsion support. C. Recently lyophilized emulsion. Oil globules can be seen in the space between the crystals. (——— = 50 μm.)

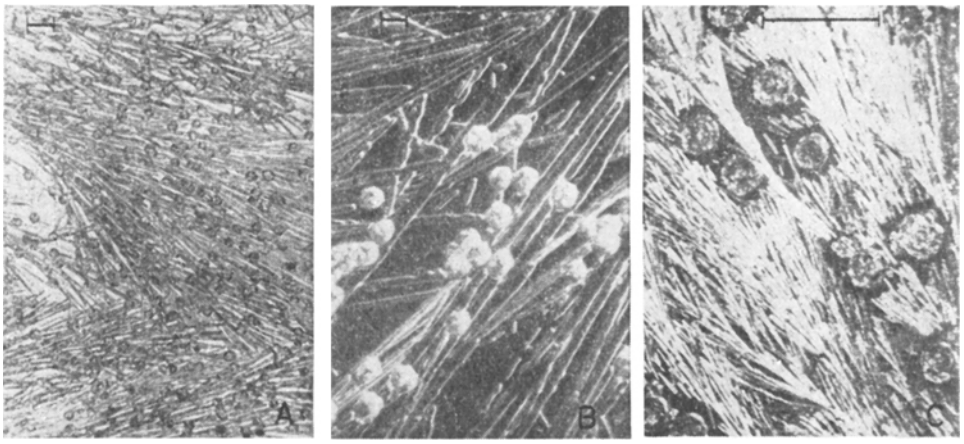

FIG. 2. Microphotograph of an emulsion with urea as support, 24 h after being lyophilized. Crystals of urea and floccules of Oil globules can be seen A, under transmitted light, B and C, under phase contrast. (——— = 50 μm.)

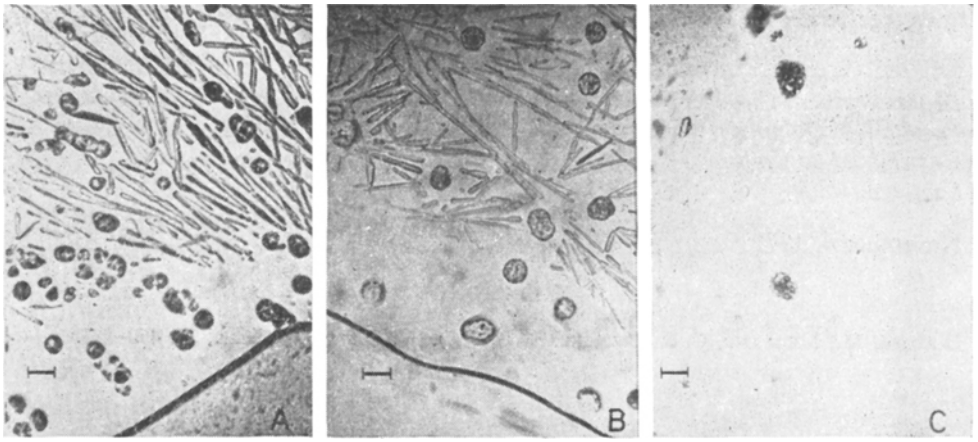

FIG. 3. Reconstitution of a lyophilized emulsion. A and B show the dissolution of the support and the disintegration of the floccules as the aqueous front advances. C. Reconstituted emulsion. Two large floccules that have not disintegrated are seen. (——— = 50 μm.)

(b) In this procedure a special chamber which allowed direct microscopic observation of the process, was employed. Here the process of freeze-drying was not controlled but was rapid, the emulsions being dry in 10–15 min. The temperature was below −32°.

When the first procedure was followed, transmitted light photographs were taken of the resultant products. With the second method, microphotographs were taken during the process.

When aqueous solutions of 13·3% of sorbitol, glucose, sucrose or lactose were lyophilized and examined microscopically (procedure b), non-crystallized; a viscous mass that bubbled and did not retain its structure as it lost water and finally shrank leaving empty spaces, was observed. Under the same conditions, mannitol, glycine and urea, showed crystals which remained unchanged during the process and in the final product. Only those substances that crystallize in a definite way during the process can be employed as emulsion supports.

Microscopically, in emulsions containing mannitol, glycine or urea as supports, these supports crystallized rapidly and the oil globules arranged themselves according to the shape of the crystals of the support used. With mannitol, which crystallizes as radial needle aggregates, the globules were distributed around the periphery of the aggregates, at the tips of the needles. In systems with glycine, which crystallizes as feathers, the globules were distributed in the spaces between the crystals. Needles of urea were observed distributed in disorderly form, leaving empty spaces that were occupied by the oil globules. Fig. 1 shows two stages of a sequence of the lyophilization process of an emulsion having urea as support (photographs A and B). The oil globules are located in the interstices left by the crystals once the process is finished (photograph C).

The system, however, suffers some modifications with time. In the same preparation 24 h after completion of the process, the oil globules become rearranged in floccules, the shape and appearance of which are retained for up to two years (Fig. 2).

These observations agree with our earlier results (Lladser & others, 1968) reporting an increase in the size of the globules when the lyophilized emulsion was reconstituted. The increase could be due to the coalescence of some of the globules to give rise to the floccules.

The reconstitution of the system by the addition of water was clearly observed microscopically. As the water advances into the lyophilized mass, a fast dissolution of the support occurs; the latter disappears from the observation field and the floccules violently disintegrate when the aqueous front reaches them, leaving the globules dispersed as before in the continuous phase with their characteristic Brownian movement, see Fig. 3.

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