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Increased binding capacity and flowability of α-lactose monohydrate after dehydration

C. F. LERK, A. C. ANDREAE, A. H. DE BOER, G. K. BOLHUIS, K. ZUURMAN, P. DE HOOG†, K. KUSSENDRAGER†, J. VAN LEVERINK†, *Laboratory for pharmaceutical technology and dispensing, State University of Groningen, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands, and †DMV, P.O. Box 13, 5460 BA Veghel, The Netherlands*

Coarse and regular grade sieved crystalline fractions of α-lactose monohydrate, spray-dried lactose and commercially available anhydrous lactose, consisting of an excess of β- over α-lactose, are widely used as direct compression filler-binders. None of these products however, can be characterized as an ideal excipient for direct compression because of moderate binding properties (α-lactose monohydrate), reduced ability to form tablets on inadequate storage and handling (spray-dried lactose) or borderline flowability (anhydrous product). In an attempt to optimize lactose to an excipient with high flowability as well as good compactability and stability, α-lactose monohydrate was gradually processed into products with decreasing water content. Dehydration was performed by thermal treatment and by desiccation with methanol. Sieve fractions of 100–125 μm of these products were compressed at 15 000 N by means of a hydraulic press into 500 mg tablets having a diameter of 13 mm. The compacts were tested on crushing strength (Schleuniger, model 2E). The thermally dehydrated samples showed strongly increasing binding properties with decreasing water content (Fig. 1). Desiccation by methanol gave a much steeper increase in crushing strength.

X-Ray analysis on a single crystalline particle containing 2·5% of water, showed the diffraction patterns of both α-lactose monohydrate and stable anhydrous α-lactose. This points to a gradual transition within each particle from the hydrous into the anhydrous form during treatment. Scanning electron micrographs illustrated the change of single particles into aggregates of anhydrous lactose. Compaction of both the thermally dehydrated and methanol dessicated product resulted in tablets with an almost equal overall porosity, when compared with tablets compressed from the original

* Correspondence.

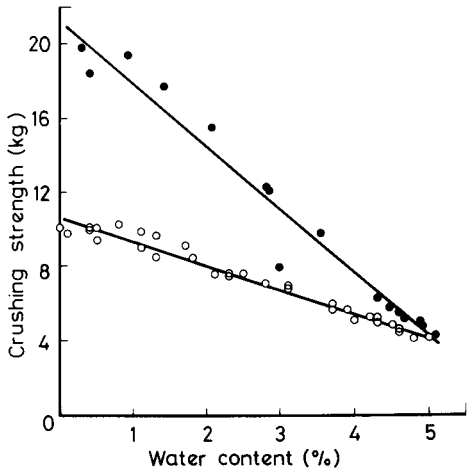

FIG. 1. Relation between crushing strength and percentage water content of, respectively, thermally dehydrated ○ and methanol desiccated ● α-lactose monohydrate samples, compressed (15000 N) into 500 mg (13 mm) tablets.

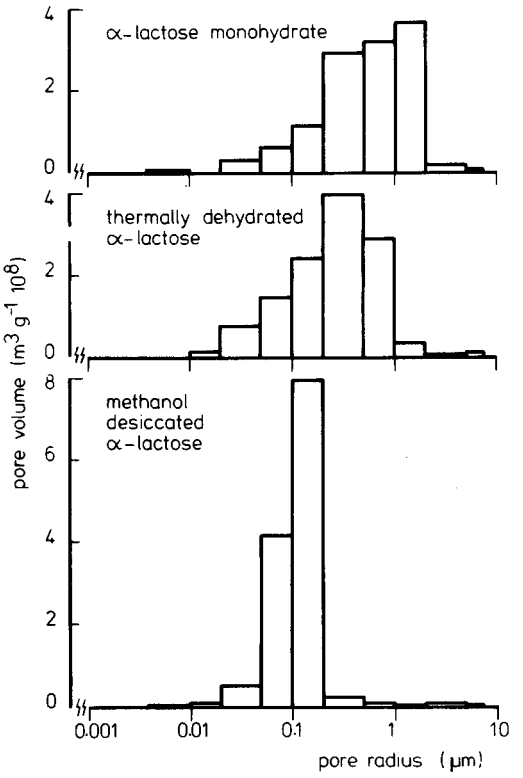

FIG. 2. Representation of the pore size distribution of tablets compressed at 15 000 N from α-lactose monohydrate, thermally dehydrated and methanol desiccated α-lactose, respectively (sieve fraction 100–125 μm).

material, but with totally different pore size distributions (Fig. 2). These results point to a strongly increased fragmentation during compression and explain the tremendous increase in binding capacity with increasing dehydration.

A comparative evaluation of the flow properties of the dehydrated product with other commonly used lactose products showed the former to be even better than the very good fluidity of sieved crystalline (100 mesh) α-lactose monohydrate. The flow properties were characterized by the flow through funnels of standard dimensions (Klein 1968), the Hausner ratio and the variation coefficient of the weight of 100 tablets (500 mg), by compression on a single punch tablet machine (Indola HOKO KJ) at 15 000 N compression force.

In conclusion, thermal dehydration or desiccation by means of organic solvents, like methanol, can convert crystals of α-lactose monohydrate into a stable anhydrous product with much increased binding capacity and excellent flowability.

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Preliminary report on the antimicrobial activity of honey distillate

E. E. Obaseiki-Ebor†, T. C. A. Afonya‡, A. O. Onyekweli*, †*Department of Pharmaceutical Microbiology*, ‡*Department of Pharmaceutical Chemistry*, **Department of Pharmaceutics, Faculty of Pharmacy, University of Benin, Benin City, Nigeria*

Honey is used officially in pharmaceutical preparations as a sweetening and demulcent agent. Some Nigerian natives use it as an antitussive. It also has antimicrobial activity and has been suggested (World Health Forum 1981) for use in enhancing the healing of wounds and pressure sores and was reported in the Pharmaceutical Journal (1982) to be bactericidal to many Gram-positive and Gram-negative bacteria and *Candida albicans*.

Several mechanisms have been suggested to explain the antimicrobial activity. Sugar in honey being the cause of high osmotic pressure at the wound surface and the induction of an unfavourable low water activity thereby inhibiting microbial growth as well as the fermentation of the honey to produce alcohol in-situ have been suggested.

To exclude the possibility of the activity being due to the putative effect of sugar. This paper presents a preliminary report on the antimicrobial activity of honey distillate.

Materials and methods

Preparation of the honey distillates. Samples of locally obtained honey from different geographical zones in Nigeria, and imported honey for commercial consumption from England and West Germany, were purchased and destructively distilled under dry nitrogen, the distillates being obtained in fractions.

Organisms. The organisms and their properties are listed in Table 1.

Antibiotics and antimicrobial agents. Streptomycin (Glaxo Laboratories), nystatin suspension (Squibb & Sons Ltd.) and 5% w/v phenol as a laboratory reagent, were used.

Media. used were: Diagnostic Sensitivity Test agar (Oxoid) pH 7·4, Nutrient broth (Oxoid) pH 7·2, Sabouraud-glucose agar (Oxoid) pH 7·3, Sabouraud-glucose liquid media (Oxoid) pH 7·3.

Determination of minimum inhibitory concentration (MIC). 10^5–10^6 bacteria colony forming cells of overnight broth cultures, or 10^{-2} dilution in sterile 0·9% NaCl of the two-day fungal cultures, were spotted respectively on to a series of overdried D.S.T. or Sabouraud agar plates containing progressively increasing concentrations of the antimicrobial agents. The plates inoculated with bacteria were incubated at 37 °C while those with fungal organisms were incubated at 25 °C for about 48 h. The MIC of an antimicrobial agent was the lowest concentration inhibiting growth.

Antimicrobial assay. This was by measurement of zones of inhibition on agar plates seeded with appropriate organisms and incubated at 35 °C for 24 h.

Results and discussion

A yellowish-brown oil, easily solubilized in water, sugarless, b.p. 123–126 °C, pH 4·8, exhibited a broad spectrum antimicrobial activity to the test organisms (Table 2). Similar activity was produced by honey from all sources.

The MIC of the fraction was 0·5% v/v irrespective of the presence of chromosomal or R-plasmid-mediated resistance genes on the bacterial strains. At 0·5% v/v, the fraction was also fungicidal to *Candida albicans* and fungistatic to *Penicillium spp* and *Aspergilus niger*.

† Correspondence.