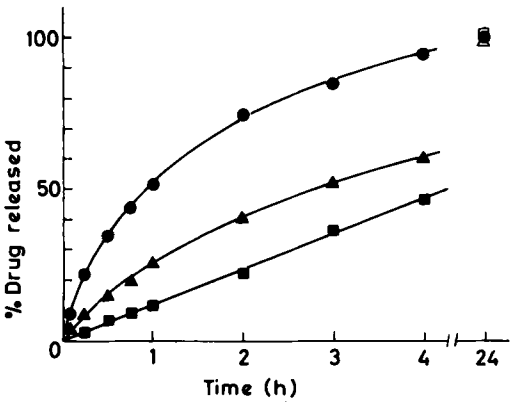

FIG. 2. The percentage of isoniazid released from 1000–800 μm microcapsules against time (0·500 g microcapsules; 2000 ml water) ● sample B ▲ sample D, and ■ sample E. Ordinate: Drug released (%). Abscissa: Time (h).

microcapsules prepared by technique D, was found during the complete observation time (4 h). Deasy et al (1980) have shown the suitability of the sealant treatment of microcapsules with paraffin wax in retarding the release of core material. In our opinion the fractional application of the wall material provides a very useful sealant treatment of the primarily formed wall and provides a mean in sustaining the drug release.

In conclusion, a small change during the preparation procedure can greatly influence the deposition of wall material around the core, and therefore affect the release of a drug. Taking into consideration a very high t50% value for the D sample, it would appear that the large holes or pores may not extend through the wall to the core and therefore do not provide a direct transport of the drug into the surrounding sink solution.

REFERENCES

Deasy, P. B., Brophy, M. Regina, Ecanow, B., Joy, Mary M. (1980) J. Pharm. Pharmacol. 32: 15–20

Donbrow, M., Benita, S. (1977) Ibid. Suppl. 29: 4P

Jalšenjak, I., Nixon, J. R., Senjković, R., Štivić, I. (1980) Ibid. 32: 678–680

Nozava, Y., Higashide, F., Ushikawa, T. (1979) in: Kondo, T. (ed.) Microencapsulation, Techno Inc., pp 79–91

J. Pharm. Pharmacol. 1981, 33: 666–668
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A technique for investigating changes in the surface roughness of tablets during film coating

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Surface roughness parameters determined by stylus instruments such as the Talysurf (Rank-Taylor-Hobson), Surfcom (Ferranti Ltd) and Hommel (Hommelwerk G.m.b.H) are important in the interpretation of tablet film coating adhesion data (Nadkarni et al 1975; Rowe 1978a, 1979) and in quantifying the physical appearance of the coat during formulation and process optimization (Rowe 1978b; 1981). By using parameters including the arithmetic mean roughness (R_a) defined in BS 1134 (1972) and others defined by Rowe (1979), it has been demonstrated that the surface roughness of a film coated tablet is related to tablet porosity, polymer concentration and molecular weight, pigment size and concentration and film thickness (Rowe 1978b, 1979, 1981).

This approach however is severely limited due to the large variations inherent in the surface topography of tablets, which unlike metals, do not exhibit a regular machine finished profile (BS 1134, 1972). In coating studies involving standard commercial equipment it is extremely difficult to ensure that the same tablet core is measured before and after coating. Even if this difficulty can be resolved by, for example, using a marked core, the problem of determining the roughness of the identical section of surface, 2·5 μm wide and 3·8 mm long, is still to be overcome. Thus the values reported in the literature for these roughness parameters are averages of a large number of different profiles and will only indicate general trends during coating.

Relocation profilometry (Grieve 1970; King & Thomas 1978) can overcome this disadvantage by allowing the specimen to be precisely remounted on the instrument enabling the identical profile to be recorded. This communication describes the development and application of a relocation technique to the study of tablet and tablet coating surface roughness. The use of this technique in conjunction with a laboratory model system which allows individual tablets to be coated under conditions pertaining to those which may be found in a 24″ Accela-Cota (Prater et al 1980) enables the precise effect of film coatings on surface roughness to be readily assessed.

Surface roughness measurements were made using a Talysurf 3 surface measuring instrument (Rank-Taylor-Hobson) fitted with a specially developed relocation table and stage (Figs. 1,2, and 3). The removable top of the relocation table (D) and the stage (B) were clamped together and three 4 mm diameter holes accurately drilled and

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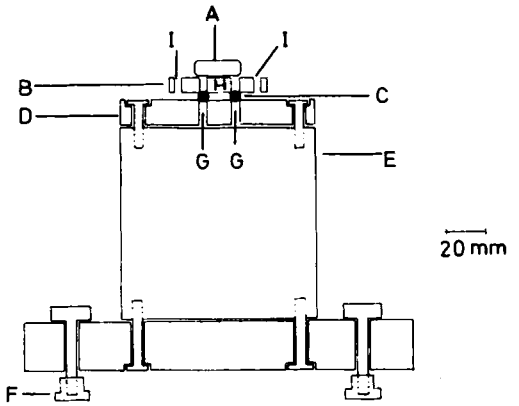

FIG. 1. Side view of relocation table and stage. Key: A. 25·4 mm flat bevelled edge compact. B. Relocation stage—(5/16" mild steel gauge plate). C. 5 mm Diameter hardened steel balls. D. Removable top of relocation table. (½" × 4" × 4" mild steel). E. Relocation table (4" × 4" × 4"+ 4" × 8" × 2" mild steel). F. T-slot nuts (mild steel). G. and H. 4 mm diameter drilled and reamed holes. I. 4 mm diameter drilled holes for fixing relocation stage to belt of model coating system.

reamed out (G & H). The relocation table (E) and its top (D) were reassembled and bolted firmly to the Talysurf using T-slot nuts (F). Cyanoacrylate adhesive (Radio Spares Ltd) was applied to the edges of the holes (G), in which 5 mm diameter hardened steel balls (C) were placed, and the relocation stage (B) placed on top until the adhesive had set. Thus relocation to better than 2·5 μm (the stylus width) was obtained by a three point contact of the balls (C) and holes in the stage (H). The tablets under investigation were attached to the relocation stage using cyanoacrylate adhesive. To minimize damage to the tablet surface during measurement, it was found necessary to replace the standard tungsten carbide skid fitted to the Talysurf 3 with one machined from nylon 12 block.

Tablets (porosity 18·1%) consisting of lactose and microcrystalline cellulose were compressed at a compaction pressure of 197 MPa using a rotary tablet machine (D3RY, Manesty Machines Ltd) fitted with 25·4 mm diameter flat bevelled edge punches. Fig. 4 shows the surface roughness profiles for one of these tablets, relocated on seven separate occasions and demonstrates clearly that satisfactory relocation is occurring. The minor changes which occur in certain regions of the trace can be attributed to damage by the

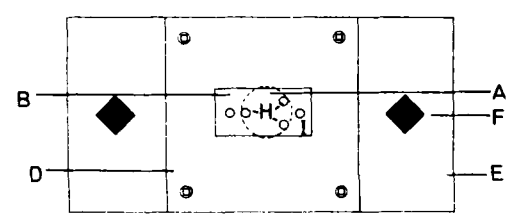

FIG. 2. Plan view of relocation table and stage. Key: As Fig. 1.

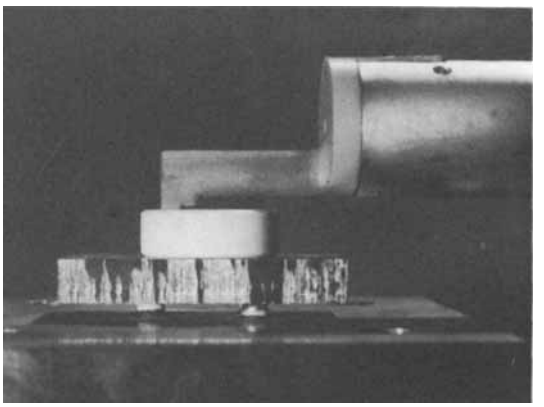

FIG. 3. Photograph of Talysurf 3 surface measuring instrument fitted with the nylon skid and relocation rig.

repeated passage of the diamond stylus under a load of 100 mg, since these did not occur on relocation of a metal surface. Not withstanding these small changes the value of R_a recorded by the triple cutoff average meter was a constant 2·85 μm (standard deviation, zero) during the successive relocations. For similar surfaces on lactose-starch tablets Rowe (1978a), who did not use relocation, found coefficients of variation ranging from 14–30%

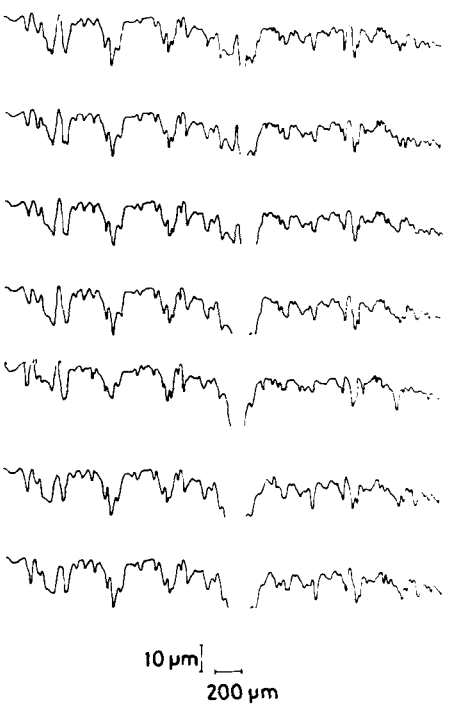

FIG. 4. Surface roughness traces of a 25·4 mm diameter lactose-microcrystalline cellulose tablet, showing seven consecutive relocations.

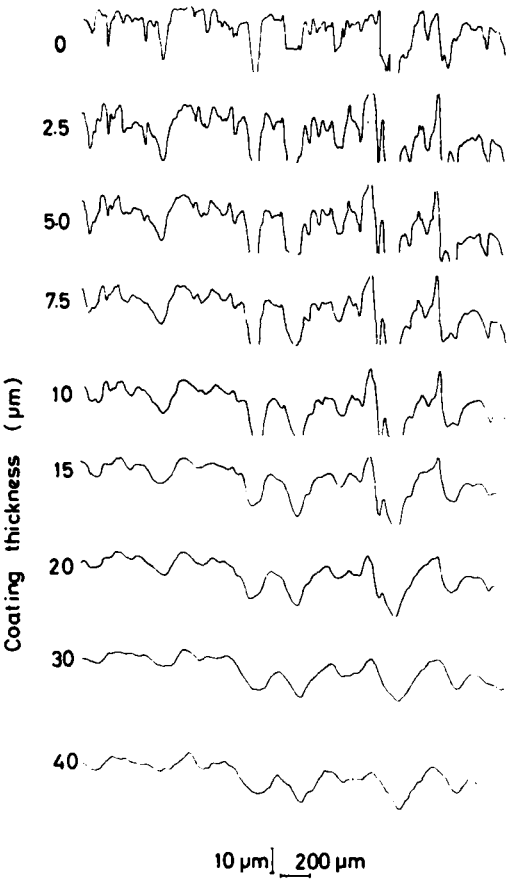

FIG. 5. Surface roughness traces of a 25·4 mm diameter lactose-microcrystalline cellulose tablet during the build-up of a film coating 40 μm thick.

To follow the changes in surface topography during film coating, the relocation stage and tablet were bolted to a backing plate which had been attached to the belt of the model coating system (Prater et al 1980). A 5% w/v aqueous solution of hydroxypropyl methylcellulose (Pharmacoat 606, Shinetsu Chemical Co. Ltd) was applied under the following conditions which were those successfully used in a 24" Accela Cota; pneumatic spray nozzle (Spraying Systems Co 1/4 JCO 2050 fluid and 120 air nozzles), drying air flow rate 4·13 m^3 min^{-1}, compact surface temperature 45 °C, exhaust capacity 10·05 m^3 min^{-1}, nozzle to compact surface distance 200 mm, compact cycle time 25 s, dwell time in spray 0·12 s, spray rate 35 ml min^{-1}. At stages during the build-up of the coating, the relocation stage was removed and the surface profile of the tablet recorded. The film thickness was measured using a high precision micrometer (Starrett Ltd).

Fig. 5 shows the changes in surface topography which occur as the coating increases in thickness up to 40 μm. Minor irregularities are rapidly obliterated and the major peaks and valleys become more rounded. However, even at a film thickness of 40 μm, it is the presence of large irregularities in the core which determine the roughness of the coating. This obvious reduction in surface roughness is accompanied by R_a decreasing from 2·80 μm to 1·80 μm. These R_a values were again constant for each trace, (5 determinations gave zero standard deviation).

Because this technique eliminates variation arising from an inability to monitor the same sections of surface from the same tablets, it thus allows the deposition of film coatings to be closely followed, enabling the influence of formulation and processing conditions on surface roughness to be studied in greater detail. Furthermore since the core surface profile is constant, changes during coating can be quantified by analysis techniques such as cumulative peak height distributions, peak and valley distributions, slope curvature distributions and power spectra (King & Thomas 1978).

We wish to thank Mr A. E. Carter of the Department of Mechanical Engineering, University of Bath, for his help in developing the relocation technique.

REFERENCES

B.S. 1134 Parts I and II (1972) British Standards Institute, London

Grieve, D. J. (1970) Ph.D. Thesis, University of Birmingham

King, M. J., Thomas, T. R. (1978) J. Coat. Tech. 50 (643): 56–61

Nadkarni, P. D., Kildsig, D. O., Kramer, P. A., Banker, G. S. (1975) J. Pharm. Sci. 64: 1554–1557

Prater, D. A., Wilde, J. S., Meakin, B. J. (1980) J. Pharm. Pharmacol. 32S: 90P

Rowe, R. C. (1978a) Ibid. 30: 343–346

Rowe, R. C. (1978b) Ibid. 30: 669–672

Rowe, R. C. (1979) Ibid. 31: 473–474

Rowe, R. C. (1981) Ibid. 33: 1–4