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COMMUNICATIONS

Surface topography of microcapsules and the drug release

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Recently, Nozava et al (1979) have suggested that the presence of large holes (1–10 μm in diameter) on the surface of microcapsules plays a significant role in drug release which occurs mainly through these holes. We have prepared three batches of the ethylcellulose microcapsules with different surface characteristics by the separation of the polymer from cyclohexane.

Isoniazid was used as the core material, and the ethylcellulose sample had a viscosity of 50 mPas when dissolved in toluene–ethanol (80:20 w/w). The core to wall ratio was 1:2 in all preparations. Techniques B (standard method) and D (fractional application of ethylcellulose) were the same as described previously (Jalšenjak et al 1980), and a modification from the technique B was made by addition of polyethylene (Technique E). Polyethylene was used in an amount equal to one half of ethylcellulose, because the usage of a synthetic macromolecule that is highly solvated in cyclohexane was suggested to act as a protective colloid in the coacervation preventing the formation of large agglomerates of ethylcellulose (Donbrow & Benita 1977).

The mean diameters ($\pm\sigma_g$) at 50% cumulative undersize were graphically determined from their individual logarithmic probability plots, and they were as follows: 977 ± 241, 1050 ± 293, and 1047 ± 277 μm for the B, D, and E samples, respectively. Although, quite a broad distribution of sizes was obtained in each sample, the technique B produced smaller microcapsules, whereas the use of polyethylene did not minimize agglomeration in the system.

The size fraction which remained between sieves 1000 and 800 μm was separated, and used in further investigations. Scanning electron micrographs were prepared with a Stereoscan 600 (Cambridge) type apparatus. Samples of microcapsules were vacuum-coated with a thin gold film. Considerable difference in the appearance of the microcapsules surfaces was found (Fig. 1) especially when the relative number of large holes present on the surfaces of microcapsules is taken into consideration.

The release of isoniazid from 1000–800 μm microcapsules (0·500 g) was monitored by the method of Jalšenjak et al (1980). The percentage of the drug released was plotted against time (Fig. 2). The maximum release rate was obtained with the B sample of capsules, which also contained the greatest number of holes over their surfaces. The times for the 50% release of the drug graphically determined from their plots (Fig. 2) were as follows: 56, 260, and 170 min, for the B, D, and E samples, respectively. The t50% value obtained for the D and E samples indicates that, in our range of experiments, the relative number of holes was not of such an importance as suggested by Nozava et al (1979). The linear drug release (zero-order), from the

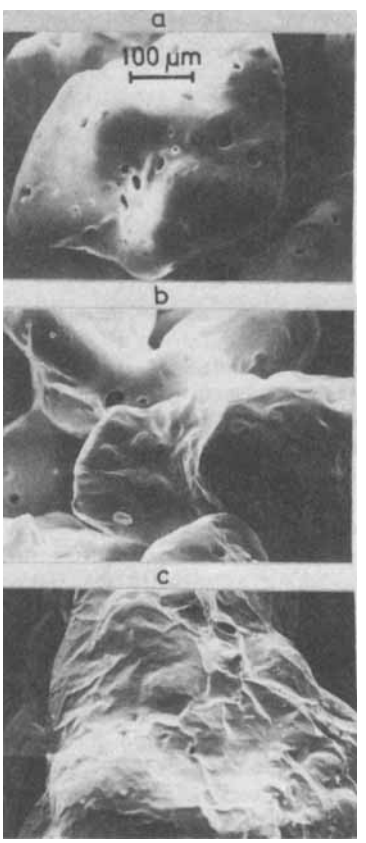

FIG. 1. Scanning electron micrographs of ethylcellulose microcapsules containing isoniazid: a, sample B, b, sample D, and c, sample E.

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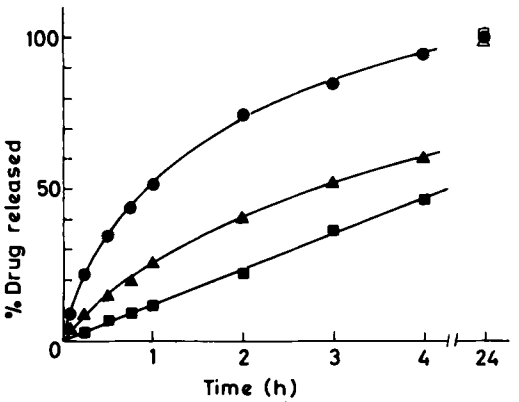

FIG. 2. The percentage of isoniazid released from 1000–800 μm microcapsules against time (0·500 g microcapsules; 2000 ml water) ● sample B ▲ sample D, and ■ sample E. Ordinate: Drug released (%). Abscissa: Time (h).

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

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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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