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COMMUNICATIONS

A new method for film coating granules

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The film coating of granules is difficult, because of their large specific surface area, and the presence of many fine holes or cracks. It has been found that amounts of coating materials of over 50% of the weight of uncoated granules are required to effect sufficient covering, for example, for enteric coating (Omata 1978).

Recently, fluidized bed coating has been widely used for the film coating of granules. The method generally uses a counter flow system in which the granules are fluidized by blowing hot air up into the bed and the coating solution is sprayed downward. Another procedure, developed by Wurster (1953) and applied to a variety of pharmaceutical products, is a system in which the granules and the coating solution are blown in parallel with each other. It is effective in coating the granules because the time of contact of the granules with the coating solution spray is longer than that with the counter flow system. But with both systems the drawback is the time necessary to coat the granules, for example, over 5 h for enteric coating. Furthermore, there is a distinct possibility of a breakdown or attrition of the granules occurring during the coating operation.

We now present an evaluation of a new device in which a pneumatic transport system is used for applying a film to granules in order to mask the taste of a bitter drug.

The device (Fig. 1) is made from a thin iron plate. The pneumatic transport tube is 5 cm in diameter except for that portion in which the spray nozzle was installed, this is 10 cm in diameter, and 4 m long at the linear portion, T. The radius of curvature is 50 cm on both sides of the tube. A tube of acrylic resin (Perspex) one metre long is installed in both linear portions, T(A) and T(B), to allow observation of the state of transportation of the granules. The lever, L, can be turned to the transport tube during coating, and to the collecting cyclone at the end of the operation. The blower, B, is a small-sized fan with an air capacity of 2·3 m^3 min^{-1} at 12 500 rev min^{-1} and 300 W at 100 V. Two blowers of the same kind in parallel are used to circulate the granules. At full working, the air flow rate is 20 m s^{-1} in the 5 cm diameter tube. The air temperature is about 70°C at the back of main heater, H_1, and the exhaust air at the top of main cyclone is about 50°C.

The spray nozzle used for coating is of a two-fluid type and 1 mm in diameter. It is fed using a roller pump and a compressor at a suitable spray rate and pressure.

The uncoated granules are poured into the main cyclone, C_1, from the top. When the temperatures described are attained, the coating solution is sprayed. These temperatures are lowered about 10°C at this time due to evaporation of the liquid.

The variable factors in the system and optimal conditions are as follows. The coating operation is carried out at a spray rate of 10 ml min^{-1} because excess coating solution adheres to the wall near the nozzle and the peeling dried thin flakes disturb circulating motion of the granules which also agglomerate on them. For the same reason, the shape of spray mist should be a narrow angle cone. The maximum fan width of the nozzle is 115 mm at 3 kg cm^{-2} pressure, but we have used

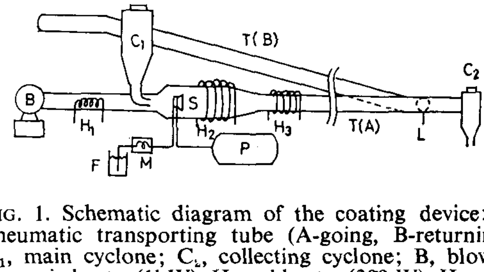

Fig. 1. Schematic diagram of the coating device: T, pneumatic transporting tube (A-going, B-returning), C_1, main cyclone; C_2, collecting cyclone; B, blower; H_1, main heater (1kW); H_2, subheater (300 W); H_3, subheater (500 W × 2); S, spraying nozzle; L, changing lever; P, compressor; M, rollerpump; F, spraying solution.

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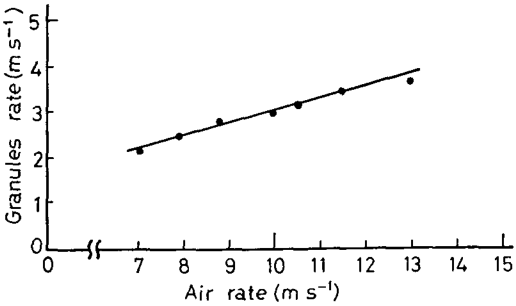

FIG. 2. Relationship of circulating rate between the air and the granules; the measured values at 10 cm in diameter.

2·5 kg cm^{-2} because it is the minimum at which a good mist can be obtained.

It has been found necessary to prolong the contact time of the coating spray with the granules in order to improve the coating efficiency. For this purpose it would be necessary for the transport rate of the granules to be similar to that of the spray. By using photography we found that the differences between the rates of granules and air became smaller with the decrease of air rate (Fig. 2). Where the air flow rate is less than 8 m s^{-1} the granules cannot be maintained in circulation but at 10 m s^{-1} there is no problem. The degree of attrition of the granules is related to air flow to a small extent, e.g. the amount of powder passing through a 35 mesh sieve (< 420 μm) was only 0·2, 5 and 7·3% after 1, 3 and 5 h respectively.

Fine granules have the advantage of a higher transport rate than larger granules. The energy involved in the pneumatic transport of particles has three components (Jotaki 1968), floatation, transportation and collision. These decrease with decreasing particle size. When optimal conditions for each granule type are attained it may be possible to achieve a covering effect of near to 100% from the present 65–70%.

To show that the device actually works, we used it to mask a bitter drug. The granules were a 1 : 1 mixture of commercial corn starch and lactose to which a bitter drug, sodium dichloxacillin (MDI-Na), was added to the extent of 20%. Three parts of the mixture were kneeded with two parts of a solution of ethylcellulose (49% ethoxy, 10 cps) dissolved in dichloromethane to give a final concentration of 3% in the mixture. The wet mass was granulated and dried at a room temperature (20°C) for 24 h, then at 90°C for 5 h. The granules were sifted through 28 and 35 mesh sieves to give a size range of 420–600 μm. Ethylcellulose, as used for binding, was dissolved in dichloromethane to a concentration of 5% for the coating solution. The following method was used to determine the amount of coated layer.

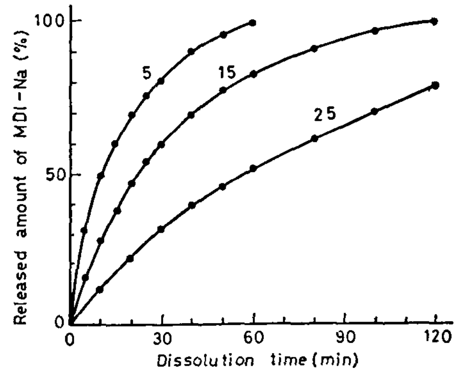

FIG. 3. Release of MDI-Na into distilled water from the coated granules; binder amount, 3%; numbers on the curves indicate the coated amount of ethylcellulose.

If b_0 g of MDI-Na is contained in a_0 g of uncoated granules, the amount of MDI-Na in a unit weight of granules is b_0/a_0. If after coating a_1 g of coated granules contained b_1 g of MDI-Na, the following equation can be derived:

$$\frac{b_0}{a_0} = \frac{b_1}{a_1}(1 + \alpha) \qquad (1)$$

where α is the coated amount based on the weight of uncoated granules. From equation (1), equation (2) is obtained, where α is expressed as a percentage

$$\alpha = \left(\frac{b_0/a_0}{b_1/a_1} - 1\right) 100 \qquad (2)$$

Instead of calculating the exact amounts of drug released, optical densities from u.v. were used. When the u.v. reading was constant it was assumed that 100% had been released and these values were used for b_0 and b_1. The quantity of MDI-Na dissolved in water was measured at regular intervals, by a colorimetric procedure that makes use of the drug, having a maximum peak at 275 nm. Fig. 3 shows the release of MDI-Na from the coated granules. The bitterness could not be tasted when the coat was formed with ethylcellulose at 5% and above. The time needed to effect coating was about 1 h.

It seems that this coating device has the elements for making rapid coating of granules possible.

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