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THE GRANULATION OF A HYDROPHOBIC POWDER USING A MODIFIED STARCH

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ABSTRACT

Granules have been prepared using a hydrophobic powder and a modified starch as binder. Granules suitable for tabletting could be prepared using either water and 25% modified starch or a surfactant solution and not less than 5% modified starch. Compacts produced from a coarse size fraction of these granules disintegrated readily only if the granulation liquid contained surfactant. All compacts had adequate strength to withstand handling but those containing surfactant were weaker.

INTRODUCTION

The production of granules by the wet massing and screening process involves the mixing of powders with a suitable binder liquid. This liquid may contain a suitable binder, for example, hydrolysed starch or gelatin. Alternatively a substance that will form a binder after the addition of liquid, can be mixed with the powders. Granule agglomerates are formed, providing the powders are adequately wetted, without a binder but frequently insufficient material dissolves to hold together the agglomerates after they have been dried.

When a tablet is to be prepared, containing a high dose of hydrophobic powder,a binder liquid of low surface tension is required or a viscous liquid may be used to act as an adhesive between the particles (1). However, the use of a viscous liquid can inhibit mixing (2) and the addition of accurately measured amounts is extremely difficult.

Granulations using liquids of low surface tension can be performed using either organic solvents (3) or wetting agents. In this study a hydrophobic powder blended with up to 25% of a modified starch has been granulated by the addition of water or aqueous surfactant solutions. The granules that were prepared, and compacts prepared from them,have been studied with respect to their suitability for tabletting.

MATERIALS AND METHODS

Granules were prepared from 200g of a mixture of a hydrophobic polyvinylchloride (Pevikon D-42, Fosfatbolace, Stockholm, Sweden) 3.3μm, 1.422 g cm^{-3},contact angle with water 128°; blended with different proportions of a modified starch (Sta-Rx 1500, Colorcon Ltd., Orpington, Kent, England) 17.0μm 1.49 g cm^{-3}. The two powders were pre-mixed for four minutes using a 'Z' blade mixer (Winkworth, Wishaw, Scotland). The chosen volume of water or surfactant solution, dioctyl, sodium sulphosuccinate 1% $^{w}/_{v}$, surface tension 24.2mNm^{-1} was then added and the whole was massed for 5,10 or 20 minutes. In each case massing was stopped 1 minute from the total time and the sides of the mixer were scraped before completing the massing. The damp mass was forced through a 1.4mm screen using an oscillating granulator and the granules were dried to constant weight at 50° in a hot air oven. The dry granules were fractionated using sieves and the 50% size calculated.

Compressed discs, 19.05mm diameter, were prepared at 100MNm^{-2} from the 1.0mm - 0.5mm size fractions of selected

batches. The hardness and disintegration time of these discs were measured using a Schleuniger hardness tester and the British Pharmacopoeial method, respectively.

RESULTS

In order to assess the effects of variation in liquid volume and Sta-Rx 1500 content, granules were made using liquid volumes from 100-130cm^3 and the Sta Rx 1500 content was varied from 2.5% $^w/_w$ to 25% $^w/_w$. At the lowest Sta Rx 1500 content granules formed but after drying they were too soft to fractionate without significant abrasion. The mean granule sizes for the various batches are given in Table 1.

Compressed discs were formed from selected batches using the 1.0 - 0.5mm size fraction. The minimum porosity of these fractions and the properties of the discs that were prepared from them are listed in Table 2.

DISCUSSION

The results in Table 1 show that use of the modified starch makes it possible to granulate a hydrophobic powder without the addition of a wetting agent. The surface tension of the aqueous phase formed from 250cm^3 water and 25g Sta-Rx1500 was 66 mNm^{-2}. The results in Table 1 also show that the major effect of massing time. Using 100cm^3 water and prolonged, 20 minute massing, gave an overwet mass, whereas after 5 minutes massing almost no granule was formed. However, discs prepared from granules, that had been massed using water, disintegrated very slowly in water at 37°. Table 2. Addition of surfactant, 1% to the disintegrant fluid had an insignificant effect on disintegration time.

TABLE 1

The Mean Granule Sizes of Batches prepared using water or 1%^{w}/v dioctylsodium sulphosuccinate.

		Mean Granule Sizes (μm)					
Massing time (min)		5	5	5	5	10	20
Sta-Rx 1500 %		5	15	20	25	25	25
Binder liquid (cm^3)							
Water	100	-	-	-	<100	510	w
"	105	-	<100	-	230	660	w
"	125	-	<100	-	550	w	p
"	130	-	<100	-	800	-	-
Surfactant	105	-	120	-	120	120	120
"	125	540	-	-	280	610	w
"	130	920	400	375	335	w	-

w = significant,<80%, worming

p = paste in mixer

TABLE 2

Minimum Porosities of 1.0 - 0.5mm Size Fractions, Mean Hardness and the Disintegration Time for Fine Discs Compressed at 100 MNm^{-2} Binder volume 130 cm^3, Massing Time 5 minutes.

Binder liquid	Surfactant1%				Water
Sta-Rx %	5	15	20	25	25
Porosity	0.24	0.23	0.22	0.21	0.20
Hardness (tp)	13.8	13.2	13.1	14.0	> 20
Disintegration time (seconds)	305	45	45	45	>1800

Granulations carried out using surfactant solution required more liquid, than water used alone, in order to produce large granules. However, these could be prepared using 5% Sta-Rx1500 and the compressed discs had satisfactory disintegration characteristics. Table 2.

The results in Table 2 indicate, in addition, the weakening effect of the surfactant on the compacts and the decreasing porosity with both increasing Sta-Rx content and the source of surfactant.

Granulation in the absence of the surfactant is the result of the formation of a paste by the modified starch, this is a high viscosity binder that sticks the hydrophobe particles together. With a surfactant, sufficient starch is required to form solid bridges on drying but adequate wetting occurs to give satisfactory damp granules.

The failure of prolonged massing to produce large granules with 52.5% $^{v}/_{w}$ surfactant solution is possibly due to the formation of weaker damp agglomerates with a binder liquid of low surface tension.

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