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Effect of Temperature of Binding Liquid on Some Tablet Properties

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The effect of temperature of the granulating fluid on some physical properties of lactose granules and tablets was investigated. Checks on granule size, flow rate and tap density of the granules and hardness, friability and disintegration time at temperatures between 20° and 60°C were carried out. Also, temperature effect on the viscosity of the granulating fluids, water and maize starch mucilage, was observed. The viscosity of maize starch mucilage was found to decrease as temperature increased, while there was no noticeable effect on water. Also, it was found that the granule size increased with temperature up to about 50°C after which there was no more increase. The flow rate followed the same pattern, except that there was a decrease beyond 40°C. The tap density was not significantly affected, thus signifying that flow of granules from the hopper to the die in the tabletting machine was not affected equally. The tablet hardness increased as the temperature decreased from 60° to 25°C while friability showed a reverse. Standardization of the temperature of the granulating fluid is therefore essential.

Key words: Temperature effect, Granulating fluid, Granules, Tablet properties.

Introduction

Most pharmaceutical powder excipients have poor cohesive properties. Therefore, in order to successfully formulate them as tablets, binders must be incorporated into them. Binders are cohesive materials which are added to poorly cohesive or non-cohesive powders to aid their granulation. Provided sufficient quantity of the binder is added, the granules formed usually have minimum quantities of fines and enhanced flow characteristics. They can also be compressed into hard tablets without employing excessive force. The efficiency of a binder can be affected by various factors. The volume and concentration of binders significantly affect tablet characteristics (Shubair and Dingwall 1977; Stanley-Wood and Shubair 1979). Cellulosic gums as well as natural gums when used at high concentrations increase disintegration time and decrease dissolution rate of drugs from tablets.

The method of incorporation of binder (Hill 1976; Shubair and Dingwall 1976) and the massing time (Tiamraj and Dingwall 1978) have been shown to affect binder efficiency. Binders may be added as solution in the granulating fluid or as solid in the wet granulation or direct compression methods of tablet manufacture.

Starches are popular as binder in the manufacture of tablets. Commonly used ones include maize, rice and potato. Others are cassava, tapioca, wheat and yam starches. Starch is used as a binder in the form of a mucilage prepared by adding boiling water to a suspension of starch powder in cold water. It is usual to allow the hot mucilage to cool before being used but the temperature to which it is allowed to cool is usually not specified. Since the temperature of starch mucilage may affect some of its physical characteristics such as viscosity, the temperature of its use in the wet granulation process may affect its efficiency as a binder.

The effect of temperature on the binding efficiency of cassava and yam starch pastes has been reported recently (Eradiri and Nasipuri 1985). Our study investigates the effect of pasting temperature of maize starch mucilage on some physical characteristics of lactose tablets.

Materials and Methods

Materials used were maize starch from BDH Chemicals, UK; lactose and liquid paraffin from Halewood Chemicals, UK; modified cellulose gum NF (Ac-Di-Sol) from FMC Corporation, PA, USA; and magnesium stearate powder from Hopkin and Williams, UK.

Preparation of starch mucilage. Five gram of maize starch were made into a slurry with ml10 of distilled water, and sufficient quantity of boiling water was added to the suspension with continuous stirring to prepare 100 ml. The mucilage was further boiled for a few minutes to ensure complete gelatinization of the starch granules in suspension. The mucilage formed was left to cool to the desired temperature before use.

Determination of viscosity of starch mucilage. The Ubbelohde suspended level viscometer was used to measure the viscosity of starch mucilage in accordance with B.P. 1980 method (British Pharmacopoea 1988). The viscometer was

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placed vertically in a thermostated water bath in order to determine the viscosities at various temperatures. The viscometer constant, c, was calculated by using liquid paraffin.

Preparation of lactose granules. Forty eight gram of lactose powder and 2g of Ac-Di-Sol (disintegrant) were mixed for 10 min in a planetary mixer (Kenwood, UK). 20 ml freshly prepared maize starch mucilage (or distilled water) at a temperature 10°C higher than the required temperature was added gradually with continuous mixing to produce a wet mass of acceptable consistency. The total wet mixing time was 10 min. The wet mass was then granulated by passing through a 1.4 mm aperture sieve, and dried in a tray oven (Kottermann, Germany) at 60°C for 6 h. The moisture content was determined and found to be between 0.94 and 1.06% w/w after heating to constant weight. All the granules were stored in a desiccator prior to characterisation.

Characterisation of granules. Bulk densities (at zero tap) and tap densities (after 100 taps) were determined in an automatic tapping device (Onyekweli 1997) similar to that earlier described (Newmann 1967). The ratio of tap density over the bulk density (i.e. Hausner ratio) of each of the samples was calculated. The mean of three replicates was calculated.

Using BSS410 test sieves, the average granule size of various batches was computed in three replicates from the cumulative weight percentage oversize. The fraction of each batch which passed through a 0.250 mm sieve was calculated as the percentage amount of fines.

The flow characteristics of granules were determined by measuring the time taken by a known weight of the granules to flow through a 1.0 cm diameter orifice. Measurements were carried out in three replicates and the mean calculated.

Compression of granules. The granulations were mixed with 0.5% w/w/ magnesium stearate (as lubricant) for 10 min in a tumbling mixer (Rotomixer, Foster Equipment, UK). Enough granules to produce tablets weighing about 400 mg were compressed in a single punch tabletting machine (Type F 3, Manesty, UK) at a fixed compression dial reading of 38.5 units. The tablets were stored in the desiccator for at least 24 h to allow complete recovery before characterisation.

Characterisation of tablets.(a) Friability: 10 tablets from each batch formulated with starch mucilage (or water) as granulating fluid were caused to cascade in a Roche friabilator (Erweka TA, Germany) at 25 rpm. for 4 min. The percentage loss in weight was computed as the friability. The mean of three replicates was recorded.

(b) *Hardness:* The force required to crush a tablet placed between two motorised platens of an electronic hardness tester (Schlueniger, Switzerland) was determined. The values listed are the mean of ten replicates.

(c) *Disintegration time:* Six randomly selected tablets from each batch were individually assessed in a BP disintegration testing apparatus (Manesty, UK) containing distilled water at 37 ± 0.2°C. The mean of the recorded times was calculated.

Results and Discussion

Viscosity determinations for the starch mucilage at temperatures between 25°C and 60°C (Table 1) showed a decrease with the increase of temperature . An equation analogous to Arrhenius equation of chemical kinetics expresses approximately the dependence of viscosity of a liquid on temperature thus:

$$\eta = Ae^{-E/RT} \text{ of } \log n = \log A - E/2.303RT$$

where η is the viscosity of the system, A is a constant which depends on the molecular weight and molecular volume of the liquid, E is the activation energy required to move one

Table 1

Temperature effects on the viscosity of starch mucilage

Temp (°C)	Viscosity (Centipoise)
25	17.1×10^4
30	1.7×10^4
40	11.15×10^4
50	6.45×10^4
60	2.45×10^4

Table 2

Temperature effects on some physical properties of lactose granules

Binder type and conc.	Temp. (°C)	Bulk density ($g^{-1}cc$)	Tap density ($g^{-1}cc$)	Hausner ratio	Flow rate ($g^{-1}cc$)
Maize starch mucilage (5% w/w)	25	0.56	0.71	1.27	0.30
	30	0.56	0.71	1.27	0.41
	40	0.57	0.77	1.35	0.42
	50	0.57	0.77	1.35	0.42
	60	0.57	0.77	1.35	0.32
Water		0.56	0.69	1.28	0.30
		0.56	0.71	1.27	0.31
		0.56	0.71	1.27	0.31
		0.56	0.74	1.32	0.30
		0.56	0.74	1.32	0.40

Table 3

Granule size of lactose expressed as weight (g) at various temperatures

Sieve size (mm)	25°C		30°C		40°C		50°C		60°C	
	Water	Starch mucilage	Water	Starch mucilage	Water	Starch mucilage	Water	Starch mucilage	Water	Starch mucilage
>1.18	1.10	0.09	1.08	1.83	1.14	6.91	1.15	4.48	1.13	7.37
>0.71	10.21	13.80	10.25	16.06	8.53	8.64	9.92	24.67	1.13	28.99
>0.50	2.50	5.17	3.98	5.61	3.02	3.83	3.23	5.36	3.73	9.23
>0.25	3.72	5.30	4.00	6.08	3.22	6.28	3.41	7.56	3.69	5.83
>0.125	1.51	2.62	3.28	4.06	2.12	0.66	2.71	5.64	4.36	3.15
>0	0.39	2.17	1.03	2.87	0.19	2.32	1.91	4.47	1.93	2.11

molecule past another, T is the absolute temperature and R is the gas constant (Rawlings 1977). It is evident from this equation that a rise in temperature causes a decrease in viscosity and data in Table 1 confirms this.

Data obtained from the tap and bulk density measurements of the granules (Table 2) show that temperature does not significantly affect these properties and consequently the Hausner ratios of these granules does not vary significantly. Hausner ratio (HR) predicts the degree of densification that granules may undergo during compression into tablets as a result of machine vibration. High densification (i.e. high HR) adversely affects the flow of granules from the hopper to the die. Onyekwili (1981) using cohesive powders, obtained HR values > 1.6 at temperatures between 20° and 50°C. Although no official limits have been set as acceptable for HR values, the values of 1.30-1- 35 for granules with maize starch mucilage and 1.28-1.32 for granules obtained with water as the granulating fluids respectively seem pharmaceutically acceptable. Differences in the range of the HR values obtained for the mucilage and water respectively, were due to higher bulk and tap density values recorded for the starch mucilage.

The mean granule size was affected by both the type of granulating fluid and the temperature (Table 3). 5% maize starch mucilage produced larger granules than water. The average granule size increased with the temperature up to about 50°C after which there was a decrease. The flow rates of granules formed by starch mucilage were found to be dependent on temperature, increasing from 25° to about 40°C before decreasing. Because there was no noticeable change in the size of granules formed by water at temperatures between 25° and 60°C, their flow rates were not affected.

The larger granules produced by maize starch mucilage can be attributed to superior binding ability of the mucilage over water. The increase in granule size with the increase of temperature can also be attributed to the ease with which the mucilage coat the particles at higher temperature (decreasing viscosity with increasing temperature) thus encouraging granule growth. This was however not observed beyond 50°C.

The friability and hardness of tablets formulated with different granulating fluids are illustrated in Figure 1. Tablets made with water were more friable than those made with starch mucilage. For both tablets, friability increased as the temperature of the granulating fluids increased. The hardness of both tablets decreased as the friability increased in accordance with earlier findings (Hill 1976; Onyekweli 1985). Since harder and less friable tablets were produced as the temperature of the granulating fluid decreased, it implies therefore, that temperature affects the magnitude of interparticle bond strength. Also, since all the batches of granules were compressed under similar conditions, the variations in friability and hardness must have been influenced directly or indirectly by the temperature of the binding fluids. For example, the viscosity of the starch mucilage contributed to the bond strength of the granules depending on the operating temperature. As the temperature decreased and the viscosity increased, tablets obtained from the granules became harder. Sakr *et al* (1972) reported a proportional increase in crushing strength of tablets with increase in binder viscosity as a result of increase in binding force between the particles. The granules thus produced with the mucilage formed stronger tablets than those produced with water as granulating fluid.

Disintegration time results (Table 4) show that tablets formed with starch mucilage had longer disintegration times than those produced with water as the granulating fluid at all the temperatures. Also, tablets formed with both granulating fluids at 60°C disintegrated faster than those formed at 25°C. Maize starch is insoluble in water; rather, it forms a mucilaginous viscous barrier round the granules thus retarding its

Table 4
Effect of temperature on disintegration time of lactose tablets.

Binder type & conc.	Temp.(°C)	Mean disintegration time (min).	Standard deviation
Maize starch mucilage (5%w/w)	25	6.2	0.80
	30	5.7	0.49
	40	5.6	0.68
	50	5.5	0.69
	60	5.4	0.78
Water	25	6.3	0.37
	30	5.4	0.76
	40	4.0	0.99
	50	2.7	0.30
	60	2.5	0.30

disintegration (Esezobo and Pilpel 1976). At higher temperatures, the low viscous mucilage provides a thin film of binder around the granules. Therefore, penetration of water into the tablets is easier and as a result disintegration is faster.

The temperature of the granulating fluid markedly affects its viscosity as well as some properties of the granules and tablets such as granule size, tablet friability, hardness and disintegration time. It is therefore necessary for a manufacturer to standardize the temperature at which granulating fluid is used in order to minimize batch to batch variation in the quality of the products.

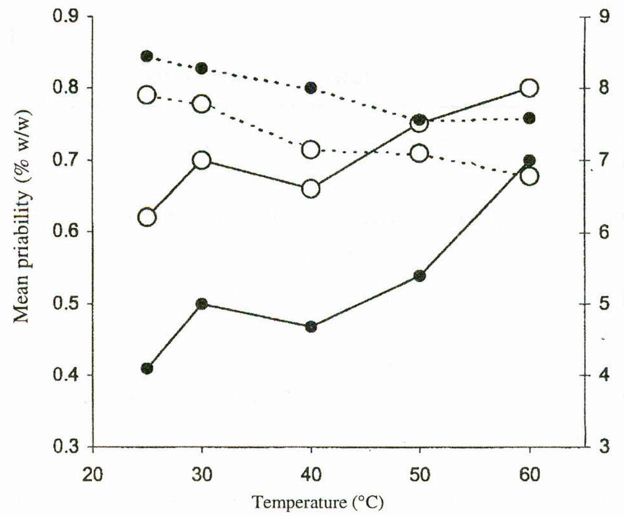

Fig 1. The effect of temperature of friability and hardness of lactose tablets.

Hardness/starch mucilage-----●-------;Hardness/water------o-------;
Friability/starch mucilage-----●-------;Friability/water------o-------;

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