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INFLUENCE OF STARCH STEEPING PERIOD ON DIMENSIONLESS DISINTEGRATION VALUES OF A PARACETAMOL TABLET FORMULATION

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Abstract: In this study, tapioca starches obtained after different steeping periods, i.e. TS 24, TS 48 and TS 72, were used as disintegrants with corn starch BP as the standard disintegrant in a paracetamol tablet formulation. Two dimensionless disintegration quantities, T_N and T_C were used in the determination of the influence that steeping period of starch disintegrant would have on the crushing strength friability – disintegration time ratio (CSFR/DT). These quantities were used to assess the influence of steeping period, relative density and disintegrant concentration on CSFR/DT as well as to compare disintegrant efficiency. The results suggest that the CSFR/DT is more dependent on the disintegrant concentration than on steeping period and relative density. The study further showed that TS 72 is a more reliable disintegrant because its activity would not be influenced by changes in relative density of tablets. This work concludes that the T_N would be more useful for quantitative assessment while T_C is more relevant for qualitative assessment.

Keywords: tapioca starch, steeping period, disintegrant, crushing strength – friability/ disintegration time ratio

Disintegrating agents are added to tablets to promote breakup of the tablets when placed in an aqueous environment, in order to increase the surface area of the tablets for release of the drug. Disintegrants can act by swelling in the presence of an aqueous phase to burst open the tablet. Traditionally, starch has been the disintegrant of choice in tablet formulations, and is still widely used, but several new disintegrants like cellulosic agents, hydrogels, yeast cells, surfactants etc., are now being employed (1, 2). Starch, which is still the commonest disintegrant, is believed to act by swelling (3). Formulation and processing variables like the mode of addition of disintegrants; relative density/compression pressure, disintegrant concentration, size and type have been shown to have significant effects on disintegrant properties – e. g. disintegration time and the crushing strength – friability/disintegration time ratio, of formulated tablets (4-6).

The crushing strength – friability to disintegration time ratio (CSFR/DT) is an index of measuring tablet quality which is not only measuring the crushing strength (tablet strength) and friability (tablet weakness), but also, in addition, evaluates the negative effects of these two parameters on the disintegration time of the tablets (4, 7). In comparing the efficiency of different disintegrants, Vadas et al. (8) defined two dimensionless constants T_N and T_C to quantify the activities of disintegrants using the disintegration times of tablets as the test parameter. T_N facilitates comparison of disintegration time within a given tablet formulation, while T_C is used to evaluate a test disintegrant's efficiency using a standard disintegrant as a control.

In this work, CSFR/DT is the test parameter and T_N is defined as:

$$T_N = T_{sample\ n} / T_{sample\ 1} \qquad \text{(Eq. 1)}$$

where $T_{sample\ n}$ is the CSFR/DT of the nth member of a series of tablets all containing the same disintegrant with different relative densities, and $T_{sample\ 1}$ is the CSFR/DT of the tablet processed at the lowest relative density within the series. The CSFR/DT must be at the same disintegrant concentration. The second dimensionless quantity, T_C is defined as:

$$T_C = T_{sample} / T_{control} \qquad \text{(Eq. 2)}$$

where T_{sample} is the CSFR/DT of a tablet containing a specific disintegrant with a given relative density and $T_{control}$ is the CSFR/DT of a tablet which contains the standard disintegrant and have the same relative density with the tablets containing the test disintegrant. Both T_{sample} and $T_{control}$ must be at the same disintegrant concentration.

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The aims of this paper were to find out whether the steeping period used for extracting tapioca starch would affect the disintegrant ability of the starch, and to relate the above two defined dimensionless quantities to the application of CSFR/DT in evaluation of disintegrants in tablet formulations. This was with a view to reveal information concerning the performance of the starch disintegrant under test. Our aim was also to determine whether seemingly obvious similarities/differences in observed results would give room for a prediction of the behavior of a test disintegrant in a formulation. Tapioca starch was used for this type of study because of its high plasticity (9) and good swelling properties (10).

EXPERIMENTAL

Materials

The materials used were: paracetamol powder BP, corn starch BP and acetone (BDH Chemicals Ltd., Poole, UK), lactose BP (AB Knight and Co., London, UK), gelatin BP (Type A), (Hopkin and Williams, UK), and tapioca starch extracted from *Manihot utillisima* in our laboratory.

Extraction of tapioca starch

The starch was extracted from root tubers of cassava (*Manihot utillisima* L.) according to the method of Alebiowu (9) using established procedures (11). Cassava tubers were peeled, washed and cut to small pieces. These small pieces were then soaked in distilled water for different periods of time i.e. 24 h, 48 h and 72 h to give three batches (TS 24, TS 48, and TS 72). At the end of the steeping period, the softened tubers were milled to a pulp, and more distilled water was added to give dilute slurry which was sieved using mesh size 100 µm. This process was repeated three times until starch was fully extracted from the tubers as confirmed by iodine test on the remaining chaff, which was negative. The extracted starch was dried at 50°C in a hot air oven (Gallenkamp, Model OV-335, Vindon Scientific Ltd, Oldham, U.K) for 72 h. The dried mass was powdered in a laboratory mill (Christy and Norris Ltd; Chelmsford, UK). The starch was then passed through a no. 120 mesh sieve (125 µm) and stored in an amber colored screw capped bottle before use.

Preparation of gelatin solution

A gelatin solution was prepared by weighing the required amount of gelatin granules that would produce a 4.0% w/w concentration of starch disintegrant in the formulation. The weighed amount of gelatin was suspended for 10 min in distilled water in a beaker with continuous stirring to allow hydration before heating. The solution was used while still hot for more effective binding.

Swelling and water retention capacity tests

The method described by Bowen and Vadino (12) was used for swelling capacity determination. The method of Ring (13) was used for water retention capacity determination. Both determinations were done in triplicate. Swelling capacity and water retention capacity values are shown in Table 2. Statistical analysis (standard error of the mean at a confidence level of 0.95) of the results in this Table revealed low variability between them.

Preparation of granules

The wet granulation method of massing and screening was used. Three hundred gram batches of formulation mixtures of paracetamol, lactose and starch (Table 1) containing various concentrations of starch disintegrants (1% w/w, 3% w/w and 5% w/w) were prepared by dry mixing the required quantity of paracetamol, lactose and each starch for 5 min in a planetary mixer (Hobart Canada Inc., Don Mill, ON, Canada). They were then moistened with gelatin binder solution to yield 4% w/w gelatin in the final dried granulation. The resulting wet masses were granulated by passing them manually through a 12 – mesh (1400 µ) sieve, dried at 60°C for 6 h, and then resieved through a 16 – mesh (1000 µ) sieve. Particle densities were determined using the pycnometer method with acetone as the displacement fluid.

Preparation of tablets

Quantities (550 mg) of granules from each batch were compressed into tablets with three predetermined loads (25, 50 and 75 $kpcm^{-2}$) on a Pharma 100 multi-station rotary tablet press (Korsch Maschinen Fabrik, Berlin, Germany) with a 10.5 mm die and flat faced punch assembly. A set of tablets were produced from each pressure. After ejection, the tablets were stored in airtight containers to allow for elastic recovery and hardening, and prevent falsely low yield values before the tablets were subjected to analysis. Their masses (w) and dimensions were then determined to within ±1 mg and 0.01 mm, respectively, and their relative density was calculated using the equation;

$$RD = w/V_t\rho_s \qquad \text{(Equation 3)}$$

where V_t is the volume (cm^{-3}) of the tablet and ρ_s is the particle density of the solid material. The volume reduction which increased with successive increase

in compression pressure led to variable relative density.

Disintegration test

Tablet disintegration time (DT) was determined in distilled water at 37 ± 0.5°C in a BP Manesty (Manesty Machines, UK) disintegration test unit. The tablets were placed on the wire mesh just above the surface of the distilled water in the tube. The time taken for each tablet to disintegrate and all the granules to go through the wire mesh was recorded. The results were expressed as an average of three determinations.

Determination of tablet crushing strength and friability

A Monsanto hardness tester (Monsanto Chemical, USA) was used at room temperature to determine the load required to diametrically break the tablets (crushing strength) into two equal halves. Tablets with signs of lamination or capping were not used. The percent friability of the tablets was determined using a Roche friabilator (Erweka Apparatebau, Germany) operated at 25 rev×min^{-1} for 4 min; ten tablets were used at each relative density. The average of three determinations was taken for the crushing strength and friability values.

RESULTS AND DISCUSSION

Physical properties

Table 3 shows the effect of relative density on the following physical properties – friability, crushing strength and disintegration time of the tablets prepared. It also shows the effect that the concentrations of disintegrant and steeping period have on the physical properties of the tablets.

The values of friability obtained reflect a general trend of a decrease with an increase in relative density and disintegrant concentration of the tablets for all the batches. It is also seen from the Table that the friability values are starch steeping period dependent. Lower values of friability are observed for tablets containing starch disintegrant obtained at higher steeping periods. .This observation could be due to the binding ability of the starches obtained at higher steeping periods (9). This binding ability will enhance the bonding strength of the tablets, and hence reduce the friability values of the tablets.

The crushing strength values obtained were found to be relative density dependent. This could be due to the fact that with an increase in relative density, there will be more particle-particle contact and enhanced interparticulate bonding (14, 15) leading to higher crushing strength. Tablets containing the disintegrants had their crushing strengths lower than those without disintegrant at higher relative density. This could be due to the effect of the starch disintegrant acting as a binder. This action as a binder was, as a result of increased particle – particle contact, brought about by an increase in relative density. The crushing strength of tablets containing disintegrants did not reflect any particular general trend, but for tablets with TS 24 and TS 48, the rank order of crushing strength for disintegrant concentration is 1.0% > 3.0% > 5.0%, while for TS 72 and CS disintegrants, the rank order is 5.0% > 1.0% > 3.0%. These rank orders suggest a similarity in the influence of these disintegrants, i.e. TS 24/TS 48 and TS 72/CS on the crushing strength of the tablets.

Table 1. Formulae of tablets prepared*

Ingredients	Batches											
	1	2	3	4	5	6	7	8	9	10	11	12
Paracetamol	90	90	90	90	90	90	90	90	90	90	90	90
Gelatin (binder)	4	4	4	4	4	4	4	4	4	4	4	4
Lactose	5	3	1	5	3	1	5	3	1	5	3	1
TS 24	1	3	5	–	–	–	–	–	–	–	–	-
TS 48	–	–	–	1	3	5	–	–	–	–	–	–
TS 72	–	–	–	–	–	–	1	3	5	–	–	-
CS	–	–	–	–	–	–	–	–	–	1	3	5

* The values are expressed as percentages.

The disintegration time of the tablets was found to be dependent on the relative density of the tablets and the disintegrant concentration for all the batches. With the increase in relative density an increase is observed for the disintegration time. This could be due to the reason given earlier, i.e. the increased relative density leads to enhanced interparticulate bonding (14, 15). This would reduce the penetration of the tablet matrix by the disintegration fluid, hence a reduced disintegration time with increased relative density. Table 3 shows that generally the disintegrant concentration considerably influenced the disintegration time, with lower disintegration times obtained for higher disintegrant concentration. This is not strange, since a higher starch disintegrant concentration would lead to a higher swelling of the tablet matrix and faster breaking of the tablet (16, 17). The starch steeping period/disintegrant type also affected the disintegration times of the tablets with the following rank order: TS 48 < CS = TS 72 < TS 24. This rank order could be due to the swelling ability and water retention capacity of the starches. Swelling has been confirmed to be one of the mechanisms of disintegrant action, but it should be noted that the reduction in disintegration time with an increase in disintegrant concentration is higher for tablets containing starch disintegrants with lower steeping periods, i.e. TS 24 and TS 48, than for those containing starch disintegrant with higher steeping period (TS 72) and CS. This could be due to their swellability and water retention capacity (Table 2). The higher swellability and water retention capacity of TS 72 and CS could have contributed to the lower reduction in the disintegration time of tablets containing them. Higher swellability of starch disintegrants has been implicated in clogging of pores in a tablet matrix (16). This clogging effectively reduces capillarity, hence the decrease and reduction observed in disintegration of tablets.

Crushing strength friability/disintegration time ratio

The CSFR/DT results are presented in Table 4. The Table shows the effects of disintegrant concentration, relative density and steeping period on the CSFR/DT. Generally, the CSFR/DT increased with an increase in relative density. This implies that the increase in relative density favors the tablet mass, since a higher value of CSFR/DT indicates a better balance between the tablet's binding and disintegrant properties (7). Though, this is not in agreement with earlier observations, it could be due to the increasingly high disintegration time which might have resulted from the activation of the starch disintegrant binding ability during wet granulation (on application of moisture and heat), which would assist in not only breaking down the tablets but also in bonding the tablet mass (18). The rank order of the effect of disintegrant concentration on the CSFR/DT for the different disintegrants is, for TS 24 – 1.0% < 3.0% = 5.0%, while for TS 48, TS 72 and CS is – 1.0% < 3.0% << 5.0%. These rank orders are in agreement with earlier observation (4) and implie that higher concentration of disintegrant will generally lead to a better balance between binding and disintegrant properties of a tablet mass.

Dimensionless disintegration value, T_N

The CSFR/DT values were normalized to that of tablets with the lowest relative density (0.880) in each series according to Equation 1, in order to facilitate comparison among tablets of different compositions. The values of T_N are plotted in Figure 1. A direct comparison of trends in tablet behavior is possible with a dimensionless quantity such as T_N. It particularly shows the influence of formulation and processing variables on the tablet's CSFR/DT. In using T_N to quantify the influence of a variable on CSFR/DT, the CSFR/DT of the first tablet of the series (tablet with the lowest relative density) becomes unity. Values of

Table 2. Swelling and water retention capacities of starches

Starch	Swelling capacity (V_2/V_1)[a]	Water retention capacity (m_1/m_2)[a]
TS 24	1.42 ± 0.03	3.31± 0.13
TS 48	1.56 ± 0.07	3.38 ± 0.06
TS 72	1.60 ± 0.03	3.51 ± 0.11
CS	1.57 ± 0.01	3.06 ± 0.09

[a] The mean ± SEM, n = 3. V_1, V_2 = initial and final volume (after swelling) of starch powder. w_1, w_2 = weight of residue before and after drying at 70°C.

Table 3. Physical properties of tablets

Disintegrant	Concentration (% w/w)	Relative density	Friability (%) (± SEM)	Crushing strength (kg) (± SEM)	Disintegration Time (min) (± SEM)
TS 24	1.0	0.880	1.12 (0.16)	1.62 (0.11)	13.51 (0.35)
		0.900	0.93 (0.11)	3.97 (0.09)	32.73 (0.51)
		0.912	0.48 (0.03)	8.91 (0.15)	43.86 (0.23)
		0.925	0.21 (0.07)	14.17 (0.22)	70.50 (0.48)
		0.936	0.10 (0.02)	9.60 (0.19)	93.03 (0.41)
	3.0	0.880	0.82 (0.08)	4.98 (0.06)	8.57 (0.19)
		0.900	0.60 (0.09)	6.40 (0.13)	11.62 (0.25)
		0.912	0.46 (0.10)	7.25 (0.09)	16.49 (0.21)
		0.925	0.36 (0.07)	7.50 (0.11)	20.54 (0.49)
		0.936	0.14 (0.02)	9.05 (0.18)	28.18 (0.33)
	5.0	0.880	0.83 (0.10)	5.90 (0.09)	9.36 (0.33)
		0.900	0.76 (0.11)	6.34 (0.13)	10.05 (0.10)
		0.912	0.56 (0.07)	6.70 (0.15)	12.70 (0.22)
		0.925	0.48 (0.06)	7.02 (0.10)	14.51 (0.18)
		0.936	0.35 (0.08)	7.25 (0.26)	18.55 (0.29)
TS 48	1.0	0.880	0.60 (0.09)	1.32 (0.06)	4.16 (0.11)
		0.900	0.50 (0.10)	5.56 (0.12)	6.58 (0.09)
		0.912	0.38 (0.08)	8.25 (0.08)	15.57 (0.25)
		0.925	0.18 (0.02)	11.50 (0.17)	25.00 (0.32)
		0.936	0.11 (0.02)	14.56 (0.11)	32.07 (0.28)
	3.0	0.880	0.57 (0.07)	2.48 (0.02)	1.41(0.03)
		0.900	0.48 (0.05)	6.99 (0.13)	4.20 (0.15)
		0.912	0.30 (0.07)	9.50 (0.21)	7.48 (0.09)
		0.925	0.19 (0.07)	12.15 (0.18)	12.29 (0.13)
		0.936	0.11 (0.03)	14.17 (0.16)	20.84 (0.18)
	5.0	0.880	0.62 (0.10)	3.24 (0.05)	1.29 (0.05)
		0.900	0.49 (0.06)	6.50 (0.15)	3.06 (0.05)
		0.912	0.38 (0.08)	8.12 (0.23)	4.35 (0.12)
		0.925	0.12 (0.02)	11.12 (0.17)	6.46 (0.09)
		0.936	0.07 (0.02)	12.41 (0.19)	8.29 (0.17)
TS 72	1.0	0.880	0.49 (0.08)	2.38 (0.11)	4.89 (0.03)
		0.900	0.33 (0.02)	5.07 (0.09)	8.48 (0.15)
		0.912	0.19 (0.02)	9.81 (0.17)	0.83 (0.13)
		0.925	0.11 (0.02)	12.73 (0.15)	30.95 (0.36)
		0.936	0.05 (0.01)	17.16 (0.20)	41.53 (0.27)
	3.0	0.880	0.49 (0.02)	3.40 (0.10)	2.04 (0.02)
		0.900	0.39 (0.03)	7.30 (0.08)	4.78 (0.17)
		0.912	0.18 (0.02)	9.43 (0.15)	12.75 (0.14)
		0.925	0.09 (0.01)	11.74 (0.11)	29.28 (0.20)
		0.936	0.04 (0.01)	14.10 (0.09)	35.10 (0.31)
	5.0	0.880	0.68 (0.06)	4.05 (0.05)	1.94 (0.06)
		0.900	0.30 (0.03)	6.51 (0.21)	6.30 (0.19)
		0.912	0.18 (0.02)	10.02 (0.17)	9.53 (0.15)
		0.925	0.10 (0.01)	13.79 (0.24)	13.22 (0.20)
		0.936	0.05 (0.01)	18.83 (0.21)	18.04 (0.29)
CS	1.0	0.880	0.44 (0.09)	2.12 (0.02)	4.05 (0.12)
		0.900	0.35 (0.09)	4.61 (0.11)	7.08 (0.10)
		0.912	0.22 (0.05)	9.34 (0.19)	18.66 (0.23)
		0.925	0.13 (0.03)	12.70 (0.15)	25.36 (0.19)
		0.936	0.05 (0.01)	15.96 (0.22)	33.45 (0.27)
	3.0	0.880	0.62 (0.08)	3.05 (0.08)	1.39 (0.02)
		0.900	0.42 (0.09)	7.15 (0.13)	3.55 (0.15)
		0.912	0.28 (0.05)	9.50 (0.11)	6.85 (0.11)
		0.925	0.17 (0.02)	10.93 (0.20)	12.10 (0.11)
		0.936	0.05 (0.01)	14.27 (0.18)	28.65 (0.28)

Table 3. cont.

Disintegrant	Concentration (% w/w)	Relative density	Friability (%) (± SEM)	Crushing strength (kg) (± SEM)	Disintegration Time (min) (± SEM)
	5.0	0.880	0.72 (0.08)	3.58 (0.05)	1.98 (0.08)
		0.900	0.40 (0.05)	5.97 (0.13)	4.94 (0.15)
		0.912	0.21 (0.02)	9.11 (0.20)	7.61 (0.10)
		0.925	0.11 (0.02)	14.05 (0.17)	14.76 (0.25)
		0.936	0.05 (0.01)	17.38 (0.13)	18.58 (0.13)
No disintegrant		0.880	1.12 (0.10)	1.87 (0.15)	23.85 (0.36)
		0.900	0.81 (0.06)	3.12 (0.10)	37.32 (0.29)
		0.912	0.69 (0.08)	9.64 (0.11)	55.67 (0.41)
		0.925	0.41 (0.04)	18.29 (0.20)	89.79 (0.35)
		0.936	0.37 (0.07)	37.55 (0.36)	121.54 (0.49)

Table 4. Crushing strength friability/disintegration time ratio (CSFR/DT) as a function of relative density and disintegrant concentration

Disintegrant	Relative density	CSFR/DT		
		1% w/w	3% w/w	5% w/w
No disintegrant	0.880	0.070	–	–
	0.990	0.103	–	–
	0.912	0.251	–	–
	0.925	0.497	–	–
	0.936	0.835	–	–
TS 24	0.880	0.107	0.709	0.759
	0.990	0.130	0.918	0.830
	0.912	0.423	0.956	0.942
	0.925	0.957	1.014	1.004
	0.936	2.107	2.293	1.117
TS 48	0.880	0.528	3.085	4.051
	0.900	1.690	3.464	4.332
	0.912	1.962	4.234	4.912
	0.925	2.555	4.943	14.345
	0.936	4.099	6.181	21.385
TS 72	0.880	0.993	3.401	3.040
	0.900	1.812	3.916	3.444
	0.912	2.479	4.096	5.841
	0.925	3.739	4.455	10.431
	0.936	8.264	10.043	20.876
CS	0.880	1.190	3.504	2.511
	0.900	1.860	4.795	2.591
	0.912	2.275	4.953	5.700
	0.925	3.852	5.314	8.654
	0.936	7.952	9.962	18.708

$T_N > 1$ are indicative of a beneficial effect of the variable on CSFR/DT, while values of $T_N < 1$ indicate a detrimental effect on CSFR/DT (higher values of CSFR/DT implies a better balance between binding and disintegrant properties).

In addition to presenting a direct comparison of trends, it was shown how the different disintegrants are sensitive to the relative density of tablets and disintegrant concentration (two variables used in this work). Figure 1 as an example, shows the sensitivity of the disintegrants to concentration and relative density of tablets. Inclusion of TS 24 in a tablet mass resulted in a high sensitivity of CSFR/DT to disintegrant concentration and relative density at 1.0% concentration whereas at 3.0% and 5.0% concentrations, a poor sensitivity to the two variables is seen. From Figure 1, it is seen that TS 48, TS 72 and CS have similar sensitivities to both disintegrant concentration and relative density in the following rank order 1.0% > 5.0% and 3.0%. Although, this rank order does not show which disintegrant is more sensitive to these two variables, it implies that CSFR/DT is disintegrant concentration dependent and confirms it. The values obtained from the application of T_N suggest that T_N would be useful for quantitative assessment of the disintegrants.

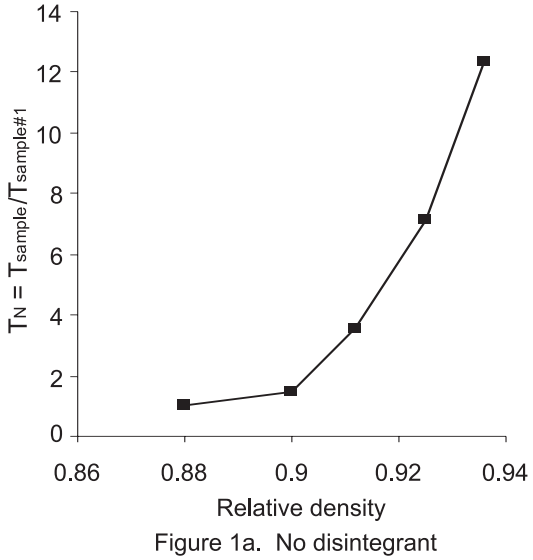

Figure 1a. No disintegrant

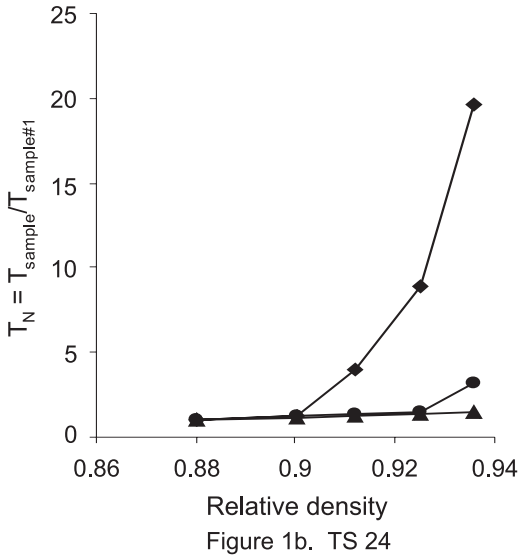

Figure 1b. TS 24

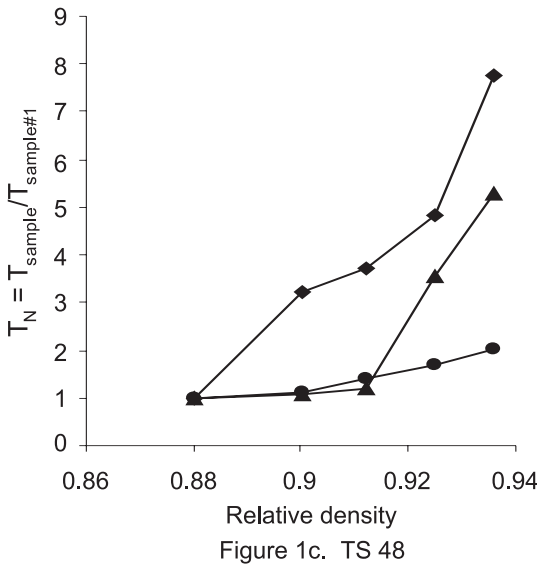

Figure 1c. TS 48

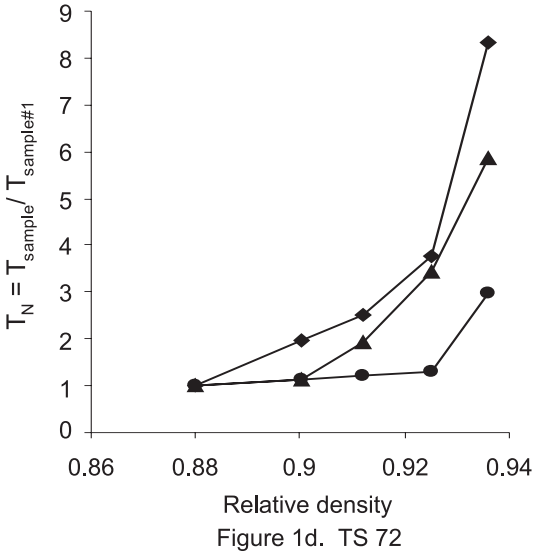

Figure 1d. TS 72

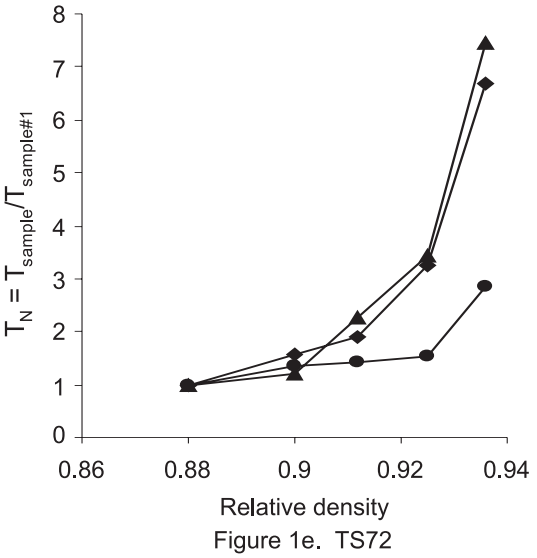

Figure 1e. TS72

Figure 1. Plots of the dimensionless disintegration quantity T_C as a function of relative density and disintegrant concentration for paracetamol tablets containing (a) no disintegrant (b) TS 24 (c) TS 48 (d) TS 72 (e) corn starch. Key: (■) 1% w/w disintegrant; (●) 3% w/w disintegrant; (▲) 5% w/w disintegrant.

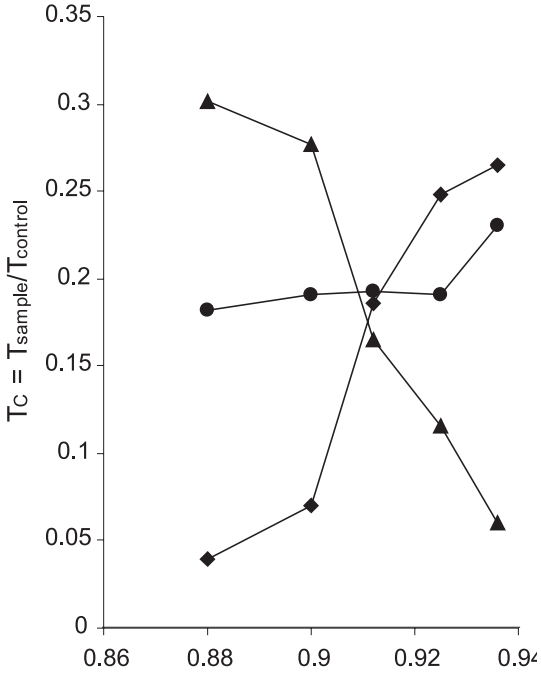

Figure 2a. TS 24

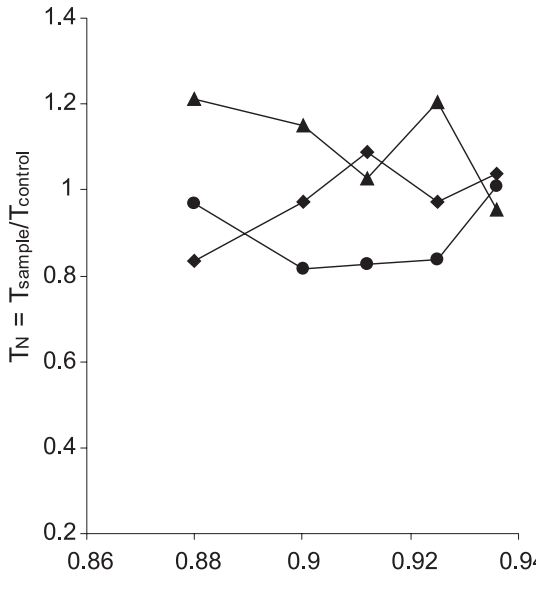

Figure 2c. TS 72

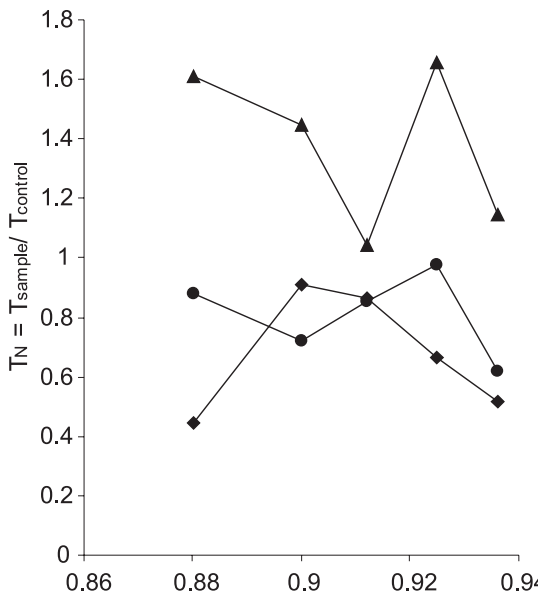

Figure 2b. TS 48

Figure 2. Plots of the dimensionless disintegration quantity T_N as a function of relative density and disintegrant concentration for paracetamol tablets containing (a) TS 24 (b) TS 48 (c) TS 72. Key: (■) 1% w/w disintegrant; (●) 3% w/w disintegrant; (▲) 5% w/w disintegrant.

Dimensionless disintegration value, T_C

In the second dimensionless value, i.e. T_C, the CSFR/DT of tablets containing the tapioca starch disintegrants, is normalized to that of tablets containing corn starch BP as disintegrant. The values obtained allow one to quantitatively assess and qualitatively compare disintegrant efficiency.

Plots of T_C against relative density are shown in Figure 2. The first dimensionless quantity T_N allows direct comparison of disintegration behavior of tablets with the same formula and different relative density, while T_C gives a clear indication of disintegrant performance (qualitative assessment) with respect to concentration, i.e. whether the tablet is effectively designed to give a better balance between binding and disintegrant properties of the tablet at particular disintegrant concentration. It also allows one to evaluate the performance of a test disintegrant relative to a standard disintegrant.

To demonstrate the importance of T_C, the behavior of tablets (containing tapioca starch disintegrants) at a relative density of 0.90 is compared. At 1.0% disintegrant concentration, the T_C of tablet containing TS 24 is 0.070, i.e. the CSFR/DT of the tablet is 7% of the standard matrix at 1.0% disintegrant concentration. The tablet containing TS 48 disintegrant has a T_C value of 0.909 while that of TS 72 disintegrant is 0.974. Clearly the most efficient disintegrant at these conditions, i.e. relative density of 0.90 and 1.0% disintegrant concentration, is TS 72. At 3.0% disintegrant concentration, the T_C values for the three different disintegrants, i.e. TS 24, TS 48 and TS 72, is 0.191, 0.723 and 0.817, respectively. This shows that tablets containing TS 72 have a better balance between tablet strength and disintegration time at the stated conditions. However, at 5.0% disintegrant concentration, the T_C values are 0.277, 1.448 and 1.151 for TS 24, TS 48 and TS 72, respectively. This observation suggests that T_C has a particular steeping period at which it will be optimal. This observation at 5.0% disintegrant concentration was not only made for relative density of 0.90 but for all other relative densities studied in this work.

Apart from the usefulness of T_C in determining the above, it will assist in understanding the level of dependence of CSFR/DT on relative density of the tablet and concentration of disintegrant. It was stated earlier that CSFR/DT is dependent on both variables, however, the plots presented in Figure 2 (especially 2b and 2c) do not reflect a distinct dependence on the relative density of the tablets but rather show that T_C is concentration dependent Furthermore, for the three different disintegrants, it is observed (Figure 2) that the effect which the disintegrant concentration has on T_C is not uniform for the three disintegrants. For TS 24 at 1.0% disintegrant concentration the T_C increases with an increase in relative density, whereas at 5.0% disintegrant concentration the T_C is reduced. But at 3.0% concentration a clear-cut difference in T_C values is not fully reflected except at the highest relative density employed. For TS 48 and TS 72, at each of the disintegrant concentrations studied, no particular trend for the T_C values is observed with an increase in relative density.

On examining the T_C values of CSFR/DT for the tablets containing the tapioca starch disintegrants, it is seen that though the T_C values of tablets with TS 48 as starch disintegrant has higher values at 5.0% disintegrant concentration than other tablets, but the tablets with TS 72 as disintegrant have T_C values that show more of less dependence on relative density (Figure 2). This less dependence on relative density is common to all the disintegrant concentrations employed in this work. Hence, it could be inferred that TS 72 is a more reliable disintegrant than TS 24 and TS 48 when used in a tablet formulation, because its disintegrant activity would not be influenced by changes in pressure especially during industrial tablet manufacturing, where changes in the machine cam tracks may affect the pressure (relative density) setting of the machine.

CONCLUSIONS

It can be concluded from the results in this study that the relative density of tablets, concentration of disintegrant and the steeping period of starch will have noticeable effects on the friability, crushing strength and disintegration time of tablets produced. The crushing strength result presented suggests that there could be a similarity in the influence of disintegrants on the crushing of tablets.

The use of the dimensionless quantities for the assessment of the disintegrant activity suggests that a disintegrant would have optimal activity at a particular steeping period (disintegrant type) and relative density of tablets (as shown by TS 48 at 5.0% disintegrant concentration and relative density of 0.90). The results also imply that TS 72 would serve as a better disintegrant compared to TS 24 and TS 48 if used in a tablet formulation. Furthermore, the values obtained with the application of T_N suggest that CSFR/DT is concentration and relative density dependent, e.g. at 1.0% disintegrant concentration, a higher sensitivity was observed, while at 3.0 and 5.0% disintegrant concentrations a lower sensitivity

was seen. For the values obtained with the application of T_C, steeping period and disintegrant concentration were observed to affect CSFR/DT. These, i.e. T_C and T_N values, imply that obvious similarities/differences in observed results would not be appropriate for predicting the behavior of a test disintegrant in a formulation.

Also, this type of analytical method, i.e. the use of dimensionless disintegration quantities, would be useful in quantitative and qualitative assessment of new disintegrants/excipients in optimization studies and may allow selecting appropriate processing and formulation variables in order to achieve an optimal result for a particular disintegrant or excipient when used in a formulation.

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