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Uptake of water by excipients in tablets

Lucy S.C. Wan and Kanneganti P.P. Prasad

Department of Pharmacy, National University of Singapore, Singapore (Singapore)

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Summary

Disintegrants such as sodium starch glycolate (NaSt glycolate), crospovidone (PVPP) and silicon dioxide (SiO_2) play an active part in influencing water uptake and disintegration time (*DT*) of sulphanilamide tablets containing methylcellulose (MC) of varying viscosity grade as a binder. The disintegrants used were at the 1.25%, 2.50% and 5% level. The DT of tablets containing NaSt glycolate decreased with an increase in the viscosity of MC due to enhanced water uptake. Tablets without MC but only the drug and NaSt glycolate were observed to have a higher DT and lower water uptake at higher concentrations of the disintegrant. With PVPP, the DT increased with increasing viscosity of MC. This occurs despite an increase in water uptake by tablets containg higher viscosity MC. For tablets containing SiO_2 and MC, DT is extremely high. In the absence of MC, water uptake is slightly higher with the higher concentration of SiO_2 but DT still remained high. Water uptake alone does not determine the disintegration process. The choice of excipients, especially binders such as methylcellulose, plays a crucial role in influencing disintegrant action.

Introduction

Cellulose ethers are widely used as tablet excipients. Methylcellulose (MC), a hydrophilic colloid used as a binder, has properties such as thickening, thermal gelation, film formation and adhesion (Greminger et al., 1980) which can influence the water penetration, disintegration, dissolution and mechanical strength of tablets. One of the mechanisms suggested for the action of tablet disintegrants is the phenomenon of swelling following the uptake of water by the tablet (Lowenthal, 1973). Disintegrants such as microcrystalline cellulose and cross-linked CMC when used in hydrophilic matrix tablets containing water-soluble polymers tend to expand the gelatinous layer and cause more drug to be released in the early stages of dissolution (Alderman, 1984). On contact with water, MC hydrates readily and swells (Wan and Prasad, 1987a). This swelling effect and the subsequent adhesive action can affect the disintegrant action. Earlier studies were focussed on the action of different viscosity grade MC on the water uptake, disintegration and dissolution properties of tablets containing disintegrants such as maize starch (Wan and Prasad, 1986a and b), cross-linked sodium carboxymethylcellulose (Wan and Prasad, 1988a) and microcrystalline cellulose (Wan and Prasad, 1988a).

Correspondence: L.S.C. Wan, Department of Pharmacy, National University of Singapore, 10 Kent Ridge Crescent, Singapore 0511, Singapore.

The purpose of this investigation was to examine the action of sodium starch glycolate (NaSt glycolate), crospovidone (PVPP) and colloidal silicon dioxide (SiO_2) on the water uptake and disintegration of tablets containing various viscosity grades of MC.

Materials and Methods

Materials

Sulphanilamide (B.P.) fine powder was used as a model drug. Disintegrants used were sodium starch glycolate (Primojel; Avebe, Foxhol, The Netherlands), crospovidone NF XV (Polyplasdone XL; GAF, New York, NY, U.S.A.) and colloidal silicon dioxide (Aerosil 200; Degussa, Frankfurt, F.R.G.). Methylcellulose (Tokyo Kasei, Tokyo, Japan) used as a binder was of different viscosity grades: 20–30, 80–120, 350–550, 800–1200, 4000 and 7000–10,000 cps.

Preparation of tablets

Tablets were prepared according to the procedure described in an earlier publication in this journal (Wan and Prasad, 1988a). The drug, disintegrant and binder were mixed together and moistened with distilled water. All disintegrants were incorporated at 3 fixed concentrations: 1.25%, 2.5% and 5%.

Water penetration into tablets

The method adopted was the same as described earlier (Wan and Prasad, 1986a). The tablet was placed on a sintered glass filter connected to a horizontal graduated capillary containing distilled water. Volume of water (V) taken up by the tablet was measured by noting the change in the capillary reading with time.

Disintegration

The disintegration time (DT) of individual tablets at $37 \pm 0.5\,^{\circ}C$ was determined using a B.P. disintegration test apparatus (Van-Kel, model 71, U.S.A.) without the disc. The mean $\pm$ S.D. of 5 replicates were calculated.

Results and Discussion

Sodium starch glycolate

Tablets containing sulphanilamide alone without any excipients, did not disintegrate even after 30 min (Wan and Prasad, 1986a). Addition of 1.25% NaSt glycolate resulted in the DT being reduced to 10 s. However, the use of 2.50% and 5% NaSt glycolate led to slightly higher disintegration times of 18 and 27.2 s, respectively (Table 1). The penetration of water into these tablets is shown in Fig. 1. The concave nature of the plots of V^2 vs time is thought to be due to the slow wetting rate of the disintegrant particles, a similar case being observed when 10% starch was used as the disintegrant (Wan and Prasad, 1986a). During the first 5 s of water uptake, there is no difference in the rate of water penetration into tablets containing various amounts of NaSt glycolate. After 10 s, however, the value of V^2 for tablets containing 1.25% and 2.50% NaSt glycolate, respectively, is about 8 times that of tablets containing sulphanilamide alone (Table 1). Tablets containing 5% NaSt glycolate have a V^2 value that is 6 times higher. After 30 min, uptake of water by tablets formulated with 1.25%, 2.5% and 5% NaSt glycolate is more than 30, 20 and 15 times, respectively, in comparison to formulations that do not have any disintegrant. This clearly demonstrates the affinity of NaSt glycolate for water.

The entry of water into tablets containing 1.25% NaSt glycolate and 2% MC was rapid, the rate being influenced by the viscosity grade of the MC. A linear relationship between V^2 and t in accordance with the Washburn equation (Washburn, 1921) was observed for the low viscosity grade MC (Fig. 2). The high viscosity grades showed deviations from linearity especially after water penetration had proceeded for some duration of time. This could possibly be due to the swelling action of these MC. It was discussed earlier (Table 1) that small amounts of NaSt glycolate improve water uptake properties of the tablet to a great extent by virtue of the affinity of the disintegrant for water. NaSt glycolate facilitates the entry of water into the tablet interior and this water is utilised by the MC to hydrate. Higher viscosity MC polymers have a greater capacity to hydrate.

TABLE 1

Water uptake into and disintegration of sulphanilamide tablets containing sodium starch glycolate, crospovidone, colloidal silicon dioxide in the absence of methylcellulose

Disintegrant conc. (%)	V^2 ($\times 10^{-4}$ cm^6)			Disintegration time (s)
	10 s	20 s	30 s	
NaSt glycolate				
0	5.36 ± 0.19	9.38 ± 0.22	10.35 ± 0.24	**
1.25	40.25 ± 3.94	190.07 ± 10.33	*	10 ±0
2.50	42.09 ± 2.96	110.61 ± 4.31	199.10 ± 8.95	18 ±0
5	32.25 ± 3.55	80.53 ± 11.78	148.57 ± 17.26	27.20 ± 0.84
PVPP				
1.25	66.90 ± 4.56	80.22 ± 2.60	86.74 ± 2.52	5.80 ± 0.88
2.50	119.35 ± 5.95	138.48 ± 3.70	148.20 ± 2.59	6.00 ± 0.71
5	186.53 ± 23.23	232.62 ± 15.55	*	6.00 ± 0.71
SiO_2				
1.25	11.00 ± 2.32	12.32 ± 2.47	13.10 ± 2.27	**
2.50	8.73 ± 1.84	13.06 ± 1.69	14.98 ± 1.04	**
5	24.53 ± 3.71	29.88 ± 2.90	30.60 ± 3.05	**

* Water penetration measurements were discontinued as uptake exceeded capacity of equipment.
** Disintegration test not completed as *DT* exceeds 1800 s.

Thus tablets containing the higher viscosity grade MC also have higher water uptake (Fig. 2).

Water uptake by tablets containing 2.5% NaSt glycolate and 2% MC was rapid. The rate of penetration was at least twice as high as when 1.25% NaSt glycolate was used. Again, tablets

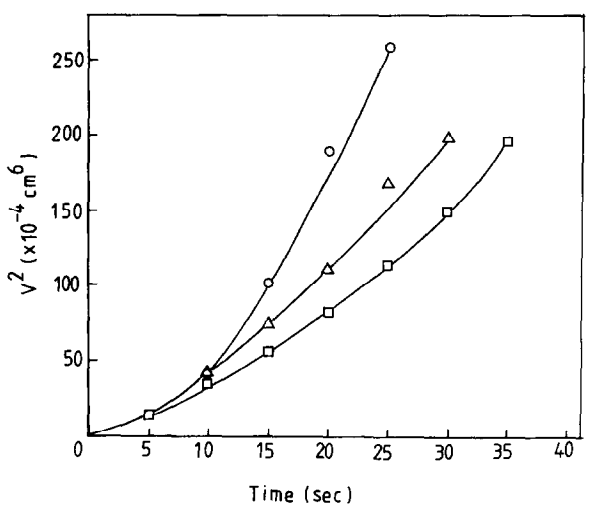

Fig. 1. Water penetration into sulphanilamide tablets containing different amounts of NaSt glycolate in the absence of methylcellulose: ○, 1.25%; △, 2.50%; □, 5%.

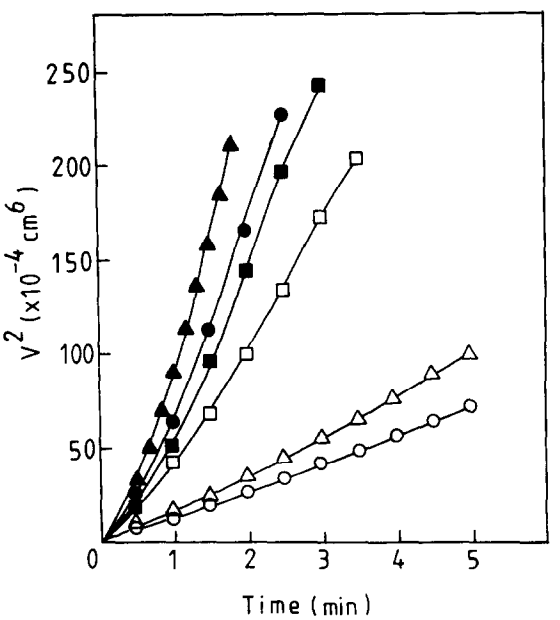

Fig. 2. Penetration of water into sulphanilamide tablets formulated with 1.25% NaSt glycolate and 2% methylcellulose (MC) of varying viscosity: ○, MC 20–30; △, MC 80–120; □, MC 350–550; ●, MC 800–1200; ▲, MC 4000; ■, MC 7000–10,000.

containing higher viscosity grade MC exhibited higher uptake of water. The incorporation of 5% NaSt glycolate also produced similar patterns of water penetration.

An observation worth noting is that while the entry of water is reduced when 2.5% and 5% of NaSt glycolate are used in tablets which do not contain MC (Table 1), no such effect is observed when MC is present. The large amount of disintegrant available within the tablet assists rapid absorption of water by the tablet initially. MC particles in contact with this water hydrate and swell. Tablet pores may be blocked and as a result the interior could be relatively inaccessible to water. But water absorption still continues on account of the slow hydration of the MC polymer molecules, sometimes at the tablet surface.

An increase in the NaSt glycolate concentration causes increased water uptake in tablets containing different viscosity MC. In the presence of MC, adhesive forces due to NaSt glycolate do not play a dominant role in influencing water uptake.

The *DT* of tablets with 2% MC and varying amounts of NaSt glycolate decreases with increasing viscosity of the MC due to increased water uptake (Table 2). The order for *DT* is 2.5% < 1.25% < 5% for most viscosity grades of MC. Although a higher water uptake is observed for 5% NaSt glycolate, the *DT* is longer. The optimum amount of NaSt glycolate is 2.5% because at 1.25% level, the amount of disintegrant is insufficient to overcome the adhesive action of MC while at the 5% level, the adhesive effects of the disintegrant are more dominant than its disintegrating activity.

TABLE 2

Disintegration time of sulphanilamide tablets containing various viscosity grades of methylcellulose (2%) and varying amounts of NaSt glycolate

MC grade	Disintegration time (s)		
	1.25%	2.50%	5%
MC 20–30	87.20 ± 1.48	92.20 ± 2.05	69.80 ± 2.28
MC 80–120	83.20 ± 1.30	49.20 ± 0.84	61.20 ± 1.30
MC 350–550	52.60 ± 0.55	48.00 ± 1.58	107.80 ± 1.64
MC 800–1200	40.80 ± 1.30	38.60 ± 1.14	40.20 ± 0.84
MC 4000	34.20 ± 1.48	29.60 ± 1.14	44.20 ± 1.30
MC 7000–10000	50.60 ± 1.14	29.60 ± 1.82	33.60 ± 1.14

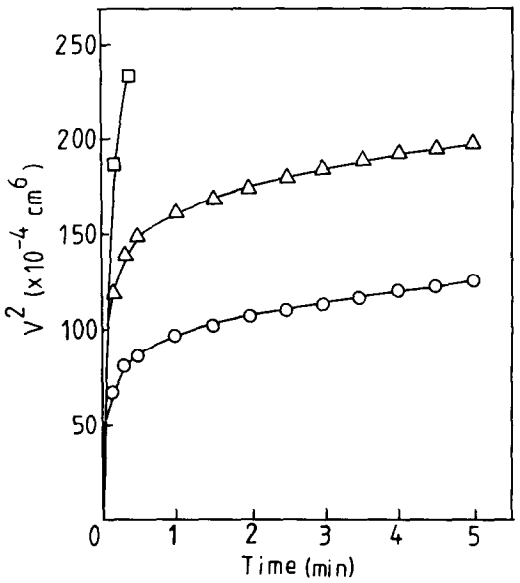

Fig. 3. Uptake of water by sulphanilamide tablets containing various amounts of PVPP in the absence of methylcellulose: ○, 1.25%; △, 2.50%; □, 5%.

Crospovidone

Fig. 3 shows the uptake of water by tablets containing different amounts of crospovidone (PVPP) and no MC. Plots of V^2 vs time are convex-shaped indicating that wetting of the material is fast. There is an initial rapid uptake followed by a slowing down of the rate of water penetration as saturation volumes are attained. Also, the V^2 values at various times are higher than those encountered when similar amounts of NaSt glycolate are used (Table 1). Unlike the case of NaSt glycolate, the use of larger amounts of PVPP results in higher water uptake. As discussed earlier, viscous forces came into action when high concentrations of NaSt glycolate were used. This was not found when high concentrations of PVPP were used. A similar observation was made in an earlier study in which tablets containing greater amounts of maize starch had higher water uptake (Wan and Prasad, 1986a).

At a fixed level of 1.25% PVPP and 2% MC, no definite relationship can be established between the viscosity of MC and the rate of water penetration (Fig. 4). In the case of the low-viscosity grades, MC 20–30, MC 80–120 and MC 350–550,

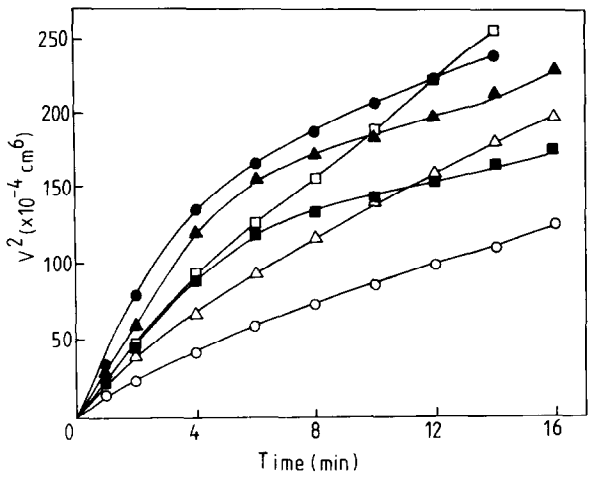

Fig. 4. Water penetration profiles of sulphanilamide tablets with 1.25% PVPP and 2% methylcellulose (MC) of varying viscosity: ○, MC 20–30; △, MC 80–120; □, MC 350–550; ●, MC 800–1200; ▲, MC 4000; ■, MC 7000–10,000.

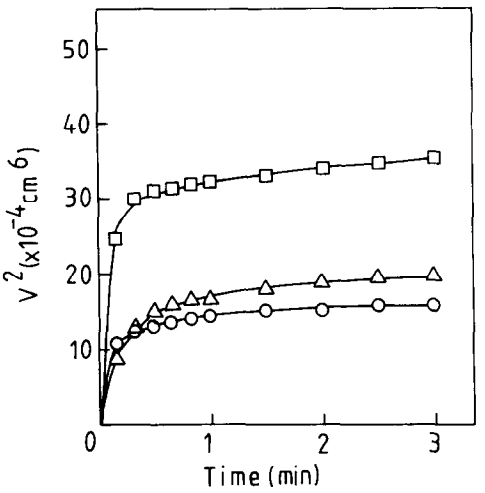

Fig. 5. Water penetration into sulphanilamide tablets containing different amounts of colloidal silicon dioxide in the absence of methylcellulose: ○, 1.25%; △, 2.50%; □, 5%.

the uptake of water increases with the viscosity of MC. But for the high-viscosity grades, MC 800–1200, MC 4000 and MC 7000–10,000, the water uptake decreases with the viscosity of MC. Extremely viscous MC in this case retards water penetration by successfully blocking tablet pores. The use of 2.50% PVPP improved the rate of water uptake. However, certain formulations containing a high viscosity MC have a lower uptake of water than those containing a low-viscosity MC. A similar trend is observed when 5% PVPP was used. An increase in the amount of PVPP resulted in an increase in water uptake for each viscosity grade of MC.

The *DT* of tablets containing PVPP and no MC is much lower than those of plain compacts of sulphanilamide. The *DT* remains almost unchanged with concentration of PVPP (Table 1), although the water uptake increases. The low value of the *DT* (about 6 s) makes it difficult to judge the small differences between these formulations. The *DT* of tablets with 2% MC and varying amounts of PVPP increases with viscosity of the MC (Table 3). This occurs despite an increased water uptake by the low-viscosity grades. For each viscosity grade, the use of a higher concentration of PVPP lowers the *DT*.

Colloidal silicon dioxide

Addition of SiO_2 to the tablets in the absence of MC did not influence the *DT* (Table 1). The *DT* of these tablets was high just like that of plain

TABLE 3

Disintegration time of sulphanilamide tablets containing various viscosity grades of methylcellulose (2%) and varying amounts of PVPP

MC grade	Disintegration time (s)		
	1.25%	2.50%	5%
MC 20–30	104.00 ± 8.63	24.00 ± 1.41	23.20 ± 1.92
MC 80–120	150.80 ± 12.24	45.40 ± 1.67	27.60 ± 2.07
MC 350–550	316.00 ± 11.73	129.00 ± 8.40	46.00 ± 1.22
MC 800–1200	497.00 ± 20.99	239.20 ± 16.13	48.80 ± 3.11
MC 4000	1045.20 ± 27.52	331.20 ± 24.10	52.60 ± 4.83
MC 7000–10000	> 1800	567.20 ± 17.96	141.40 ± 18.20

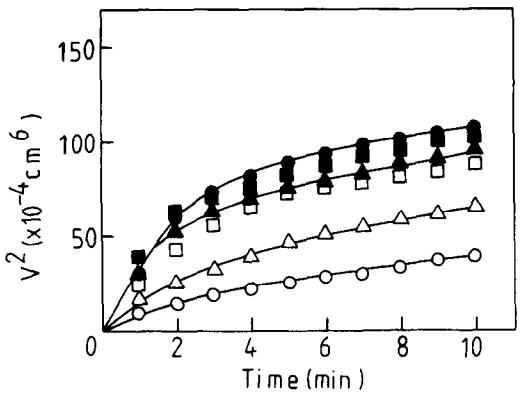

Fig. 6. Penetration of water into sulphanilamide tablets formulated with 1.25% SiO_2 and 2% methylcellulose (MC) of varying viscosity: ○, MC 20–30; △, MC 80–120; □, MC 350–550; ●, MC 800–1200; ▲, MC 4000; ■, MC 7000–10,000.

sulphanilamide compacts containing no excipients. In formulations without MC, water uptake increases with the increase in the quantity of SiO_2 (Fig. 5). The volume of water taken up by tablets containing SiO_2 is much smaller in comparison to tablets containing NaSt glycolate and PVPP (Figs. 1, 3, 5).

Water penetration into tablets containing 2% MC of different viscosity and 1.25% SiO_2 is slow (Fig. 6). The volume of water that penetrates into the tablets is also lower than that observed in similar formulations containing NaSt glycolate and PVPP. The uptake of water increases with the viscosity of MC in tablets containing SiO_2. The high-viscosity grade MC-containing tablets have water uptake rates that are similar. Water penetration in most cases falls with an increase in concentration of SiO_2. The *DT* in all cases is above 1800 s. Slow uptake of water encourages adhesive action by MC. Due to its large surface area, colloidal silicon dioxide coats the granules and its hydrophobic nature results in high *DT*.

Swelling of disintegrants

Individual particles of NaSt glycolate when observed under the microscope were found to have a 217% increase in perimeter diameter on wetting (Prasad and Wan, 1987; Wan and Prasad, 1988b). Most particles required only about 6 s to attain peak size on wetting. This high rate and extent of swelling could have resulted in the low *DT* observed (Table 1).

PVPP particles, on the other hand, do not swell to a great extent. There is only a 19% increase in perimeter diameter of particles of PVPP on wetting (Wan and Prasad, 1988b). Swelling action in the case of PVPP is minimal. This disintegrant seems to aid the transport of water into the tablet through intraparticular capillary spaces. The wetting of the tablet interior leads to collapse of the tablet structure and disintegration results. Some of the findings concerning the action of NaSt glycolate and PVPP have been reported earlier (Wan and Prasad, 1987b). Colloidal silicon dioxide is a poor disintegrant in the system used as shown by the low aqueous uptake and high *DT*.

Thus, from these studies, it can be concluded that a higher water uptake does not lead to a shorter *DT*. It is the influence of excipients individually and the resultant effect of excipients in combination that produces a correlation between water penetration into and disintegration of tablets. This relationship can differ with variations in systems.

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