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Liquid Penetration into Tablets Containing Surfactants

LUCY SAL CHEONG WAN* and PAUL WAN SIA HENG

Department of Pharmacy, National University of Singapore, Lower Kent Ridge Road, Singapore 0511, Singapore

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Aqueous penetration into starch based sulphonamide tablets was reduced when surfactants were included in the formulations. This is probably due to the liquid uptake being dependant on the disruption of the tablet matrix as the volume of liquid uptake was much larger than the pore space in the intact tablet. Starch swelling also affects this penetration process. In tablets containing microcrystalline cellulose, the surfactant improved liquid penetration by improving the wettability of the tablet interior facilitating liquid access. For tablets with sodium calcium alginate, the surfactant retarded the initial uptake of liquid markedly. The strongly swelling sodium calcium alginate appeared to 'waterproof' the tablet interior when wetted. The influence of surfactant on aqueous penetration may be governed by the porosity of the tablet and the nature of the excipient(s) incorporated in the formulation.

Keywords——aqueous penetration; sulphonamide tablets; surfactant; starch; microcrystalline cellulose; sodium calcium alginate

Application of Washburn equation to liquid penetration into tablets containing surfactant can provide a qualitative profile of the penetration process. Nogami *et al.*[1] reported that water penetration into microcrystalline cellulose powder bed was about 14 times greater than that into potato starch. Singh *et al.*[2] using inert plastic matrix containing salicylic acid found that contact angle appeared to be more important than surface tension in determining solvent penetration.

The process of water penetration is preceded by the wetting of the tablet surface. For promoting wetting, hydrophilic and sometimes surface active substances are used in tabletting. The present study is to examine the effect of surfactant on penetration of water into tablets.

Experimental

Materials——Sulphanilamide, sulphaguanidine and sulphathiazole of B. P. grade were used as received. The disintegrants were maize starch (Corn Brand), microcrystalline cellulose PH101, 102 and 301 (Asahi Chemical Industry) and sodium calcium alginate (Alginate Industries) and the binder was polyvinylpyrrolidone (GAF Chemicals). The surfactants employed were polysorbate 80 (Honeywill Atlas Ltd.) and sodium lauryl sulphate (British Drug Houses Chemicals).

Tablets——Granules were prepared by moist granulation. The surfactants and polyvinylpyrrolidone (PVP) when used, were incorporated with a fixed volume of granulating liquid, water. Dried granules, 0.71—1.0 mm fraction, were used for compressing (Manesty, E2) into tablets to contain 250 mg sulphonamide by calculation and to a specified thickness so calculated to give uniform porosity of 0.16.

Disintegration——Disintegration times were determined according to the B. P. method except the disintegration time for single tablet was measured without using the disc. The mean of at least 5 determinations was taken as the disintegration time.

Liquid Penetration——Aqueous penetration into tablets was carried out using the apparatus shown in Fig. 1. The penetration for single tablet was measured at 37 °C and the uptake rate was read from a calibrated capillary tube of internal diameter of 0.124 cm. The mean of at least five determinations was taken to represent the uptake value.

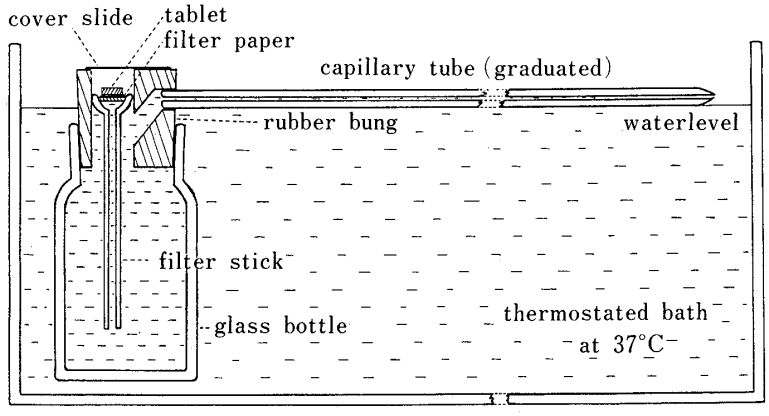

Fig. 1. Apparatus for Determination of Liquid Penetration into Tablets

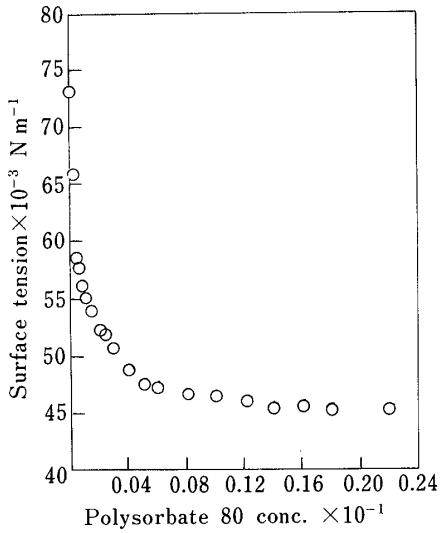

Fig. 2. Surface Tension of Aqueous Polysorbate 80 Solutions at 25 °C (±1 °C) as a Function of Surfactant Concentration

Surface tensions determined using the drop-weight method.

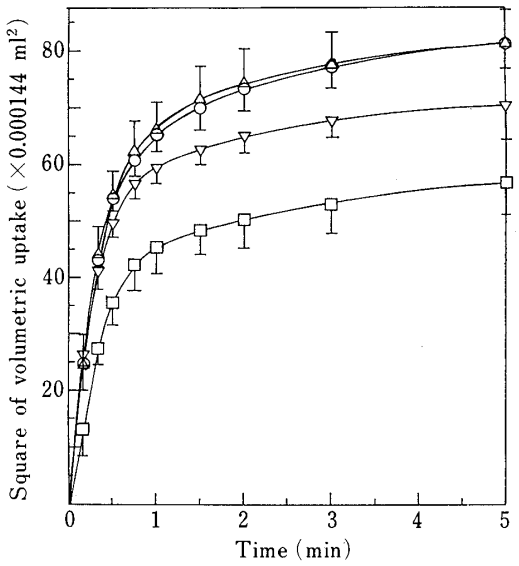

Fig. 3. Aqueous Penetration into Sulphanilamide Tablets Containing 2% Starch, 1% PVP and Varying Concentrations of Polysorbate 80

Vertical lines represent standard deviations.

Polysorbate 80 concentration: ○, 0%; △, 0.002%; ▽, 0.02%; □, 0.2%.

Results and Discussion

Surfactant Concentration

From preliminary studies it was found that the use of small quantities of polysorbate 80, 0.002, 0.01 and 0.02% in sulphanilamide tablet formulations containing 2% starch had little or no effect on water penetration. However, with polysorbate 80 concentration of 0.05% and greater, a marked reduction in water penetration was noted. Polysorbate 80 was found to have a critical micelle concentration (cmc) of 0.0044% (Fig. 2).

Starch and Surfactant

Studies on water penetration into sulphanilamide tablets containing 2% starch, 1% PVP and varying amount of polysorbate 80 showed decreased water uptake with increasing surfactant content (Fig. 3). For those containing 0.002% polysorbate 80, water penetration was unaffected. Similarly with the more hydrophobic sulphonamides, sulphathiazole and

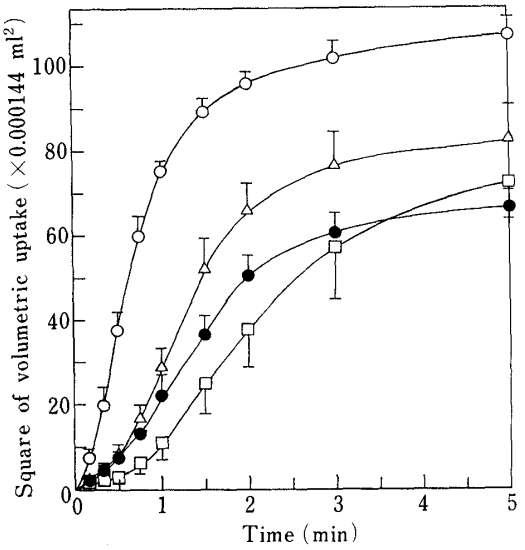

Fig. 4. Aqueous Penetration into Sulphaguanidine Tablets Containing 2% Starch, 1% PVP and Varying Concentrations of Surfactant

Vertical lines represent standard deviations.
Polysorbate 80 concentration: ○, 0%; △, 0.2%; □, 0.5%; sodium lauryl sulphate concentration: ●, 0.5%.

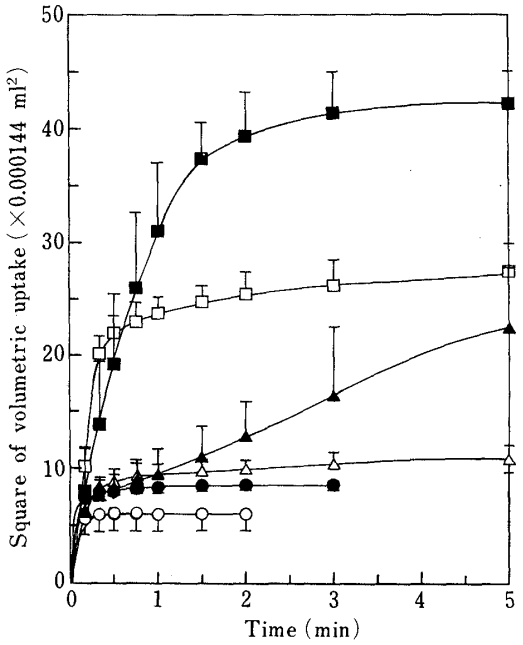

Fig. 5. Aqueous Penetration into Sulphanilamide Tablets Containing MCC PH101 with and without Polysorbate 80

Vertical lines represent standard deviations.
MCC PH101 concentration: ○, 2.5%; △, 5%; □, 10%; sulphanilamide tablets containing 2.5% MCC HP101 and ●, 2%; ▲, 0.5%; ■, 1.0% polysorbate 80.

sulphaguanidine, polysorbate 80 also depressed water penetration (Fig. 4). This was true with sodium lauryl sulphate (Fig. 4). In starch based tablet formulations, aqueous penetration could be affected by the swelling of starch. This could interfere with this penetration process since on wetting, starch swells rapidly, achieving maximum swelling in 15—40 s.[3] The swollen starch grains induce faults or cracks in the tablet matrix allowing alternative channelling of the penetrating liquid. This is probable since the disintegration times of the tablets were rather short, with 0, 0.002, 0.02 and 0.2% polysorbate 80 the disintegration times were 9.1 (±1.0), 10.0 (±1.3), 10.3 (±0.9) and 14.5 (±1.3) s (±standard deviation) respectively. Fraser and Ganderton[4] had reported large increases in aqueous uptake upon tablet disruption for tablets of magnesium carbonate and starch.

Microcrystalline Cellulose and Surfactant

With sulphanilamide tablets containing microcrystalline cellulose (MCC), increasing surfactant concentration increased the water uptake which was higher for a greater MCC concentration (Fig. 5). This is similar for MCC PH102 and PH301. With sulphathiazole tablets containing MCC PH101 (Fig. 6) or PH102, addition of polysorbate 80 also enhanced water uptake. The initial rate of water uptake was rapid for tablet formulation without surfactant although saturated volume uptake plateau was much lower.

It has been reported[1,5] that MCC promotes aqueous uptake in tablets and that it hardly swells when wetted. Lerk *et al.*[5] reported that MCC demonstrated extremely fast aqueous penetration even at low tablet porosities. The liquid volume uptake was much larger that the calculated pore volume of the tablets used. The authors conceived that the disruption of hydrogen bonds on wetting brings about a widening of pores contributing to an increased uptake.

From preliminary studies of MCC containing tablets, the optimum concentration of

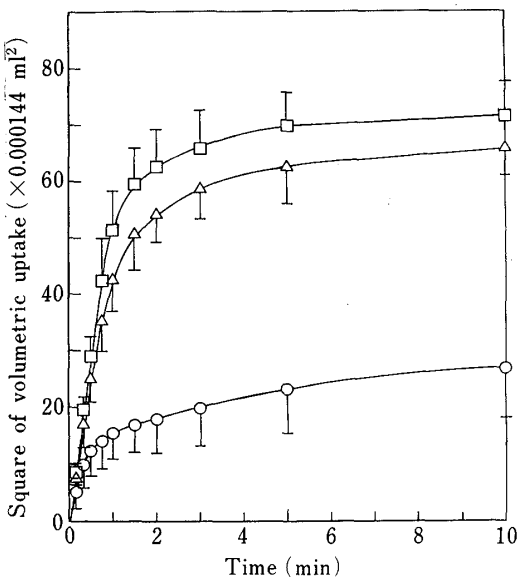

Fig. 6. Effect of Polysorbate 80 on Aqueous Penetration of Sulphathiazole Tablets Containing 5% MCC PH101

Polysorbate 80 concentration: ○, 0%; △, 0.2%; □, 0.5%.

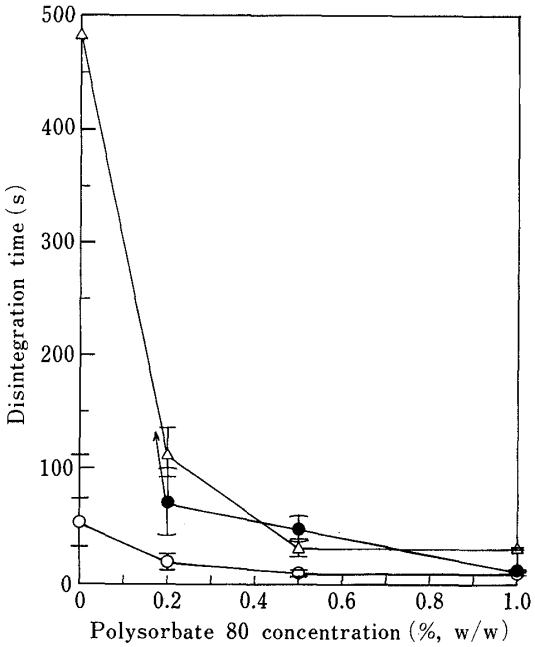

Fig. 7. Effect of Polysorbate 80 on the Disintegration of Sulphonamide Tablets Containing MCC PH101

Sulphanilamide tablets containing: ●, 2.5%; ○, 5% MCC and sulphathiazole tablets containing △, 5% MCC.

MCC for disintegration was found to be between 10% and 20%. In these studies the use of 2.5% to 5% MCC, the minimal MCC concentration for preparing tablets with satisfactory disintegration time, was still inadequate to distribute evenly throughout the tablet matrix leaving some hydrophobic areas. During aqueous penetration, liquid entry and retention was limited to the more hydrophobic channels. The incorporation of surfactant helped to 'hydrophilise' the tablet matrix and increased the aqueous uptake and retentive capacity of the tablet.

The incorporation of surfactant improved the disintegration time of tablets containing MCC (Fig. 7), a faster and more complete disruption of the tablet matrix in the presence of surfactant could occur. This would enhance penetration since this disruption increases the channels and void space within the tablet.

On wetting, the swelling of MCC is less significant than starch.[1] Liquid penetration through MCC lined capillaries would be less restricted after the initial wetting of the capillary walls. Since MCC containing tablets possess a more open network of capillaries as liquid penetrates, liquid accessibility to the various parts of the tablet by simple capillary action is possible. Terminal capillaries which are not sufficiently hydrophilic or are blocked would be left unfilled. It would be expected that the volume of liquid uptake be smaller than the void space in non-disintegrating tablet matrices. Carli and Simioni[6] showed that not all the capillaries of the tablet matrix were filled during liquid penetration. These investigators emphasized that not only the mean pore radius and wettability of inert matrices were important determinants of the water penetration process but also the pore distribution of the matrices.

The differences between starch and MCC PH101 in their characteristics on wetting were examined using discs of starch and MCC compressed to 600 kg/cm^2. A drop of water was placed on each disc and the effect of the water drop on the disc was noted and presented

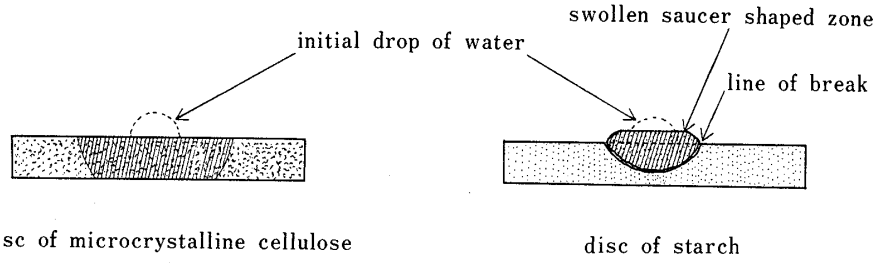

Fig. 8. Cross-Section of Compacts of MCC and Starch after Wetting with a Drop of Water

The shaded region shows the zone wetted.

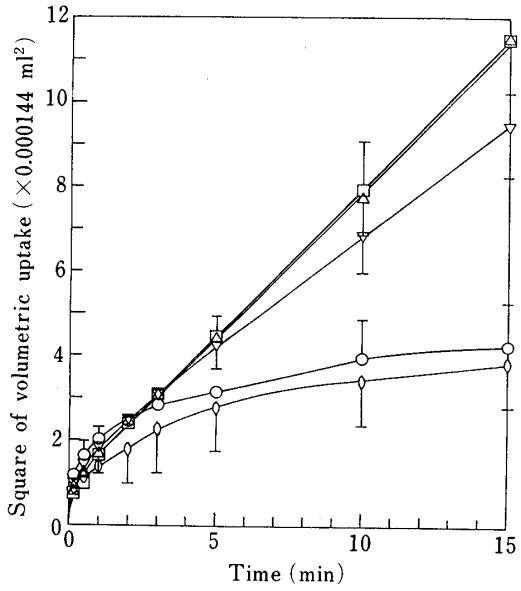

Fig. 9. The Effect of Surfactant on Aqueous Penetration of Sulphanilamide Tablets Containing 1% NaCa Alginate

Polysorbate 80 concentration: ○, 0%; ○, 0.002%; △, 0.02%; ▽, 0.2%; sodium lauryl sulphate concentration: □, 0.2%.

TABLE I. Effect of Dissolved Polysorbate 80 on the Viscosity of Distilled Water

Polysorbate 80 concentration (%, w/w)	Flow time[a] ± S.D.	n_{rel}[b]
0	3 min 51 s ± 0.04 s	
0.2	3 min 55 s ± 0.16 s	1.02
2	4 min 16 s ± 0.06 s	1.10
20	17 min 19 s ± 3.51 s	4.50

S.D., standard deviation. *a*) Average of 3 determinations. *b*) Viscosity relative to water.

diagrammatically (Fig. 8). The drop of water placed on the MCC disc was rapidly absorbed and conducted to the surrounding area while the starch showed localized swelling. The wetted and swollen region of the starch disc broke off. Examination of the surface of the MCC disc after wetting showed that the surface though powdery, was hardly raised. Thus starch swelled more significantly on wetting than MCC. Aqueous penetration in MCC was rapid with a relatively wide area wetted. For starch, swelling occurred and the spread of liquid was more limited. The swelling pressure of the starch caused the swollen portion to fracture from its base.

Sodium Calcium Alginate and Surfactant

Sulphanilamide tablets formulated with sodium calcium alginate (NaCa alginate) demonstrated a much slower water uptake pattern (Fig. 9). The formulations with surfactants had slower initial uptake rate but showed greater capacity of water uptake. It is probable that the strongly swelling NaCa alginate can 'waterproof' the tablet by its rapid swelling on the tablet' surface. The wetted NaCa alginate could form a viscous gel on the tablet surface producing an adhesive surface relatively impervious to liquid entry. The effect of NaCa

alginate 'waterproofing' the tablet interior can be seen by breaking these tablets after soaking in water containing methylene blue. The penetration of the coloured liquid was limited to a thin skin around the tablet.

Conclusions

The finding that addition of surfactant reduced water uptake of starch containing tablets appeared to contradict that with MCC containing tablets in that the effect of surfactant in 'hydrophilizing' drug surfaces would increase aqueous uptake. This could be attributed to the difference in disintegrant action between starch and MCC as discussed earlier.

Considering Washburn equation it would seem that the effect of surfactant in rendering the tablet more wettable, that is, reducing angle of contact, is opposed by the lowering of surface tension as surfactant dissolves in the penetrating liquid and the increased viscosity of the penetrating liquid as the surfactant and other substances dissolve in it. The increase in viscosity by the surfactant in water is shown in Table I. These findings suggest that surfactants have limited influence on water penetration. Of greater importance are tablet porosity and the nature of the excipient(s) used.

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