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# COMMUNICATIONS

## Characteristics of hydrogel as disintegrant in solid dose technology

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**Abstract**—A comparison between a hydrogel and the disintegrants Ac-di-sol, Avicel, maize starch and Primojel has been made using theophylline as the test drug in direct compression tableting. Results indicate that the disintegrant action of the hydrogel is comparable with that of the other disintegrants used, with no adverse effect on the dissolution of theophylline from these tablets as observed by thermal analysis study. The hydrogel's physicomechanical performance in direct compression processing appears to have no undesirable effect on the physical properties of tablets. Scanning electron micrographs of freeze-etched samples of hydrogel demonstrated its internal structure. These results strongly suggest that hydrogels have great potential as efficient disintegrants in solid dosage formulations.

Recently it has been indicated that it would be possible to use hydrogels as disintegrants in tablet formulations (Fassihi 1987).

Synthetic hydrogels are polymeric materials, exhibiting low interfacial free energies with aqueous solutions, and absorbing large quantities of water while remaining insoluble. The Flory–Huggins treatment successfully describes the swelling of a crosslinked polymer and the thermodynamics of mixing a polymer with a solvent. This has been considered in more detail elsewhere (Pouchly et al 1982; Wood et al 1983). Hydrogels are potentially useful in the controlled release of drugs and have also been used in the coating of catheters, intra-uterine devices, sensor electrodes, surgical sutures, in the production of contact lenses, wound dressings, haemodialysis membranes, and in joint replacement.

The purpose of the present report is to further investigate the compactibility and disintegrant properties of hydrogels in formulations containing active drug, and to compare these with other commercially available disintegrants in direct compression tableting.

### Materials and methods

*Materials.* Microcrystalline cellulose (Avicel PH 101) and Ac-di-sol were from FMC Corporation Philadelphia PA, USA. Maize starch, Primojel and Hydrogel were received from Unilab. Saarchem Pty Ltd RSA; Slater,Winsford, U.K. and Geistlich Pharma FRG, respectively. Aerosil 200 (Degurra AG, D6000 Frankfurt) talc, magnesium stearate (BPC), Emdex (Edward Mendell Co.) were used as other excipients in the formulation. The test drug was theophylline anhydrous BP.

*Preparation of tablets.* Theophylline was used for ease of (spectrophotometric) assay and because its solubility is not strongly pH dependent. The formula used for direct compression was % w/w theophylline, (anhydrous) 25, Emdex (moisture content 3·2% w/w) 65·5 talc (moisture content 0·53% w/v) 3, Aerosil 200 1, disintegrant 5 (or 2 in the case of Aci-di-sol). Theophylline, Emdex, talc and one of five disintegrants were sieved, and the fraction below 200 $\mu$m was used. The powders were mixed in a turbula mixer for 10 min with a rotation speed of 60 rev $min^{-1}$. Magnesium stearate was added and mixing continued for a further 5 min, after which Aerosil was added and mixed for a final 2 min. Flat-faced tablets, 12 mm in diameter and 500 mg average weight were compressed on an instrumented single punch machine (Manesty F3) giving breaking strengths of 39, 68 and 98 N. The tablet breaking strengths were within $\pm 6\%$ of their targeted values. All experiments were carried out immediately after manufacture of tablets and again four weeks later. Storage was at room temperature (20°C) and 20% RH.

*Disintegration time measurements.* The disintegration time of 10 individual tablets was determined in distilled water at 37°C using the USPXX procedure for disintegration.

*Dissolution studies.* Dissolution rates were tested using the USPXX dissolution apparatus (paddle method) from Hanson Research Corp, Northridge, CA, at a stirring rate of 50 rev $min^{-1}$, under sink conditions. The dissolution fluid (900 mL simulated gastric fluid, pH 1·2) without enzyme was maintained at $37 \pm 0{\cdot}5$°C. Samples (5 mL) were transferred by pipette at appropriate intervals through a Millipore membrane filter diluted 10-fold with fresh dissolution medium at 37°C, and analysed spectrophotometrically at 273 nm. The volume of the dissolution system was restored by adding fresh dissolution medium at 37°C. Tests were carried out for 80 min on five units of each of the tablet batches and the amount dissolved was calculated as the percentage of total drug dissolved.

*Gell Swelling Index determination.* Polymerized agar-acrylamide hydrogels were used. The degree of swelling of the gels was calculated from weights of dried and swollen samples, and expressed as the Gel Swelling Index (GSI), where: $GSI = (W_t/W - 1).\ 100\%$, where $W_t$ is the weight of the sample at time t and W is the initial dry weight.

### Results and discussion

Scanning electron micrographs of the freeze-etched samples (Fig. 1) reveal the structures of polymerized agar-acrylamide xerogel and hydrogel, respectively. The GSI value of a swollen gel after equilibration in distilled water at room temperature was found to be 2710%. It has been known that the amount of liquid bound on swelling is inversely proportional to the extent of cross-linking in the polymer network. Thus it would be easy to control the GSI value during production by addition of standardized quantities of cross-linking agent into the polymerization cycle before initiation of the process. The state of water in hydrogels has been described (Jhon & Andrade 1973) and three different states—'bound water, interfacial water, and free or bulk water' have been identified by thermal analysis. Disintegration times and tablet breaking strengths are shown in Fig. 2. It is apparent that the distintegration time of tablets containing hydrogel appears to be similar to those for tablets containing other disintegrants, irrespective of the breaking strength of the compacts. The compactibility of the particulate system used in the production of theophylline tablets was evaluated by measur-

Table 1. Physical characteristics of disintegrants investigated.

| Disintegrant* | Water content (%) w/w | Mean particle size ($\mu$m) | Bulk density (g mL$^{-1}$) | Tamped density (g mL$^{-1}$) | Apparent particle density (g mL$^{-1}$) |
|---|---|---|---|---|---|
| Ac-di-sol | 8·7 | 16 | 0·621 | 1·102 | 1·59 |
| Avicel PH 101 | 4·8 | 45 | 0·316 | 0·463 | 1·54 |
| Maize starch | 4·1 | 18 | 0·595 | 0·788 | 1·52 |
| Primojel | 2·2 | 14 | 0·606 | 0·903 | 1·62 |
| Hydrogel | 9·1 | 35 | 0·221 | 0·361 | 0·61 |

* Used at 5% w/w except Ac-di-sol which was at 2% w/w.

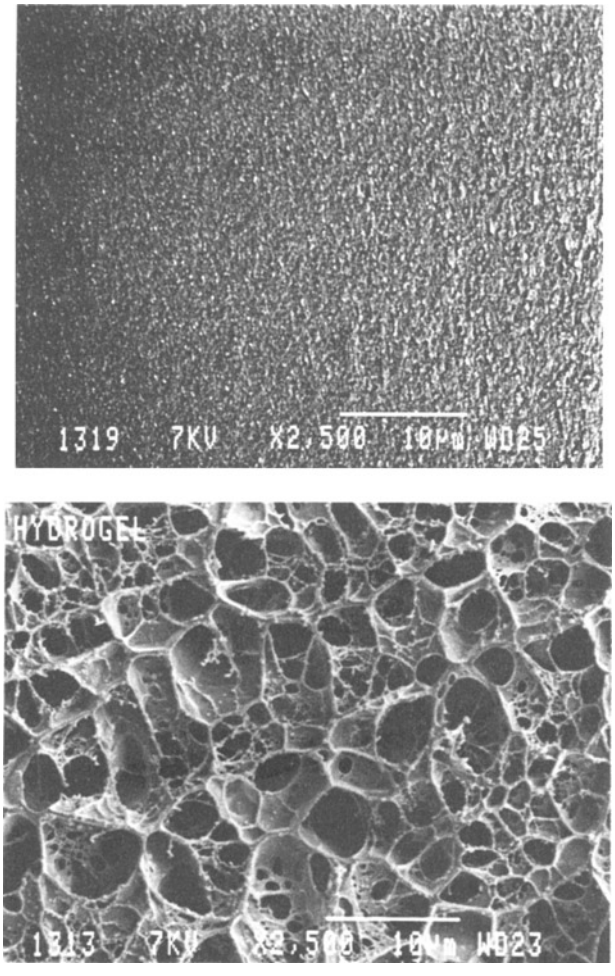


FIG. 1. Scanning electron micrograph showing top, the surface appearance of the Xerogel, bottom, the freeze-etched swollen hydrogel (X2500).

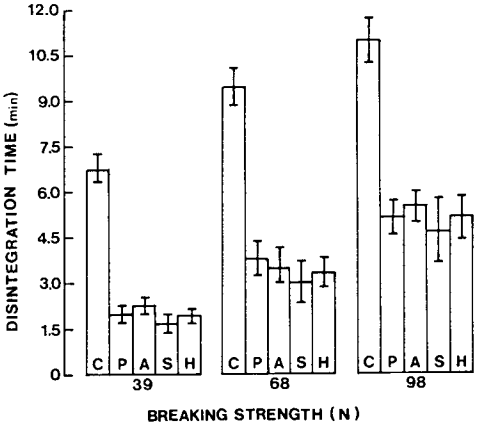


FIG. 2. Disintegration time as a function of breaking strength for tablets containing various disintegrants. All values represent the mean ± s.e.m. (vertical lines) of 10 measurements. The letters inside the columns refer to the disintegrants in Table 2.

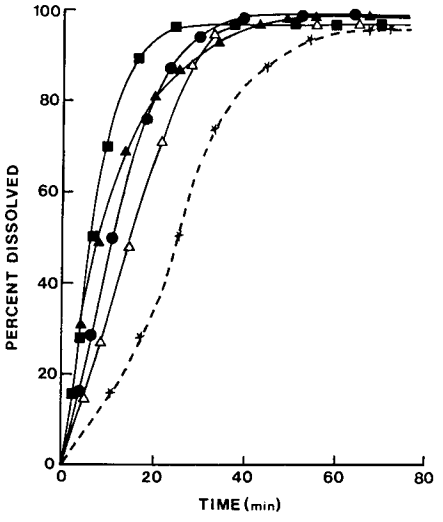


FIG. 3. Dissolution profiles for tablets of 98 N hardness containing various disintegrants: primojel (▲); Avicel (△); starch (■); hydrogel (●) and control (-*-). (USPXX paddle method; mean values n = 5 in distilled water).

ing the pressures required to produce tablets having targeted breaking strength values of 39, 68 and 98 N (Table 2). Results indicate that the presence of hydrogel in the formulation did not have any adverse effect on the compactibility of the materials used. The pressure required to produce tablets of strength 98 N demonstrated that lower pressures can be used to form compacts of similar strength to those containing Primojel and starch disintegrants. The weight variations of tablets (Table 2) show that in the tableting process tablet masses containing hydrogel flowed as well as those containing other disintegrants.

The results of the dissolution study on theophylline compacts in pH 1·2 simulated gastric fluid are shown in Fig. 3. Amount of theophylline dissolved ($T_{50\%}$) from compacts containing various disintegrants was calculated. The T50 values, in minutes, were 7 for starch, 8 for Primojel, 10 for hydrogel, 15 for Avicel and 25 for the control tablets.

Hydrogels are capable of absorbing large quantities of water-

Table 2. Effect of compactibility of various disintegrants on tablet strength.

| Disintegrant used | Weight (mg ± s.d.) | Pressure (MPa) to produce tablet[1] breaking strength of: 39 N | 68 N | 98 N |
|---|---|---|---|---|
| (C) None (control) | 500 ± 3·91 | 52 | 69 | 112 |
| (P) Primojel | 502 ± 5·33 | 58 | 73 | 124 |
| (A) Ac-di-sol[2] | 497 ± 6·01 | 49 | 70 | 108 |
| (S) Starch | 504 ± 4·22 | 61 | 76 | 127 |
| (H) Hydrogel | 501 ± 5·12 | 55 | 71 | 115 |

1 The tablet breaking strength values (using an Erweka testing machine) were within 6% of their targeted values.
2 The amount used was 2% w/w.

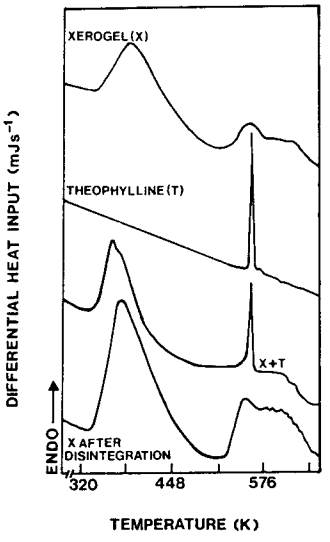


FIG. 4. DSC thermograms for xerogel (X), theophylline (T), 1:1 mixture (X + T) and (X) residue after disintegration of tablet.

soluble drugs and the drug-loaded hydrogel then releases the drug by desorption and diffusion mechanisms. These processes may delay or reduce drug availability. Fig. 3 shows that the cumulative amount of theophylline released approached 100% in approximately 40 min. The possibility of drug absorption into the hydrogel fragments during the disintegration process was investigated. The insoluble residues of hydrogels from the dissolution vessel were removed and dried under vacuum. DSC thermograms (320 to 640 K) of desiccated xerogel; theophylline; a 1:1 mixture of xerogel/theophylline, and xerogel after complete dissolution are illustrated in Fig. 4. The xerogel thermogram had a broad peak from 340 to 448 K and a lower peak near 550 K. The theophylline thermogram over the same temperature region had a narrower peak around 550 K. The xerogel/theophylline thermogram showed peaks identical to the individual components. The thermogram of residual xerogel during and after dissolution showed a peak identical to that of xerogel alone, demonstrating that no theophylline was taken up by hydrogel during dissolution.

*Conclusion*

From the results presented in this report it appears that hydrogel is a good candidate for use as a disintegrant in mass production. DSC thermograms of hydrogel residues demonstrate that they have no adverse effect on the drug dissolution process and that there is no drug uptake by the hydrogels. The physicochemical performance of hydrogels in tableting is comparable to other disintegrants used in this investigation. In addition production of closely standardised hydrogel batches would appear to present no difficulty.

## References

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