ELSEVIER

International Journal of Pharmaceutics 145 (1996) 197–201

international journal of pharmaceutics

Dynamic surface tension studies of hydroxypropylmethylcellulose film-coating solutions

Evelyn Ochoa Machiste, Graham Buckton*

Centre for Materials Science, School of Pharmacy, University of London, 29–39 Brunswick Square, London WC1N 1AX, UK

Received 16 August 1996; accepted 28 September 1996

Abstract

Film coating of pharmaceuticals involves interfacial interactions based on adhesion and spreading of the polymer over the substrate surface. The surface tension of the polymer solution will have a major influence on these interfacial events. It is known that solutions of macromolecules exhibit surface ageing; however, data are not available concerning the dynamic surface tension (DST) of such systems in the first few seconds of surface formation. In this study, the DST of hydroxypropylmethylcellulose (HPMC) has been measured using a maximum bubble pressure method. It was found that, at all concentrations, the DST was higher than the equilibrium surface tension, but that at concentrations above 6% (w/w) this difference was much greater. This can be related to difficulties in film coating which can occur with more concentrated solutions. It was shown that additions of additives, such as poly(ethylene) glycol or lactose, had a detrimental impact on DST for the high-concentration solutions only. These data provide an improved understanding of the film coating process and give a route by which film-coating formulations may be optimised. Copyright © 1996 Elsevier Science B.V.

Keywords: Film coating; Dynamic surface tension; Equilibrium surface tension; Hydroxypropylmethylcellulose

1. Introduction

Aqueous film coating of pharmaceuticals continues to be an important process, both for conventional rapid-release and also modified-release products. Film coating involves the processes of spreading, adhesion and cohesion, which can all be modelled as interfacial events. Macromolecules, such as hydroxypropylmethylcellulose (HPMC), tend to be surface active in nature; thus, the molecules preferentially adsorb at the liquid–air interface and lower the solution surface tension. These solutions exhibit what is known as 'surface ageing', as the molecules do not instantaneously come to equilibrium at the surface; hence, the measured surface tension of such a solution can fall over a long period of time prior to

* Corresponding author.

PII S0378-5173(96)04769-2

reaching the equilibrium surface tension (EST). The values of surface tension which are measured at a pre-equilibrium interface are called dynamic surface tensions (DST). Dynamic surface tension gives information on the rate of movement of the surfactant molecules to the liquid–air interface, i.e. the mechanism of surfactant adsorption, as well as offering better correlations to actual use situations. In a recent review (Chang and Franses, 1995), differences between dynamic and equilibrium behaviour of (sub-critical micellar concentration) solutions of a wide variety of surfactants have been highlighted, and examples of the fact that dynamic surface tension can control functionality were given (e.g. pesticide sprays spread more easily on leaves if they have low DST). Valentini et al. (1991) have reported on the importance of DST in the coating of slides with gelatin, demonstrating that the DST influenced wettability and the surface forces controlling flow and deformation. Chattopadhyay et al. (1995) have reported on the DST of the pharmaceutically relevant materials poly(ethylene) glycol, Poloxamer P188 (Pluronic F68) and HPMC, with respect to their ability to minimise damage to cells during air sparging of cell culture. Valentini et al. (1991) used two grades of HPMC (Methocel E50 and E4M), both at a concentration of 0.3%. These Methocel solutions were found to cause rapid lowering of DST to reach EST and, as such, gave good protection to the cells from the air-sparging damage. There are, however, comparatively few reports in the pharmaceutical literature on the use of DST, which is surprising as these experiments would be expected to relate closely to functionality.

As film coating is an event which is controlled by interfacial interactions, it is clear that changes in surface tension of the liquid with time will influence the process. Twitchell et al. (1995) have shown that the spreading of HPMC onto tablets is influenced by the concentration of the HPMC (E5) solution and also the distance of droplet fall prior to impaction on the surface. Contact angles of drops positioned on the surface were high and showed minimal variation with solution concentration (e.g. 102–108° for 6 and 12% HPMC). Those dropped on the surface from 200 mm gave contact angles of 31° and 81° (for 6 and 12% HPMC solutions, respectively). This difference between drops positioned on the surface and those dropped from a specified height will relate in part to the inertia and subsequent penetration into the tablet surface, but it could also be a function of the slightly different ages of the drop surface. The reason given for the differences between the 6 and 12% (w/w) solutions was the order of magnitude difference in viscosity. In an earlier study (Twitchell et al., 1986) it was reported that the increase in surface area which occurs during spraying may be such that the number of HPMC molecules in each drop cannot saturate the surface in the same manner as in the bulk solution (i.e. the bulk concentration in a drop is depleted rapidly due to the small numbers of molecules present). This could be expected to be important at the point of contact between the drop and the tablet surface, and in controlling coalescence of droplets on the tablet surface; however, after impingement on the surface has occurred, the phenomenon of surface ageing (DST) will also become important. It is known that the surface tension of HPMC solutions will change over many hours (measured by placing a Wilhelmy plate at the surface and measuring force as a function of time). We are not, however, aware of any measurements of DST in the time interval which will be of importance for film coating (e.g. the first few seconds of droplet life). The aim of this work is to study the effect of concentration on the DST of HPMC solutions over the first seconds of the formation of a new liquid–air interface. Furthermore, it is known that certain additives alter the performance of HPMC films and as such it would be interesting to know if they affected the DST of the solutions. Examples of additives include lactose, which has been found to increase adhesion between tablets and film, and poly(ethylene) glycol (PEG) which is used as a plasticiser.

2. Materials and methods

Solutions were prepared of 1, 3, 5, 6, 7, 10 and 12% (w/w) HPMC (Methocel E5, Colorcon) in

double-distilled water (which had a surface tension of 72.6 mN/m). The HPMC was dispersed into a small amount of heated water and then diluted with cold water, once dissolved, to give a clear solution. In the cases where additives were tested, they were added after the initial dissolution and prior to dilution of 5 and 10% (w/w) HPMC solutions. Additive levels were 10, 20 or 30% (w/w) lactose and 20% PEG 3000.

The dynamic surface tensions were measured by the maximum bubble pressure method (Sensadyne PC9000 tensiometer) at bubble rates in the range 0.1–60 s per bubble (giving corresponding surface ages for surfactant to adsorb to the liquid–air interface). The temperature of the solutions was controlled using a water circulator (25 ± 0.2°C). The Sensadyne was calibrated after every change in bubble flow rate, using water and ethanol as markers for high and low surface tension, respectively. The equilibrium surface tensions were measured using a Wilhelmy plate (Cahn DCA). In this context, equilibrium is taken as that of a solution which has aged sufficiently to yield reproducible data (typically 0.5–1 h). It is acknowledged that further reductions in surface tension would occur with extended (days) storage and this must therefore be considered an apparent equilibrium surface tension. Within the context of this study, it is regarded as reasonable to differentiate between new (a few seconds) and old (many minutes) surfaces.

All glassware was cleaned thoroughly and checked for cleanliness by adding double distilled water and measuring its surface tension. Glassware which gave 72.6 mN/m for water was regarded as clean.

3. Results and discussion

The DST data are presented in Fig. 1, with surface tension as a function of surface age. The time to reach a DST plateau was about 8 s for 1, 3 and 5%, 25 s for 6%, about 50 s for 10% and in excess of 60 s for 12% HPMC solutions. This demonstrates that the more concentrated solutions exhibit slower diffusion to the surface, presumably because of their higher viscosity. The

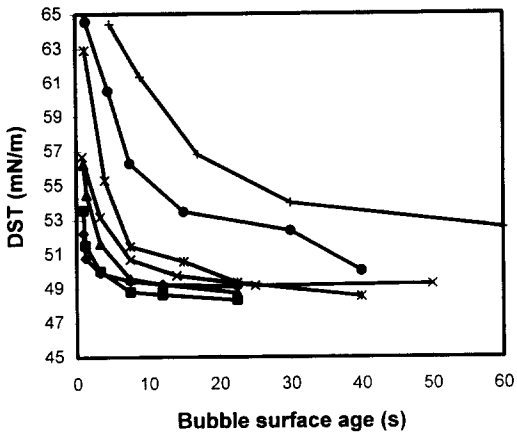

Fig. 1. DST as a function of surface age for HPMC solutions of different concentrations. (+) 12%; (●) 10%; (*) 7%; (x) 6%; (▲) 5%; (■) 3%; (◆) 1% (w/w) HPMC.

lifetime of a drop during film coating can be expected to be short, taking a small fraction of a second to reach the tablet surface and then an unknown time to coalesce and spread over the surface (this time depending upon the ease of spreading and the coating process parameters). It follows that even dilute solutions will have surface tensions higher than EST, and that this will be exacerbated for high-concentration solutions. A further demonstration of this effect is seen in Fig. 2, where the surface tension is plotted as a function of concentration at set bubble rates (surface ages). It can be seen that the EST is relatively unchanged throughout the concentration range,

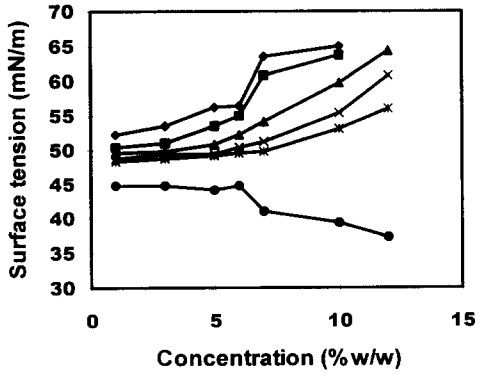

Fig. 2. Surface tension as a function of solution concentration for EST and DST with surface ages of 1, 2, 5, 10 and 20 s. (◆) 1 s; (■) 2 s; (▲) 5 s; (x) 10 s; (*) 20 s surface age; (●) EST.

showing a decrease only at the highest concentrations. The DST, however, is elevated above EST throughout, by as much as 7 mN/m for a 1-s-old surface, and as little as 3 mN/m for a 20-s-old surface when the concentration is 1% (w/w). As the concentration is increased, the difference between EST and DST is seen to diverge, especially at the highly relevant fast bubble rates (1 s old surfaces), the difference between EST and DST increasing to 26 mN/m at 10% (w/w) (1 s old surface). It would appear (Fig. 2) that 6% (w/w) is a critical point, above which the EST and DST show much greater divergence. Although Twitchell et al. (1995) do not use concentrations of HPMC lower than 6% (w/w), there is a clear difference in the measured coating contact angle (i.e. angles formed by drops which have dropped either 100 or 200 mm to the powder surface) for solutions of 6, 9 and 12% of Methocel E5, with the biggest difference (for uncoated tablets) being between 6 and 9% (w/w). This leads Twitchell et al. (1995) to conclude that "only a small amount of energy would need to be imparted . . . for low HPMC E5 solution concentrations (6% w/w and below) . . . to spread well". Whilst the age of the liquid–air interface is not known for the drops used by Twitchell et al. (1995), since there must have been a certain time needed to form the drop and to detach it from the syringe before it fell to the surface, it can be assumed that the age was within the limits of the surface ages used here (i.e. probably between 1 and 20 s old). Thus it is possible that the DST jump after 6% (w/w), which we report here for the first time, is influential in the film-coating process.

The influence of PEG 3000 on the DST of HPMC is shown in Fig. 3, from which it can be seen that PEG has minimal impact on the DST of the 5% (w/w) HPMC solution, but has a detrimental effect in the 10% solution, giving DST values consistently higher than for the 10% HPMC alone. As an indication of error, the standard deviations for all the DST data were ± 0.3 mN/m or less and often as low as ± 0.1 mN/m. It follows that PEG 3000 would be expected to neither help nor hinder the spreading of dilute HPMC solutions during film coating, but would make high-concentration HPMC solutions even less likely to spread. This is despite the fact that PEG lowers the EST of the 10% HPMC solution (Table 1).

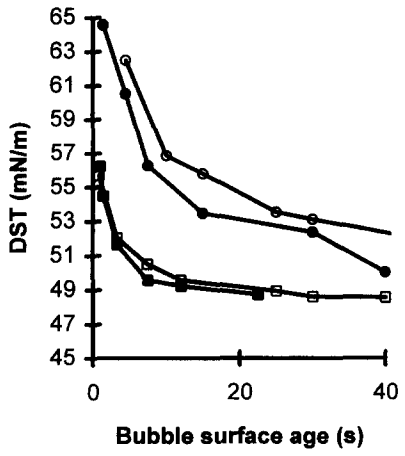

Fig. 3. DST as a function of surface age for HPMC solutions with and without PEG 3000. (■) 5% HPMC; (□) 5% HPMC + 20% PEG 3000; (●) 10% HPMC; (○) 5% HPMC + 20% PEG 3000.

There is no effect on DST of adding lactose to a 5% HPMC solution (not shown, as all data superimpose on the 5% HPMC data shown in Fig. 1). The effect of adding lactose to the 10% HPMC solution (Fig. 4) becomes detrimental (in terms of retained higher DST) when large quantities of lactose are added; however, it would seem that these effects are less noticeable at the faster bubble rates (4.5–5 s per bubble). It proved impossible to obtain reproducibility in the data for

Table 1
EST for 5 and 10% HPMC solutions alone and with added amounts of lactose and PEG 3000

Liquid	EST (mN/m)	S.D.
5% HPMC	44.1	0.7
Plus 10% lactose	43.7	0.7
Plus 20% lactose	44.0	0.2
Plus 30% lactose	39.9	0.4
Plus 20% PEG 3000	35.9	0.9
10% HPMC	39.3	0.1
Plus 10% lactose	38.3	0.7
Plus 20% lactose	38.0	0.5
Plus 30% lactose	38.4	0.7
Plus 20% PEG 3000	30.4	0.9

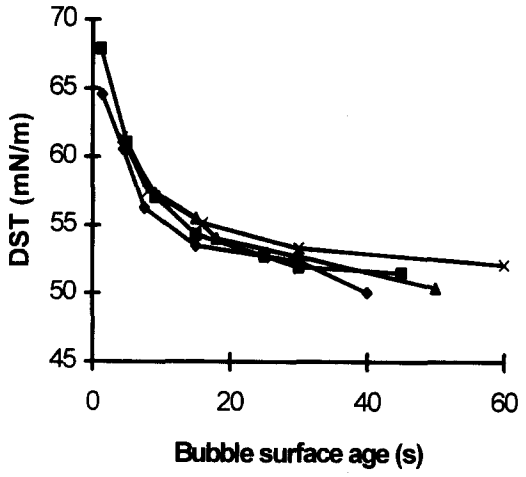

Fig. 4. DST as a function of surface age for 10% (w/w) HPMC solutions with and without lactose. (◆) 10% (w/w) HPMC alone; (■) 10% HPMC + 10% lactose; (▲) 10% HPMC + 20% lactose; (x) 10% HPMC + 30% lactose.

solutions with high lactose contents at bubble rates faster than 4.5 s per bubble, which is indicative of unpredictable movement of molecules to the surface and some surface competition between lactose and HPMC at these newly formed interfaces. It can be seen from Table 1 that lactose has relatively little effect on EST (except for a slight reduction at 30% lactose in 5% HPMC). It must be concluded that, whilst lactose is not likely to substantially hinder spreading through any influence on DST, it equally does not enhance the situation. The advantages seen with lactose-based film coating formulations are not, therefore, a consequence of any reduction in the cohesive nature of the solution.

4. Conclusion

The DST of HPMC solutions has revealed a critical concentration (6% w/w) at which the EST and DST diverge. Above this concentration, the spreading of the newly formed film coating droplets can be expected to be hindered. The addition of PEG 3000 or lactose to HPMC in high concentrations resulted in detrimental effects for 10% (w/w) HPMC solutions, but not for 5% (w/w). It is probable that these effects on DST will influence coating for such solutions. The interaction between the HPMC and additives (lactose or PEG) could be by surface competition, or by an altered structure in solution which inhibits diffusion to the surface in the already more viscous solutions.

Acknowledgements

Thanks are due to Colorcon for gifts of HPMC and to Consejo Nacional para la Investigacion la Ciencia y la Technolgia Venezuela for financial support to E.O.M.

References

Chang, C.-H. and Franses, E.I., Adsorption dynamics of surfactants at the air/water interface: a critical review of mathematical models, data, and mechanisms. *Colloid Surf. A*, 100 (1995) 1–45.

Chattopadhyay, D., Rathman, J.F. and Chalmers, J.J., The protective effect of specific medium additives with respect to bubble rupture. *Biotechnol. Bioeng.*, 45 (1995) 473–480.

Twitchell, A.M., Hogan, J.E. and Aulton, M.E., Estimated surface tensions of atomised droplets in aqueous film coating. *J. Pharm. Pharmacol.*, 38 (1986) 75P.

Twitchell, A.M., Hogan, J.E. and Aulton, M.E., The behaviour of film coating droplets on their impingement onto uncoated and coated tablets. *STP Pharma. Sci.*, 5 (1995) 190–195.

Valentini, J.E., Thomas, W.R., Sevenhuysen, P., Jiang, T.S., Lee, H.O., Liu, Y. and Yen, S.-C., Role of dynamic surface tension in slide coating. *Ind. Eng. Chem. Res.*, 30 (1991) 453–461.