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The influence of binder film thickness on the mechanical properties of binder films in tension

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Abstract—The physicomechanical properties of films of different thicknesses, made from methylcellulose and gelatinized maize starch, have been studied in tension. There was a linear relation between film thickness and tensile strength, toughness, elastic resilence and elongation at fracture. Young's modulus increased with decreasing film thickness particularly with films with a thickness of less than 15 μm.

In tablet granulations, binder films occur as thin coats with the thickness of about 0·1 or 0·2 μm. A polymeric binder, such as methylcellulose or starch, spread uniformly over 20 μm spheres, would give a theoretical thickness of about 0·05 μm; this would represent a minimum value since dissolved substrates could easily double this value.

The mechanical properties of polymeric binding agents have been examined by Schott (1970), Healey et al (1974), Aulton (1982) and Reading & Spring (1984). In general, the properties were found to be directly related to the structure of the agent and to the conditions of testing. In the present work, the changes produced in the tensile strength, toughness, Young's modulus, elastic resilience, elongation at fracture and proportional limit by variations in the thickness of binder films have been studied.

Materials and methods

Materials. The polymeric binding agents used, methylcellulose (Methocel A15, Colorcon, Orpington, Kent, UK) and Maize starch (BDH, Poole, UK), were selected because of their wide use in tablet manufacture.

Methods. The technique of preparation of binder films and the testing conditions were standardized.

Films were prepared by casting the solution of binders onto clean glass plates by means of a chromatography spreader. For maize starch, the plates were silanized.

To ensure that the wet binder did not contract after spreading, the viscosity of the solution was controlled. Binder solutions were not poured until free from air bubbles, which, for the methylcellulose solutions, was achieved by leaving the solutions covered for 24 h at room temperature (20°C), and for maize starch paste by slow stirring during preparation to prevent air entrappment. The dried film thickness was controlled by adjustment of the wet film thickness of the casting solution which was determined by the clearance of the blade in the chromatography spreader. Films were dried at 45 ± 2°C in a hot air oven for 1 to 1·5 h to a moisture level that allowed coherent films to be cut and removed. The dried films were cut in strips of 5 × 0·5 cm along the plane of spreading. The dried film thicknesses ranged from 6 to 70 μm. Films with variation in thickness greater than 5 μm along the length and/or with air bubbles or any other visible defects were rejected. Three measurements of the film thickness were taken using a micrometer. Films were conditioned by storage for 7 days in glass desiccators containing saturated salt solutions to give the required relative humidity (Winston & Bates 1960; Merck Index 1968). This ensured even conditions. The desiccators were stored in a constant temperature cabinet at 25°C.

Testing procedure. The E.L.E. Direct Shear cell apparatus model EL23-009, modified for tensile testing, was used. This involved placing one end of a piece of film, 5 × 0·5 cm, between two specimen grips attached via a coupling to a moveable loading jack while the other end was attached to a strain gauged spring beam held stationary by two vertical supports. The strain gauges were arranged to form four arms of the Wheatstone bridge so that the movement of the beam altered the electrical resistance.

Results and discussion

Graphs of tensile strength, toughness, elastic resilience and elongation at fracture showed a linear relation between the mechanical property and film thickness. The correlation coefficients and regression coefficients for these lines are given in Table 1. Student's *t*-test indicated significant ($P = 0{\cdot}05$) differences for all slopes when the results at 44% were compared with those at 81% r.h. and for all except two intercepts, when thickness = 0. The exceptions were elongation at fracture with maize starch and toughness with methylcellulose. Student's *t*-tests between materials indicated significant differences in all cases except for the slope of the graph of elongation at fracture vs thickness at 81% r.h. The methylcellulose films were clearly stronger, tougher and more elastic than those of maize starch. The correlation coefficients for maize starch films were greater than those for methlycellulose in most cases presumably indicating a more uniform film.

Variation of Young's modulus with film thickness, Fig. 1, showed a gradual increase in modulus with decreasing thickness for both materials tested. However, below 20 μm with maize starch and 15 μm with methylcellulose there was a steep rise in modulus indicating a significant increase in brittleness. Higher

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Table 1. Correlation coefficients, with standard errors in parentheses, and regression coefficients for the relation between mechanical properties and film thickness. Units are tensile strength—$Nm^{-2} \times 10^5$; toughness—$Jm^{-3} \times 10^{-5}$; Elastic resilience—Jm^{-3}; elongation at fracture—%; film thickness mm $\times 10^{-3}$.

	Slope	Intercept (thickness = 0)	r
Maize starch 44% r.h.			
Tensile strength	0·194 (0·026)	31·44 (0·83)	0·82
Toughness	0·482 (0·038)	0·94 (1·26)	0·90
Elastic resilience	0·061 (0·0051)	0·46 (0·167)	0·91
Elongation at fracture	0·224 (0·019)	1·67 (0·617)	0·90
Maize starch 81% r.h.			
Tensile strength	0·422 (0·049)	22·05 (1·48)	0·84
Toughness	0·599 (0·063)	−1·32 (2·10)	0·87
Elastic resilience	0·022 (0·0048)	0·56 (0·139)	0·65
Elongation at fracture	0·256 (0·023)	1·85 (0·72)	0·90
Methylcellulose 44% r.h.			
Tensile strength	0·221 (0·054)	44·64 (2·15)	0·57
Toughness	1·027 (0·155)	60·48 (5·42)	0·79
Elastic resilience	0·0403 (0·0078)	2·71 (0·265)	0·70
Elongation at fracture	0·512 (0·074)	26·60 (2·54)	0·81
Methylcellulose 81% r.h.			
Tensile strength	0·255 (0·052)	39·96 (1·99)	0·68
Toughness	0·724 (0·235)	62·47 (8·33)	0·54
Elastic resilience	0·0278 (0·0053)	0·996 (0·188)	0·73
Elongation at fracture	0·251 (0·081)	32·65 (2·89)	0·54

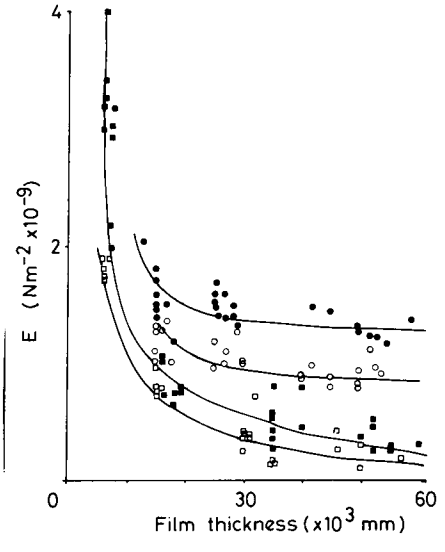

FIG. 1. Variation of Young's modulus (E) with film thickness. Maize starch 44% ■, 81% r.h. □: Methylcellulose 44% ●, 81% r.h. ○.

values for Young's modulus were obtained for films conditioned at 44% r.h. than for those conditioned at 81% r.h.

The proportional limit, Fig. 2, for methylcellulose was not affected by variation in film thickness, r = 0·074 at 44% r.h. and 0·28 at 81% r.h. for 26 and 24 degress of freedom, respectively. With maize starch the proportional limit increased sharply for film thicknesses below 10 μm. It was not possible to obtain and test films of methylcellulose thinner than 15 μm due to their fragility. A rise in Young's modulus may occur for methylcellulose as with maize starch below 10 μm.

The relations between the mechanical properties of the methylcellulose and maize starch films and film thickness are similar, which suggests that the fracture mechanism is the same in both cases. The decrease in strength with film thickness could be due to the fact that the surface skin formed on drying has

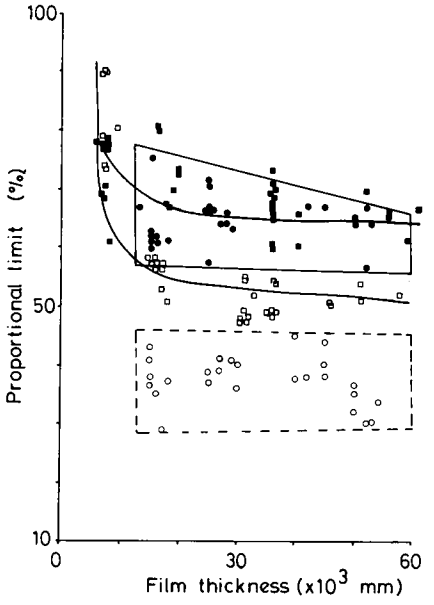

FIG. 2. Variation of proportional limit with film thickness. Maize starch 44% ■, 81% r.h. □. Methylcellulose 44% ●, 81% r.h. ○.

different properties from the bulk of the film (Abdel-Aziz et al 1975).

It is possible to estimate the value for the limiting tensile strength for methylcellulose and maize starch by plotting the ultimate tensile strength against film thickness and extrapolating to zero. This gives the limiting tensile strength for methylcellulose as $45{\cdot}0 \times 10^6$ Nm^{-2}, at 44% r.h.

This relationship may be represented by

$$\sigma = \sigma_0 + KD$$

where σ is ultimate tensile strength, σ_0 the limiting value of tensile strength, D the film thickness, and K a constant depending on the nature of the binder.

Values for K have been calculated for methylcellulose (about 3×10^5 Nm^{-3}) and for maize starch (about 2×10^5 Nm^{-3}). This index shows how related the two materials are and agrees with previous classification where methylcellulose is classified as being hard and tough, and maize starch, hard and strong. Therefore, K could be a useful parameter to determine the probable behaviour of binder film in tension. Similar expressions can be developed for toughness, elastic resilience and percentage elongation at fracture.

The increase in Young's modulus and proportional limit as the film thickness is decreased, particularly < 20 μm, may be the result of an increase in the degree of molecular orientation with decrease in diameter of the fibres as Bacon & Smith (1965) obtained similar results with carbonized rayon fibres. Jones & Duncan (1971) have attributed this type of behaviour in rayon fibres to the non-typical layer of the surface material. Jenkins & Kawamura (1976) explained the increase in Young's modulus with decrease in fibre diameter in polymeric carbon fibres of preferred orientation in the surface. However, whether molecular orientation occurs in the surface layers of spread films is a matter for conjecture, certainly the surface of cast films differ from one another (Abdel-Aziz et al 1975). The thickness of the oriented layer of fibres is almost independent of fibre diameter and it seems reasonable to assume that the surface skin formed on drying will also be of a depth that is independent of total thickness and will have a greater Young's modulus than the bulk of the film. Thus, the ratio of the depth of the surface layer to film

thickness will increase with decrease in film thickness. Assuming that the surface layer has a greater Young's modulus than the bulk film, the Young's modulus of the bulk film will increase with decrease in film thickness, this is the observed phenomenon.

It is possible, however, that the decrease in strength with film thickness is due to the weakening effect of minor imperfections being proportionately greater in the thinner films. These imperfections could arise as a consequence of the method of preparing the test samples, by cutting from a sheet, or from residual internal stresses forming during the drying phase.

Very thin films formed from polymeric binders, such as will be present in tablet granules, are much weaker and more brittle than the films that have been tested previously. However, methylcellulose films are stronger than maize starch films at all thicknesses despite the differences in slopes of the regression lines.

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The permeability of grafted human transplant skin in athymic mice

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Abstract—Human skin has been transplanted onto athymic mice and its permeability properties assessed to see if this in-vivo model would be of benefit in predicting accurately absorption of drugs or toxic chemicals through human skin. The permeability properties of the skin alone, and grafted and athymic mouse skin were assessed by measuring in-vitro absorption of tritiated water and a permanently charged cationic penetrant, paraquat. The grafted skin and athymic mouse skin had similar permeability to the tritiated water. However, the grafted skin was less permeable to paraquat but was more permeable to it than normal human skin, indicating that although histologically, the transplanted skin appeared normal, its barrier properties were impaired. The model was not, therefore, useful for assessing human percutaneous absorption.

Industrial chemicals and pesticides may accidently come into contact with human skin and drugs may be deliberately applied for beneficial effects. Sufficient quantities can be absorbed through the skin to cause toxic reactions (Davies et al 1979). Assessment of percutaneous absorption as a contribution to predicting the effect of substances in man, requires the use of animal studies. However, the structure of mammalian epidermis varies from species to species. There are microscopically obvious differences such as presence or absence of sweat glands, number of hair follicles and number of cell layers in the epidermis. Other differences, such as the amount of lipid present at different body sites may be less obvious but have also been reported (Elias et al 1980). Differences in the number of cell layers and biochemical composition are seen in the stratum corneum, the outer layer of corneocytes, which forms the primary diffusion barrier (Blank 1965). Although there is no perfect animal model for human skin permeability (Scott et al 1986a), in-vitro percutaneous absorption techniques have been developed which can predict in-vivo absorption (Scott et al 1986b). We have used such an in-vitro technique to compare the permeability properties of human and laboratory animal skins (Dugard et al 1984). The in-vitro techniques developed to date, however, have not yet replaced in-vivo methods completely and there is scope for further refinements to existing protocols.

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Recently, human cadaver and biopsy skin, transplanted onto immune-suppressed mice, has been reported to maintain a morphology similar to normal human skin (Kruger & Briggaman 1982) and to retain human microflora not found normally on the host mouse (Kearney et al 1982). If such grafted human skin is to be used to predict potential absorption in man, the permeability properties of the transplanted skin must be comparable with normal human skin. To investigate this we have measured the absorption of two test penetrants (water and paraquat ion), through the athymic mouse and grafted human skin. We have previously used these penetrants as markers for abnormal permeability properties and species differences (Dugard et al 1984; Scott et al 1986a).

Materials and methods

Chemicals. Tritiated water was obtained from the Radiochemical Centre, Amersham, UK, and diluted with distilled water to a final activity of 5 μCi mL^{-1}. Paraquat dichloride was obtained from the Radiochemical Laboratory, ICI plc, Petrochemicals Division, Billingham, UK, and added to a 1000 mg mL^{-1} solution of paraquat dichloride in distilled water to a final activity of 8 μCi mL^{-1}.

Skin graft. Cadaver skin was obtained from a hospital mortuary, between 24 and 72 h after death. Thoracic skin was transplanted onto athymic mice using published methods (Kearney et al 1982) and then, to prevent infection, the mice were housed in filter top cages at a temperature of 28–30°C and relative humidity of greater than 60%. The skin grafts were maintained on these mice for up to 6 months.

Permeability assessment. The procedure followed has previously been reported by Dugard et al (1984). Essentially, whole skin (epidermis plus dermis) membranes were mounted in glass diffusion cells. On Day 1 of the assessment the permeability of