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THE MECHANICAL PROPERTIES OF HYDROXYPROPYLMETHYLCELLULOSE FILMS DERIVED FROM AQUEOUS SYSTEMS

PART 1: THE INFLUENCE OF PLASTICISERS

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The aim of this work is to examine the effects that certain plasticisers have on the properties of aqueous based hydroxypropylmethylcellulose (HPMC) films of a type used for film coating tablets, and to investigate whether or not the inclusion of these additives is in fact beneficial in all cases.

The film former HPMC is being used increasingly as a coating for pharmaceutical tablets because of its suitable properties, not least of which is the ability to coat using a fully aqueous system. This greatly improves the method and safety of application.

The reasons for coating pharmaceutical tablets are many-fold, however we have restricted our study to an examination of certain mechanical properties of the films as an assessment of their ability to afford physical protection to the core. Two methods have been used to evaluate these properties:

a) penetration of a spherical indenter under load

and

b) deformation and fracture under tensile stress.

Indentation

One major characteristic of the indentation profile of a polymer film is its time-dependant nature. The indentation deepens continually with time with a corresponding decrease in apparent hardness. This results in it rarely being possible to state a single-valued definative hardness for a polymeric material.

Observation of indentation-time curve shapes may give an idea about the elastic, plastic and visco-elastic properties of the material. Glassy and rubbery materials are elastic and show rectangular shaped curves, viscoelastic materials show characteristically curved traces. The effects that certain additives have on the deformation characteristics of polymeric coatings are examined here.

Tensile Testing

For physical protection of a tablet core, the film coat should be hard and tough without being brittle. These properties can be defined in terms of yield point, strain at break and elastic modulus according to the classification of Lever and Rhys[1]. This is reproduced as Table 1 and suggests that an ideal film should exhibit a relatively high yield point, a high percentage elongation and a high modulus. It is possible to determine these properties by means of a tensile elongation test. Such a test was carried out on cast films of HPMC either alone or containing additives.

METHOD

The results of plasticisation were investigated by the addition of glycerol and different grades of polyethylene glycol (PEG) to the HPMC. The effect of storage and temperature were also examined.

Preparation of solutions

The polymer solutions were prepared as follows. One third of the calculated amount of water was heated in a stainless steel container. Whilst stirring, using a mechanical mixer, the desired amount of the polymeric powder (hydroxypropylmethylcellulose, Methocel E5, Dow Chemical) was added. The remaining

TABLE 1

	Yield Point	Strain at Break (Elongation)	Elastic Modulus
Soft, Weak	Low	Low	Low
Soft, Tough	Low	High	Low
Hard, Brittle	Not defined	Low	Very High
Hard, Strong	High	Moderate	High
Hard, Tough	High	High	High

amount of cold water was added only when adequate dispersion of the powdered polymer in hot water was observed. The system was stirred until complete solvation was effected. Any desired additives were added at this stage and best results were achieved if the solution was kept overnight.

Solutions were formulated to contain 15% w/v HPMC together with glycerol and polyethylene glycol 600, 1500, 4000 and 6000 as plasticisers in concentrations of 1, 2 and 3% w/v. After casting and drying this resulted in final plasticiser concentrations in the films of 10, 20 and 30% respectively, expressed as a weight percentage of the polymer.

Casting

20 ml samples were centrifuged to remove air bubbles. The solution was then cast using a thin layer

chromatography applicator. The clearance was selected to give a film thickness of about 100μm after drying. The cast was made on a dry clean glass plate and dried overnight in a leveled oven maintained at 40°C. The films were then stored for seven days at the required temperature and humidity.

Indentation Method

The indentation characteristics of the film were determined using the apparatus of White and Aulton[2]. The time of indentation was 10 minutes for the comparison study of different plasticisers. At least six readings were made for each condition. Two runs were held for three hours to investigate long term indentation. The first of these was with the polymer alone and the second one with the polymer plus 10% glycerol.

Tensile Method

After casting and drying, the polymeric films were cut using a stainless steel template (test section 20mm x 6.5mm) and scalpel. Each sample was labelled and its thickness measured using a micrometer in four places along the middle 20mm section.
The mean of these readings was used in the calculations of tensile strength and modulus[3].

In all cases, the following procedure was followed. At least five samples of each formulation were tested using an Instron 1026 testing machine. The force-time curve was recorded directly and from this ultimate tensile strength, modulus of elasticity and percent elongation at break were estimated using the original cross-section. This was done due to difficulties in measuring the cross-section just before the break. However, this is satisfactory in our case since the elongations were relatively small. Moduli of elasticity (Young's Moduli) were estimated using the first part of the stress-strain curve recorded during the tensile strength measurements.

RESULTS

Compatibility of Plasticiser

The samples were examined for incompatibilities using a low power microscope. Any sample that showed any sign of incompatibility such as spotting, was discarded at this stage. Only 9 formulae were suitable for subsequent testing. The ones containing polyethylene glycol 1500, 4000 and 6000 in concentrations greater than 10% showed signs of "blooming". This phenomena is associated with solubility; it results in some of the added plasticiser being thrown from the system. The plasticiser collects as tiny spots on the surface of the sample. This may give rise to weak spots in the film and rupture may be induced at low applied stress. All solid polyethylene glycols in concentrations above 10% in HPMC show this.

Indentation Results

It is clear that hardness, brittleness and elasticity are major mechanical properties connected with coating films in service. The results of all the experiments showed some similarity in film properties. The dry, unplasticised polymer samples were glassy in nature, but all plasticised films showed viscoelastic behaviour. Thus it was not possible to give one figure as the hardness of these polymeric films. Qualitatively the creep curves for short time gave an idea about the nature of the film system. The HPMC films tended to become softer and their viscoelastic tendencies increased as the plasticiser content was increased. Storage at the higher humidity produced a similar effect.

Figure 1 shows the indentation profiles (depth v. time) for hydroxypropylmethylcellulose alone plus curves containing 10, 20 and 30% glycerol. These films had been equilibrated at either 10% or 60% R.H. as indicated. The left-hand graph shows the glassy nature of the polymer alone in the dry state. Addition of plasticiser clearly increased the viscoelastic content of the deformation. It can be seen

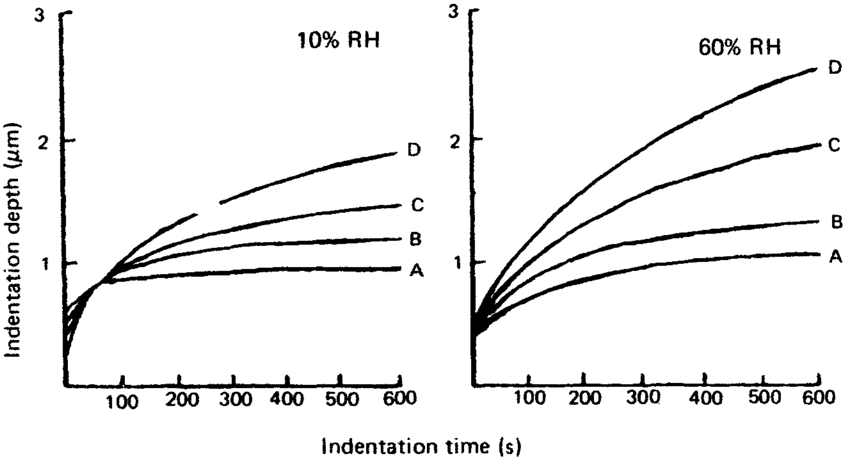

FIGURE 1
Penetration of a spherical indenter into cast HPMC films: Addition of glycerol. A=0%, B=10%, C=20%, and D=30%.

also that the depth of indentation at any time increases with the amount of glycerol added. The depth after ten minutes was doubled by the addition of 30% glycerol. Increasing the storage humidity also increased both the viscoelasticity and total depth of the indentation after ten minutes; note that even HPMC alone is clearly viscoelastic at 60% R.H.

The effect of the addition of various concentrations of polyethylene glycol 600 is shown in Figure 2. The curves are affected in a similar way to the addition of glycerol, although the measured deformations appear to be less susceptable to humidity changes.

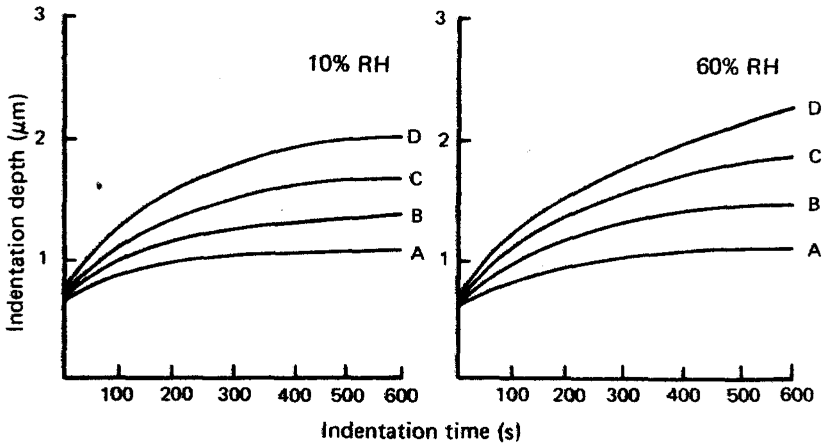

FIGURE 2
Penetration of spherical indenter into cast HPMC films: Addition of polyethylene glycol 600. A=0%, B=10%, C=20%, and D=30%.

Figure 3 shows the effect of different molecular weights of polyethylene glycol. Generally the lower the molecular weight, the greater the plasticising action. Indeed only a small increase in the indentation depth was observed with addition of the 6000 grade.

The indentation curves for the two samples tested over a long indentation period are shown in Figure 4. These long-term indents show that even the 'dry' polymer alone is viscoelastic to a certain degree, however the plasticiser-containing curve showed a more ductile deformation. These curves also reveal that there is a difference in the time needed to reach the linear viscous region. The plasticised

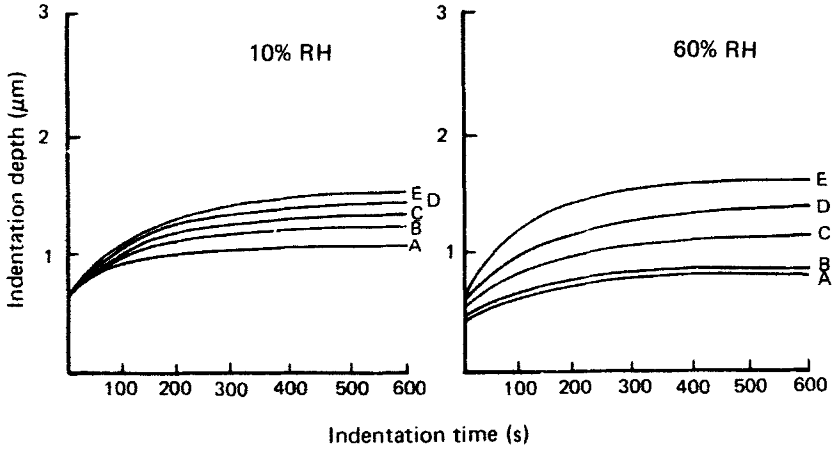

FIGURE 3
Penetration of spherical indenter into cast HPMC films: Addition of 10% polyehtylene glycols. A=0, B=6000, C=4000, D=1500, and E= 600.

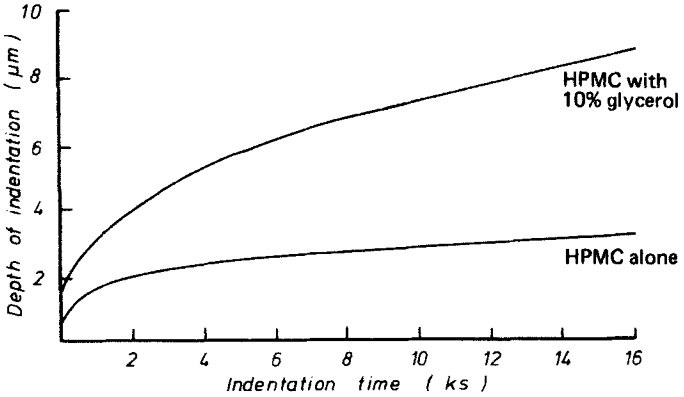

FIGURE 4
Long-term indentations of plasticised and unplasticised films of hydroxypropylmethylcellulose.

HPMC film containing 10% glycerol took 2.5 hours to reach this region; the unplasticised film needed more time, 3 hours.

Tensile Results

Glycerol

Figures 5 and 6 show that as the percentage of glycerol is increased there are significant changes in all properties measured. Ultimate tensile strength fell from 59.8 MPa with 0% glycerol to 31.7 MPa with 20% glycerol. Over the same concentration range, the percent elongation increased from 8.2% to 17.3%, i.e., an increase of more than 100%. The modulus of elasticity fell from 1703 MPa to 876 MPa, a reduction of nearly 100%.

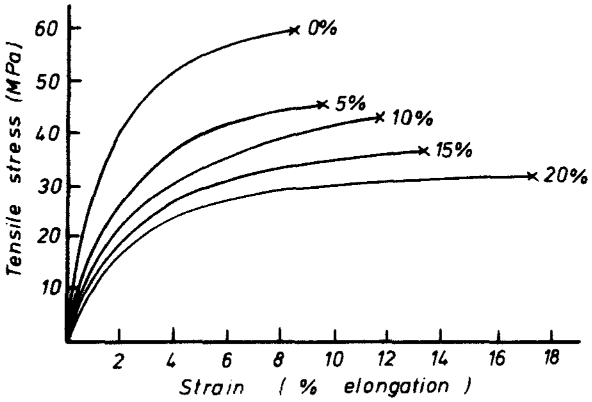

FIGURE 5
Stress-strain curves for HPMC films containing different concentrations of glycerol.

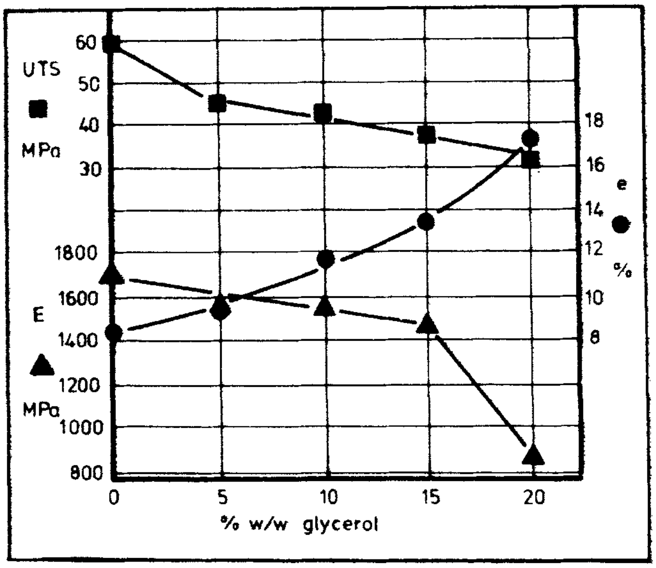

FIGURE 6
Changes in Ultimate tensile strength (UTS), percent elongation (%e) and modulus of elasticity (E) with change in glycerol content of HPMC films.

Polyethylene Glycol

Figures 6 and 7 indicate that as the grade of PEG is decreased there were changes in the properties measured. Ultimate tensile strength fell from 47.2 MP for PEG 6000 to 31.8 MPa for PEG 600. Over the same PEG grade range the percent elongation increased from 8.9% to 12.8% and the modulus of elasticity fell from 1460 MPa to 1077 MPa. As the molecular weight of PEG was increased the results approached those of the polymer alone.

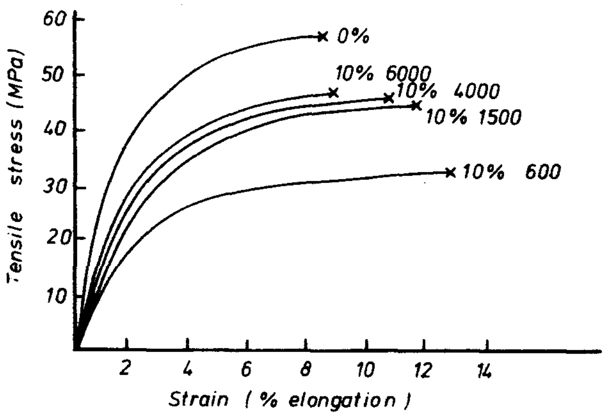

FIGURE 7
Stress-strain curves for HPMC films containing 10% of different grades of polyethylene glycol.

Humidity

The conditioning of the polymeric films at high humidity (80% R.H.) resulted in significant changes in mechanical properties. The tensile strength decreased by more than 25%. the percent elongation increased by about 40% and the modulus of elasticity decreased by nearly 10%.

Temperature

After storage at 50°C for 50 days the tensile strength of the films was found to have increased by only 3% to 61.3 MPa. The percent elongation decreased by 10% to 6.2 but there was no significant change in the elastic modulus. These observations indicate a loss of moisture from the film during storage.

DISCUSSION

It is interesting to note that the presence of glycerol (Figures 1 and 5), polyethylene glycol 600 (Figures 2 and 7) and water (humidity data) in the hydroxypropylmethylcellulose films all had similar effects. All three additives did indeed act as plasticisers with respect to their influence on the mechanical properties of the film, i.e. each of them increased the ease of deformation of the film. This was manifested in each case by an increase in the depth of penetration at any time, an increase in the time-dependant nature of the deformation, a decrease in the tensile strength of the film, an increase in the elongation at break and a reduction of the modulus of elasticity.

Porter[4] has studied the effects of a series of plasticisers on the tensile strength of aqueous derived hydroxypropylmethylcellulose (5 cps) films and reports a decrease in tensile strength with increased plasticiser concentration. It should be noted that the films in Porter's study were produced by spray techniques and not casting. Also in a recent study, Delporte[5] has looked at the influence of PEG on the modulus of elasticity and elastic limit of aqueous derived hydroxypropylmethylcellulose (5 cps) films, but only using the 400 grade of PEG. The results are in general agreement with the present work. Delporte has additionally studied the effect of PEG 400 and propylene glycol, using the same techniques, on HPMC films to which various proportions of titanium dioxide had been added. A strict comparison of results is not possible here as Delporte is using a more complex system than the present study.

There are a number of theories of plasticisation which can be used to explain such changes in mechanical properties (see, for example, Ritchie[6]). One of these, the gel theory[7], appears to satisfactorily explain our observations.

In this theory it is assumed that polymer molecules in solution are attracted to each other by forces originating from 'active centres' along the polymer chain. In solution these bonds are in a dynamic equilibrium, i.e. constantly making and breaking. As they break, solvent (i.e. water) molecules are attracted to, and are in competition for, the sites. Thus at any given time a certain fraction of these 'active centres' will be solvated with water molecules. Plasticisers, when present in the initial solution, will also be in competition for the same sites. The rigidity of an unplasticised polymer is thought to be due to a three-dimensional gel structure formed on drying by contacts between polymer molecules at these centres. The presence of plasticiser will thus reduce the number of active centres available and consequently the number of polymer-polymer contacts, thereby decreasing the rigidity of the three-dimensional structure formed on drying; this will allow generous deformation of the film before rupture. Plasticisers can be said to work by opposing the aggregation of polymer molecules during gel formation as the solvent is evaporated.

Thus, this theory explains how plasticisers work and indeed why residual water in the film has a plasticiser effect. The reduction in three-dimensional rigidity will result in the increased time-dependance of the deformations shown in Figures 1-4. Similarly, enhancement of plasticiser, as shown in Figures 1,2,5 and 6 for glycerol and PEG 600, is a clear consequence of the extra competition for active centres.

Figures 3,7 and 8 show that low molecular weights of PEG are more effective as plasticisers. This can be explained by the fact that there will be more molecules, and therefore presumably more chances of competition for an active site, per gram of added PEG.

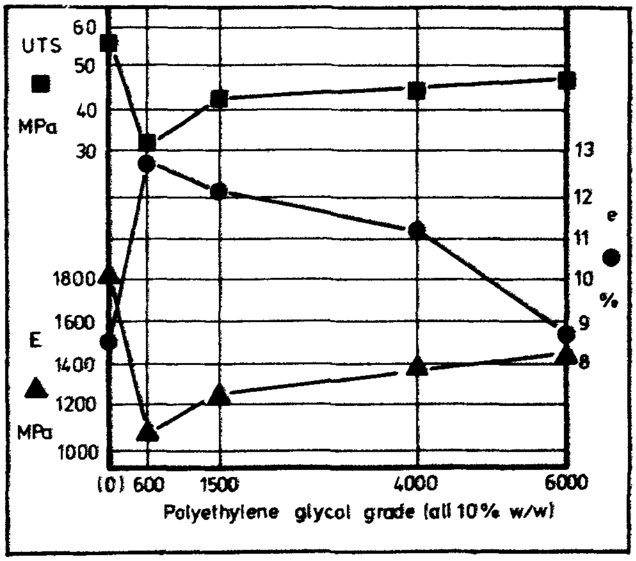

FIGURE 8
Changes of Ultimate tensile strength (UTS), percent elongation (%e) and modulus of elasticity (E) with change in grade of polyethylene glycol.

The desirable mechanical properties of polymer tablet coats have been outlined earlier in terms of yield point, strain at break and elastic modulus. HPMC films do not exhibit a distinct yield point during tensile testing (see Figures 5 and 7) and therefore a high ultimate tensile strength can be substituted in Table 1 as an alternative criterion of film quality.

As defined by Table 1, HPMC alone is a hard, brittle material, compared with HPMC plus plasticiser, particularly when there is little or no residual water acting as a plasticiser (see Figure 5, showing a strain at break of only 8%). Indeed a free 100µm thick film can be easily broken in the fingers. However storage at a high humidity makes a 100µm film ductile enough to be bent over without fracture.

Figure 6 shows the effect of the addition of glycerol on the mechanical properties. Apart from increasing the elongation at break the other changes i.e. a marked reduction in both ultimate tensile strength and elastic modulus are detrimental in terms of ideal film requirements. According to the scheme of Lever and Rhys (Table 1) the tendency is towards a soft, tough film. The increase in flexibility alone could make these films satisfactory in service although the low strength and elasticity may adversely affect the film's physical resistance to marking, scratching etc.

The effect of the addition of various grades of PEG to HPMC (Figures 7 and 8) show in all cases that the ultimate tensile strength and elongation at break were reduced. However, in the case of the higher grades, this was without a corresponding large increase in elongation. Only the lower grades of PEG had a significant effect on elongation, however this was accompanied by a marked reduction in strength.

CONCLUSIONS

This work has provided a demonstration of the plasticiser effects of water, PEG and glycerol on aqueous derived HPMC films and quantified them in terms of tensile and indentation test parameters.

Addition of plasticiser to organic solvent derived cellulosic films has long been known to be a necessity but their addition to aqueous derived coating systems should be more carefully examined.

The high degree of mechanical protection afforded by HMPC films can be modified by plasticisers to provide greater film flexibility for potentially difficult applications such as deep logos or break line.

However, from the work reported here addition of plasticiser to HPMC films is generally accompanied by a change to a softer film of decreased tensile strength.

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