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Application of intrinsic viscosity and interaction constant as a formulation tool for film coating.
III. Mechanical studies on free ethyl cellulose films, cast from organic solvents

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Summary

The mechanical properties of ethyl cellulose films, cast from different solvent systems, have been determined and the structures of the films have been visualized in order to assess the solvent systems for use in a coating process. General relationships could not be found between intrinsic viscosity or interaction constant data and the mechanical properties. However, by using the two parameters in combination, favourable solvent systems could be selected, e.g. methylene chloride and ethanol in the ratio of 60:40 (% w/w) or toluene and ethanol in the ratio of 80:20 (% w/w). Water should be avoided in solvent systems for ethyl cellulose since it accumulates in the evaporating solution and impairs the film properties by forming a spongy and porous film.

Introduction

Extended release of pharmaceutically active substances is extensively achieved by using polymers. The production of a polymer-containing formulation in many cases includes the use of solvents, e.g. for granulation or coating. A number of investigators have shown different properties of ethyl cellulose systems resulting solely from the solvent utilized to prepare the system (Haas et al., 1952; Eskilsson et al., 1976; Sina et al., 1978; Lindholm et al., 1984; Azoury et al., 1988; Iyer et al., 1990). A powerful means for predicting the impact of the solvent on the properties of polymers is, thus, of great interest.

Intrinsic viscosity, $[\eta]$, and an interaction constant, k', have been proposed as tools for solvent selection for ethyl cellulose (Arwidsson and Nicklasson, 1989, 1990). Intrinsic viscosity, $[\eta]$, is an expression of the solvent's ability to swell the polymer. A high value reflects that the polymer exists as loose coils in solution, whereas a low value is a result of the polymer being present as tight coils. Polymer films prepared from a solvent which gives a high intrinsic viscosity value might, therefore, be expected to be mechanically strong

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due to the tight intertwining between neighboring polymer molecules.

A good solvent, exhibiting a low value of the interaction constant, k', with a polymer, shows a relatively steep viscosity increase at high polymer concentrations compared to a poor solvent (Spurlin et al., 1946; Alfrey, 1947). A polymer forming a film from a solvent with a low k' value normally reaches the gel point at a more concentrated state compared to the corresponding situation with a solvent showing a high k' value. Gelation at a higher concentration results in less internal stresses in the film (Rowe, 1981, 1983; Rowe and Forse, 1982), which suggests that a low interaction constant is favourable for the mechanical properties. Hence, both parameters, $[\eta]$ and k', can be expected to influence the mechanical properties of ethyl cellulose films.

The mechanical strength of ethyl cellulose films cast from different organic solvent systems will be reported in the present paper. The role of intrinsic viscosity, $[\eta]$, and the interaction constant, k', will be discussed. Water has been shown to be favourable, regarding $[\eta]$ and k', at low concentrations when added to a mixture of methylene chloride and ethanol in the ratio of 60:40 (% w/w) (Arwidsson and Nicklasson, 1989). The effect of water concentrations up to 10% (w/w) on the mechanical properties of ethyl cellulose films will be shown.

Materials and Methods

Materials

Films were cast of a batch of ethyl cellulose 10 cps (Dow Chemical Co., U.S.A.), which has been characterized earlier (Arwidsson and Nicklasson, 1989). 1-Butanol, toluene (May & Baker Ltd, U.K.), ethanol 99.5% v/v (AB Svensk Sprit, Sweden), methanol (E. Merck, Germany), methylene chloride (ICI, U.K.), *o*-xylene (Fluka AG, Switzerland), and purified water (USP) were used as obtained. Polytetrafluoroethylene tape (Fluor-Carbon Co., U.K.) served as a substrate for the film casting.

Equipment

The films were evaluated with a film thickness gauge, Leptoskop 2011 (Karl Deutsch, Germany), a tensile testing machine (Model M30K, J J Lloyd Instruments Ltd, U.K.) fitted with pneumatic grips and a 50 N load cell, and a scanning electron microscope (Jeol JSM-25S II, Jeol Ltd, Japan).

Film casting

Films were cast from ethyl cellulose solutions in organic solvent systems. Methylene chloride, toluene, *o*-xylene, methanol, ethanol, and 1-butanol were studied as single solvent systems. Binary solvent systems were prepared from methylene chloride or toluene by mixing with ethanol in the ratios of 60:40 and 80:20 (% w/w), respectively. In addition, water was admixed to the methylene chloride/ethanol system, thus obtaining ternary mixtures of methylene chloride, ethanol, and water in the ratios of 57:38:5, 55.5:38:7.5, and 54:36:10 (% w/w).

10 ml of 7.5% (w/w) ethyl cellulose solutions were poured on a polytetrafluoroethylene tape at room temperature. The film thickness was controlled to 10–40 μm by applying an appropriate slope of the tape surface for each solvent system. The mechanical properties were shown to be independent of film thickness within this range. Immediately following the application of the solution, a hood was placed over the drying film in order to retard the evaporation of the solvent, since the evaporation rate has previously been shown to have an impact on the properties of ethyl cellulose films (Arwidsson, 1991). After 1 h of retarded drying, the hood was removed and the film was allowed to dry at room temperature for 1–3 h. Finally, the films were dried in a hot air oven at 50°C overnight. After drying, 10 mm wide strips were cut from the films. The thickness of each film strip was determined as the mean value of three measurements along the strip. The free film strips were stored at room temperature in a desiccator over silica gel prior to the tensile testing.

Tensile testing

The fracture stress, the fracture strain, and the elasticity module were determined for the free films as described earlier (Arwidsson, 1991).

Scanning electron microscope (SEM) photographs

SEM photographs were taken of the cross-sections of the fractured free films tested in the tensile testing machine.

Results and Discussion

The three mechanical properties studied, fracture stress, fracture strain, and elasticity module, were found to correlate well. Therefore, one of them, the fracture stress, was chosen for illustrations throughout.

Effects of the solvent system

All films in this study were transparent, except in the cases where water was present in the solvent system. The fracture stress of free ethyl cellulose films depends upon the solvent system from which the film was cast. This is illustrated in Fig. 1, where the fracture stress is plotted as a function of the intrinsic viscosity for each solvent system. A relationship between fracture stress and intrinsic viscosity, in accordance with the reasoning in the introduction, is indicated. However, the point representing methylene chloride does not fit in the proposed correlation in Fig. 1.

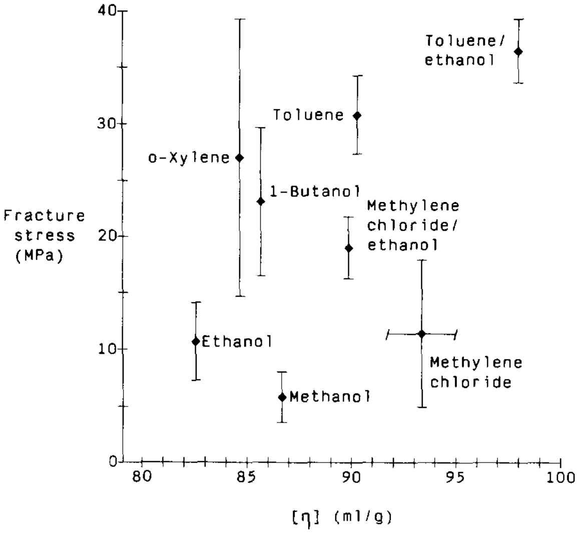

Fig. 1. Fracture stress of free ethyl cellulose films as a function of intrinsic viscosity, [η]. Horizontal and vertical bars denote 95% confidence intervals ($n = 4$–13). The solvent systems, from which the films were cast, are indicated. Intrinsic viscosity data for ethyl cellulose in the solvent systems are taken from Arwidsson and Nicklasson (1989).

Figs 2 and 3 show SEM photographs of the films cast from ethanol and toluene, respectively. The structure of the ethanol film is grainy compared to the relatively smooth structure of the toluene film, which explains the higher fracture stress of the film cast from toluene (cf. Fig. 1).

Another parameter which might affect the mechanical strength of ethyl cellulose films is the interaction constant of the solvent system used.

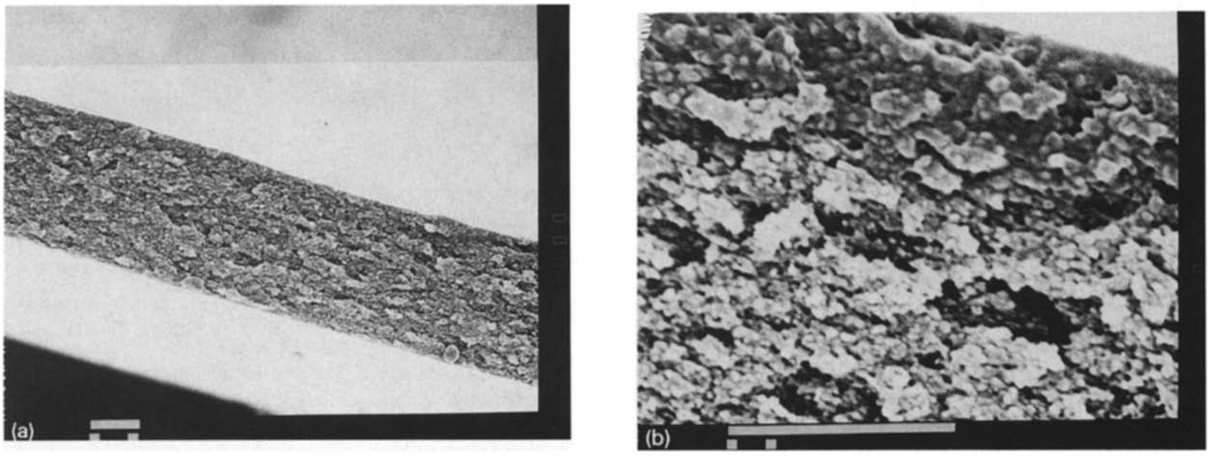

Fig. 2. Cross-section of a free ethyl cellulose film cast from ethanol, magnified (a) 1000 × and (b) 4500 × . The white bars denote 10 μm.

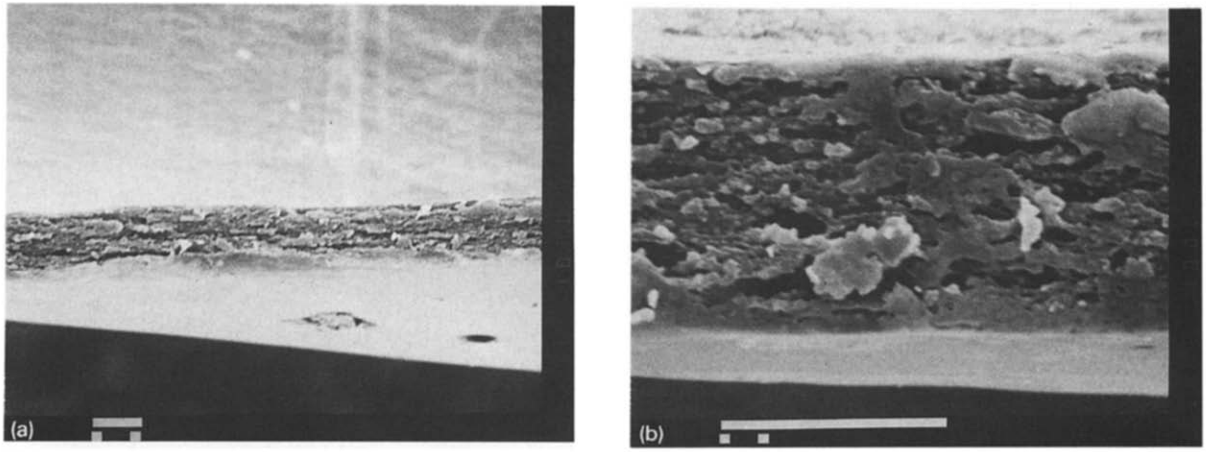

Fig. 3. Cross-section of a free ethyl cellulose film cast from toluene, magnified (a) 1000 × and (b) 4500 × . The white bars denote 10 μm.

In Figs 4 and 5, the fracture stress for cast ethyl cellulose films is shown as a function of solvent composition together with values for the interaction constant, as given by Arwidsson and Nicklasson (1989). The results show that the fracture stress exhibits maxima corresponding to minima for the interaction constant. A solvent system consisting of a poorly hydrogen bonding solvent and a strongly hydrogen bonding solvent, e.g. toluene and ethanol in the ratio of 80:20 (% w/w) or methylene chloride and ethanol in the ratio of 60:40 (% w/w) has previously been suggested as favourable for ethyl cellulose

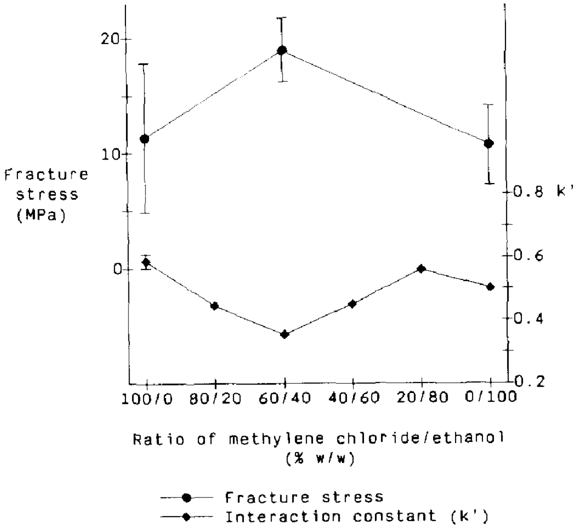

Fig. 4. Fracture stress of free ethyl cellulose films cast from methylene chloride, ethanol, and a mixture of the solvents in the ratio of 60:40 (% w/w). Bars denote 95% confidence intervals ($n = 7$–13). The interaction constants, k', for ethyl cellulose in the solvent systems are given as a comparison (Arwidsson and Nicklasson, 1989).

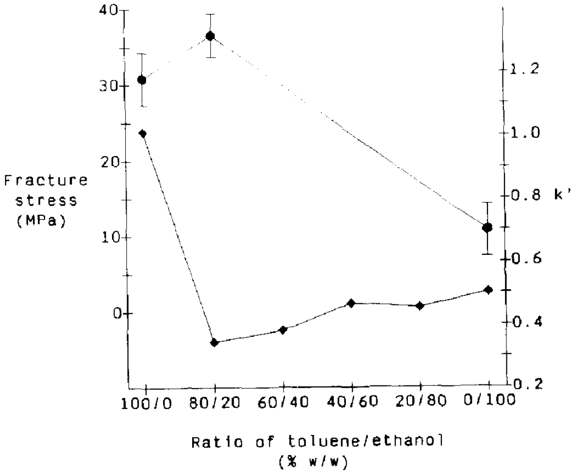

Fig. 5. Fracture stress of free ethyl cellulose films cast from toluene, ethanol, and a mixture of the solvents in the ratio of 80:20 (% w/w). Bars denote 95% confidence intervals (n = 4–7). The interaction constants, k', for ethyl cellulose in the solvent systems are given as a comparison (Arwidsson and Nicklasson, 1989).

(Arwidsson and Nicklasson, 1989, 1990) based on dilute solution properties. The results on mechanical properties exhibited by the ethyl cellulose films in the present study are consistent with these theories. However, a general relationship for all the solvent systems studied, between the interaction constant and the fracture stress, could not be found.

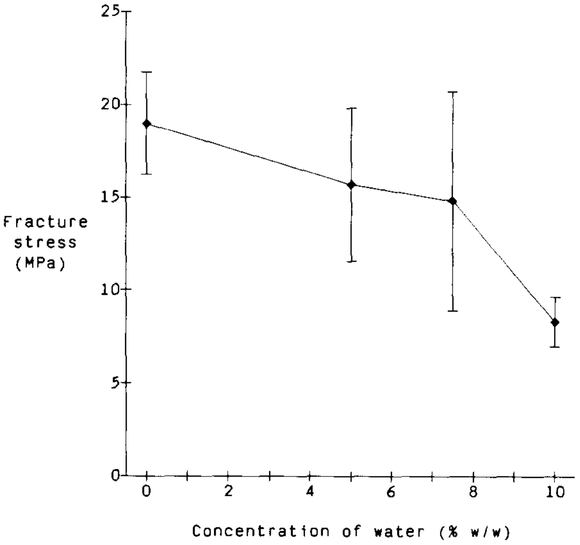

Fig. 6. Fracture stress of free ethyl cellulose films cast from a mixture of methylene chloride and ethanol in the ratio of 60:40 (% w/w) with the admixture of water. Bars denote 95% confidence intervals (n = 4–13).

Effects of water

In Fig. 6, the fracture stress is presented at different concentrations of water added to the solvent system methylene chloride and ethanol in the ratio of 60:40 (% w/w). Water has an obvious negative impact on the mechanical properties of cast ethyl cellulose films. At a concentration of 10% water, films which are less stress resistant, less ductile, and less stiff are formed, despite the fact that the addition of water up to 10% is thermodynamically favourable for an ethyl cellulose solution (Arwidsson and Nicklasson, 1989).

The cross-section of a film cast from the mixture of methylene chloride and ethanol in the ratio of 60:40 (% w/w) is shown in Fig. 7. The structure is comparable with that exhibited by the film cast from ethanol (Fig. 2). Fig. 8 shows that the structure of the film is drastically affected by the addition of water, causing a spongy and porous structure. The microstructure suggests that the solvent composition has been different at the gelation and film formation through the film. The thin and smooth parts of the structure have, thus, been formed at a water concentration less than the precipitation point, whereas the grainy parts, most clearly apparent at the higher magnification, have been formed at locally higher water concentrations. During the evaporation, the concentra-

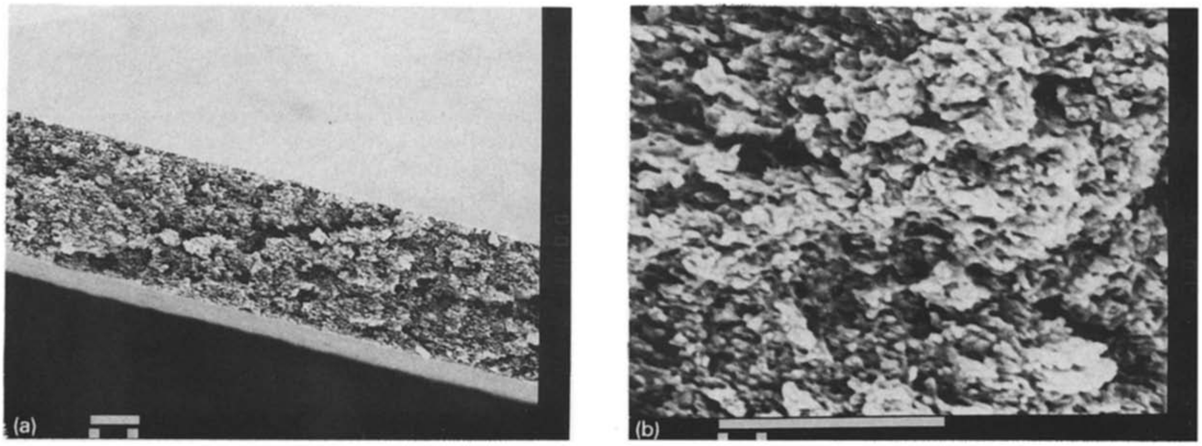

Fig. 7. Cross-section of a free ethyl cellulose film cast from a mixture of methylene chloride and ethanol in the ratio of 60:40 (% w/w), magnified (a) 1000 × and (b) 4500 × . The white bars denote 10 μm.

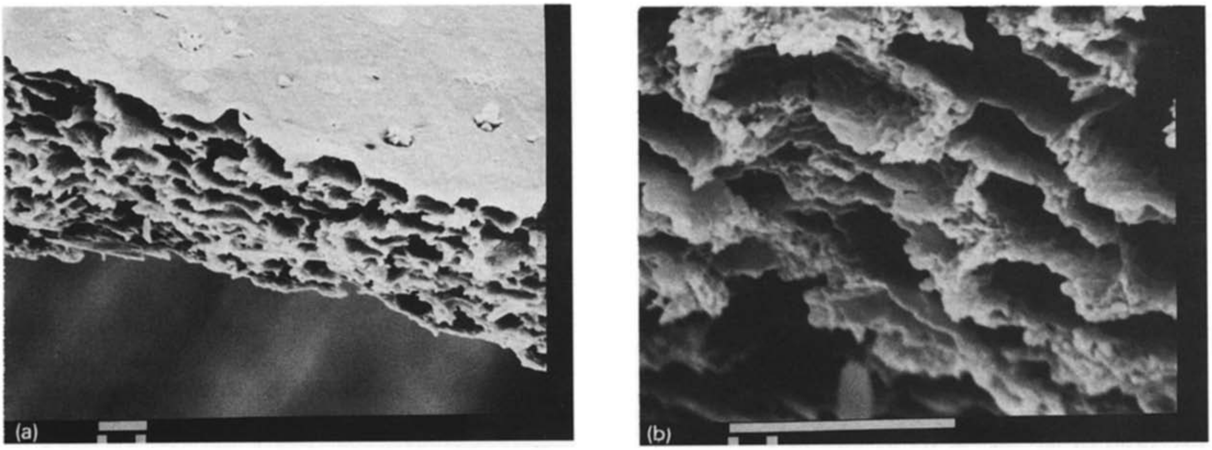

Fig. 8. Cross-section of a free ethyl cellulose film cast from a mixture of methylene chloride, ethanol, and water in the ratio of 54 : 36 : 10 (% w/w), magnified (a) 1000 × and (b) 4500 × . The white bars denote 10 μm.

tion of water is locally increased due to its relatively lower evaporation rate. Since the precipitation takes place at approx. 13% water content (Arwidsson and Nicklasson, 1989), the polymer is partially precipitating prior to the gelation and film formation. This can be visually observed as an opacity of the films, even at 5% original water concentration. The precipitated polymer molecules contribute comparatively less to the mechanical strength than the polymer molecules forming the film from a true solution via a gel, which in combination with the spongy structure produces a mechanically weaker film.

Conclusions

The mechanical properties of free ethyl cellulose films are dependent upon the solvent system from which the film was cast. General relationships between the mechanical properties and the dilute solution properties intrinsic viscosity or interaction constant could not be found. However, by using the two parameters in combination, favourable solvent systems consisting of a poorly hydrogen bonding solvent and a strongly hydrogen bonding solvent, e.g. toluene and ethanol in the ratio of 80 : 20 (% w/w) or methylene chloride and ethanol in the ratio of 60 : 40 (% w/w), could be selected.

Water, which may be present at low concentrations in e.g. ethanol, should be avoided in solvents for ethyl cellulose since it is accumulated in the solution during evaporation. The resulting film has a spongy structure and poor mechanical properties.

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