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Microwave drying of aqueous tablet film coatings: a study on free films

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Summary

Experiments were performed on free tablet coating films to evaluate microwave energy as a potential drying source for aqueous tablet film coating. Free films of 4 formulations containing either hydroxypropyl methyl cellulose or methyl cellulose were prepared using a conventional microwave oven as the drying source. Oven drying at various temperatures and convective air drying in the microwave oven at zero power setting were used as controls. Microwave drying rates were 2–22 times faster than controls. The physical properties of the films were not adversely affected by microwave drying, as indicated by water vapor permeability and tensile strength/Young's modulus measurements. The results suggest that microwave drying could be used as a substitute for conventional hot air drying in aqueous film coating.

Introduction

Successful film coating depends on the removal of the polymer solvent from the deposited film. While organic solvents have been used, there has been an increase in the use of primarily aqueous solvent systems in recent years. Water is an attractive solvent because it is safe, non-toxic, inexpensive and readily available. Relative to organic solvents, however, there are several drawbacks associated with its use. Due to its high latent heat of vaporization, energy costs and drying times are increased. Water penetration into the tablet core may degrade drugs subject to hydrolysis. The films themselves may be damaged during prolonged tumbling in fluid bed or pan coaters.

Microwave drying may alleviate some of these problems by reducing drying times and energy costs. Microwave drying is used successfully in the food industry (Decareau, 1985) and for films in the plastics industry (Stephanson, 1972). Within the pharmaceutical industry, microwave energy has been used to dry granules (Cliff, 1986), but no application to film coating has been reported.

This report presents a comparison of conventional hot air drying and microwave drying of free films formed from aqueous film coating solutions. Drying rates have been determined for microwave-dried films and for controls. Since any increase in the drying rate afforded by microwave drying is useless if film quality is compromised,

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water vapor permeability and tensile strength measurements have been used as indicators of film quality.

Materials and Methods

The film coating solution contained 3 basic components: polymer, plasticizer and solvent. A surfactant was included in all solutions to reduce foaming that can cause holes in the final film. No pigments, opacifiers or other additives were used. Four different formulations were evaluated; their compositions are summarized in Table 1. Formulation 1 contained hydroxypropyl methyl cellulose of a low viscosity grade (HPMC E3, Dow Chemical Co.) in a 10% w/v aqueous solution. Formulation 2 was identical to formulation 1, but contained no plasticizer. Formulation 3 contained hydroxypropyl methyl cellulose of a higher viscosity grade (HPMC E15, Dow Chemical Co.) in a 5% w/v aqueous solution. Formulation 4 contained methyl cellulose as the polymer (MC A15, Dow Chemical Co.) in a 4% w/v solution. Poly(ethylene glycol) was used as a plasticizer in formulations 1, 3 and 4 at 20% of the polymer weight. All formulations contained a surfactant (Antifoam AF emulsion, Dow Corning Corp.) at 0.025% of the solution volume (w/v in g/ml). Film coating solutions were prepared according to the manufacturer's instructions and then centrifuged at 2000 rpm for 5 min to remove entrapped air bubbles. Films were then cast on glass plates by pouring 1 ml of solution onto 5 cm × 5 cm squares etched in the surface of the glass.

Microwave drying was carried out in a conventional microwave oven designed for home use (Model RRL 820, Amana) at the lowest power setting. In home-use microwave ovens, microwave energy is generally supplied to the oven cavity in a square-wave 'on–off' cycle, with the power setting determining the length of the 'on' phase. At the setting used, 700 W of microwave energy were delivered to the cavity for approximately 4 s out of every 13. The plate was removed from the oven and exposed to outside air for 20 s after each minute of microwave drying. In this way, overheating of the glass plate was avoided and the films were primarily dried with microwave energy and not by conductive heat transfer. The temperature of the glass plates as measured using surface temperature-indicating labels (Markal Co., Chicago, IL) did not exceed 37 °C. Films dried using microwave energy are designated 'MWD' ('microwave-dried').

The drying rates and physical properties of MWD films were compared with two types of controls. Since a fan circulates air in the microwave oven when it is in use, control films were prepared in the oven with the fan on but without microwave heating. These films are designated 'AD' ('air-dried'). Drying rates determined for these films indicate the convective contribution to the measured microwave drying rate. As a second

TABLE 1

Summary of various film coating formulations used

Ingredient	Formulation 1	Formulation 2	Formulation 3	Formulation 4
Polymer	HPMC E3 [a]	HPMC E3 [a]	HPMC E15 [a]	MC A15 [b]
	10% w/v	10% w/v	5% w/v	4% w/v
PEG 400 [c]	20% w/w	None	20% w/w	20% w/w
Antifoam AF [d]	0.025% w/v	0.025% w/v	0.025% w/v	0.025% w/v
Distilled water	q.s.	q.s.	q.s.	q.s.

Items listed as 'w/v' indicate that the mass of the agent added in grams was the specified percentage of the total solution volume in ml. Items listed as 'w/w' indicate that the mass of the agent added was the specified percentage of the polymer weight.

[a] HPMC E3 has a low viscosity grade, whereas HPMC E15 is a high-viscosity grade polymer (Dow Chemical Co., Midland, MI).

[b] Methyl cellulose (Dow Chemical Co., Midland, MI).

[c] Poly(ethylene glycol) (Aldrich Chemical Co., Inc., Milwaukee, WI).

[d] Antifoaming agent (Dow Corning Corporation, Midland, MI).

type of control, films were dried at several temperatures in a stagnant air laboratory oven (Thelco model 16, Precision Scientific). These films are designated 'ODn' ('oven-dried at n °C'). They are intended to represent the primarily thermal drying currently used industrially. Outlet air temperatures of 35–45 °C have been reported in recent studies on industrial equipment (Mathur et al., 1984; Stafford and Lenkeit, 1984); tablet bed temperatures are generally within 1 or 2 °C of the outlet air temperatures. In the current study, films were oven-dried at 30, 50, 60, 70 and 80 °C in drying rate experiments. Physical property measurements were performed only on films dried at 30 and 50 °C (OD30 and OD50).

The plates were exposed to the different drying conditions and weighed at intervals. The rate of water loss was plotted as a function of time; the slope of the linear portion of the curve is reported as the drying rate.

The water vapor permeability of the films was measured according to the procedure specified in ASTM test E 96-80 (ASTM, 1987a). The films were clamped over small stainless-steel cups (Payne permeability cups, Fisher Scientific Corp.) filled with about 5 ml of distilled water. To produce a constant temperature and water vapor partial pressure in the surrounding air, the cups were placed in a desiccator over a saturated potassium carbonate solution. The desiccator was kept in an oven at 30 °C. During the experiments, a relative humidity of 45% was maintained within the desiccator, as measured with a digital hygrometer (Cat. no. 11-603-9, Fisher Scientific). Five cups were used in each experiment, two for microwave dried films, one each for air-dried and oven-dried films, with the last cup left open as a control. The loss of water was measured at 1, 2, 3, 4, 6, 8, 10 and 12 h. Plots of the weight of water remaining in the cups as a function of time yielded linearity: water vapor transmittance (WVT) is defined as the slope of this line. Water vapor permeability was calculated from WVT using the equations:

$$\text{Permeance} = WVT/S(R_1 - R_2)$$

$$\text{Permeability} = \text{Permeance} \times \text{film thickness}$$

where S is the vapor pressure of water at the temperature of the experiment, R_1 is the relative humidity at the source (here 100%) and R_2 is the relative humidity at the vapor sink (here 45%). Four replicate measurements of water vapor permeability were made for the MWD films; two replicates were made for each of the controls.

The thickness of the films was measured using a micrometer (Ames, Waltham, MA). Five replicate measurements were made for each film; for the 4 formulations and 4 processes (MWD, AD, OD30 and OD50) used, a total of 80 measurements were made. For all formulations and processes, the mean thickness was 0.03 ± 0.01 mm. Since the polymer content of the formulations varied, the film thickness depended on the formulation. The mean thickness values by formulation (i.e., including all four drying processes, $n = 20$) were: formulation 1, 0.041 ± 0.007 mm; formulation 2, 0.036 ± 0.005 mm; formulation 3, 0.022 ± 0.004 mm; formulation 4, 0.020 ± 0.002 mm. Thickness values were used in the calculation of water vapor permeability and tensile properties.

The tensile strength and Young's modulus of the films were measured according to the procedure described in ASTM test D 882-83 (ASTM, 1987b). Young's modulus is an indicator of the elasticity of the film, with lower values corresponding to greater elasticity. Tensile strength, as the name implies, is an indicator of film strength. Larger tensile strength values correspond to stronger films. The ideal film coating is both strong and elastic, and therefore has a large ratio of tensile strength to Young's modulus. This ratio has also been used as an indicator of the overall mechanical quality of the film.

Before tensile strength measurements were performed, the films were stored in sealed plastic bags in a desiccator over anhydrous calcium chloride for one to two days. The films were cut into dumbbell-shaped samples as specified in the ASTM procedure and examined visually for deformations or bubbles. Special care was taken to avoid jagged edges, which would produce stress concentration. The thickness of each film was measured at 5 different points using a micrometer. Films with large variations in thickness or noticeable deformities were rejected. Measurements were performed with an Instron Universal Testing In-

strument (model 1130) using a 500 g load cell and a separation speed of 0.5 cm/min. The measured force and time data were converted to stress vs strain curves by a digital computer program interfaced to the Instron. The program also calculated Young's modulus values.

The mechanical properties of microwave dried and control films were compared statistically, using the program ANOVA (Sokal and Rohlf, 1981). The data were transformed when necessary to meet the assumptions of the analysis of variance. In two cases (Young's modulus and tensile strength for formulation 4), transformation was not possible and the non-parametric Kruskal-Wallis one-way analysis of variance by ranks was used (Sokal and Rohlf, 1981). In one of these cases (Young's modulus) this test showed significance; multiple comparisons were then performed using the method of rank sums (Dunn, 1964). When a parametric analysis of variance indicated significant differences among the means, either the T-method (equal to n) or the T' method (almost equal to n) was used for multiple comparisons (Sokal and Rohlf, 1981). All statistical comparisons are at the 95% confidence level unless otherwise noted. Five replicate measurements were performed for tensile strength and Young's modulus values, 4 replicates were performed for the drying rates and 2–4 replicates were performed for water vapor permeabilities. In the latter group, 4 replicates were always used for MWD films. The water vapor permeability data were analyzed statistically to compare film and open cup values. However, due to the small sample sizes for some of the controls, statistical analysis was thought to be inappropriate for comparisons of water vapor permeabilities of films dried by different processes, and so is not reported.

Results and Discussion

Drying rates for the 4 formulations are shown in Fig. 1 for AD, MWD and OD films, and are reported as the mean of 4 experiments. Water loss curves for the methyl cellulose formulation (no. 4) are shown in Fig. 2. For all formulations, drying rates for MWD films were from 2–22 times greater

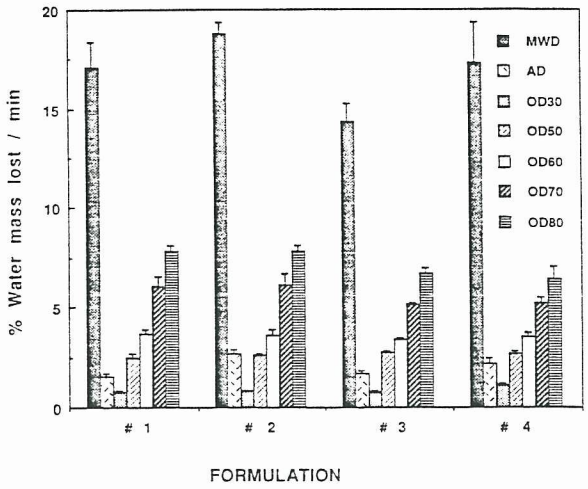

Fig. 1. Drying rates in percent of water mass lost per min of various formulations using different drying procedures; see Table 1 for formulation composition. Bars represent S.D. ($n = 4$).

than drying rates for OD controls at all temperatures. These results are significant at the 99.9% confidence level. Microwave drying could therefore offer a significant increase in drying rate over the 35–45°C hot air drying currently used industrially. Drying rates for AD controls were 9.1 to 14.3% of the drying rates for MWD films, indicating that convection contributed no more than 15% to the measured microwave drying rates.

Water vapor transmittances for all films were significantly different from the open cup values ($P < 0.01$), indicating that all films formed an intact barrier to water vapor; the water vapor permeability values for the films are presented in Fig. 3. For all formulations, the water vapor permeabilities of the MWD films were not consistently greater or less than AD or OD controls. Microwave drying therefore did not alter the ability of the films to serve as a water barrier, nor did it result in bubbles or other gross film defects that compromised film integrity. In preliminary experiments at higher microwave power settings, bubbles were formed in the films. By reducing the power setting, this problem was eliminated.

The mechanical properties of the films are summarized in Figs. 4–6. As shown in Figure 4, the Young's modulus values for MWD and OD30 films are significantly lower than those of AD and

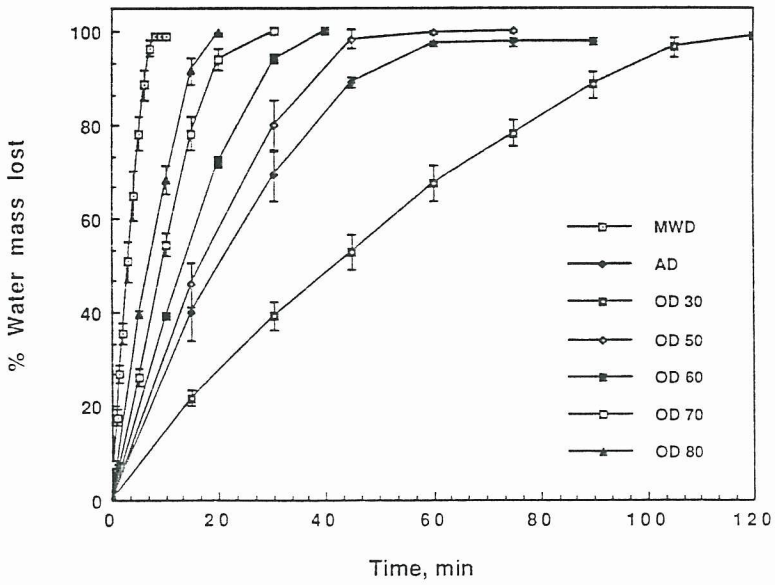

Fig. 2. Water loss in percent of water mass as a function of time for formulation 4 subjected to various drying processes; see Table 1 for formulation composition. Bars represent ± S.D.

OD50 films at the 95% confidence level. The Young's modulus values for MWD and OD30 films were not significantly different. MWD and OD30 films are therefore more elastic than AD and OD50 films.

The film tensile strengths were less dependent on the processing method than were Young's modulus values. Although the mean tensile strengths of MWD films tended to be less than those of controls, these differences generally were not significant. Specifically, at the 95% confidence level, the tensile strength of MWD films was not different from that of OD30 or AD films for any of the 4 formulations, as shown in Fig. 5. It

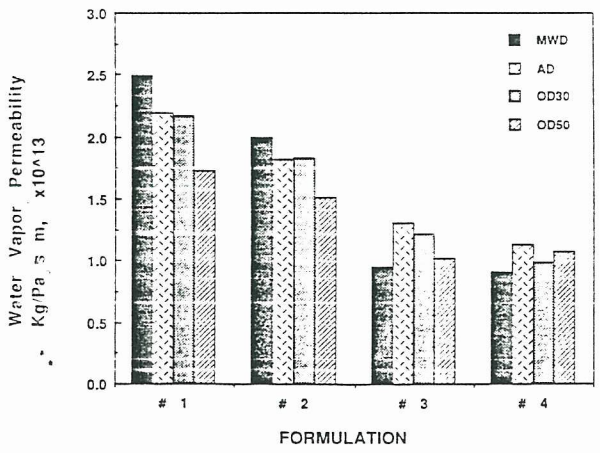

Fig. 3. Water vapor permeabilities for films prepared from various formulations using different drying processes; see Table 1 for formulation composition. $n = 4$ for MWD films; $n = 2$ or 3 for AD and OD films.

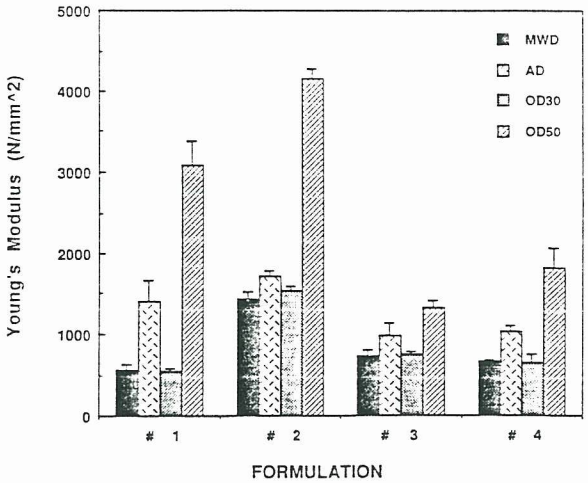

Fig. 4. Young's modulus values for films prepared from various formulations using different drying processes; see Table 1 for formulation composition. Bars represent S.D. ($n = 5$).

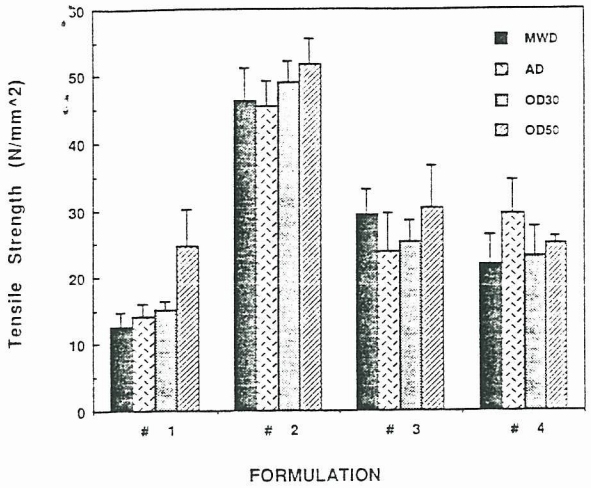

Fig. 5. Tensile strengths for films prepared from various formulations using different drying processes; see Table 1 for formulation composition. Bars represent S.D. ($n = 5$).

differed from that of the OD50 films only for formulation 1. Tensile strength is a measure of the greatest stress a film can withstand without breaking; a large value of tensile strength indicates a strong film. The data show that MWD films tend to be slightly weaker than controls, but that the difference is not statistically significant.

The ideal film coating is both strong and elastic, that is, it has a high tensile strength and a low

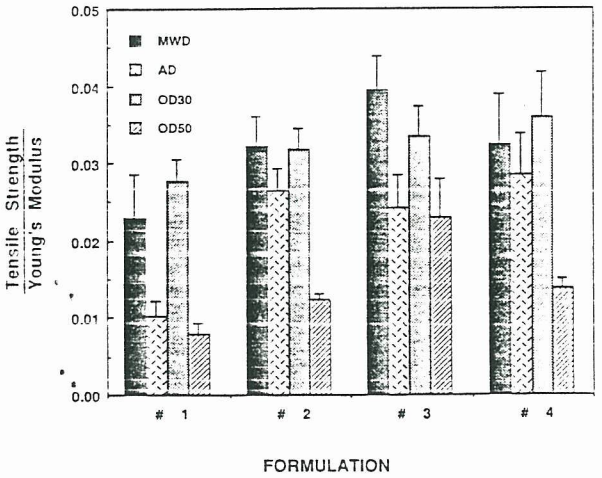

Fig. 6. The ratio of tensile strength to Young's modulus for films prepared from various formulations using different drying processes; see Table 1 for formulation composition. Bars represent S.D. ($n = 5$).

Young's modulus. The ratio of tensile strength to Young's modulus has been used as an indicator of film mechanical properties, with larger values of the ratio being more desirable (Rowe, 1983). A correlation between this ratio and the incidence of edge splitting for hydroxypropyl methylcellulose films has been demonstrated (Rowe, 1983). As shown in Fig. 6, the ratio for MWD films is comparable to that of OD30 films for all 4 formulations. The MWD and OD30 values are significantly greater than OD50 values for all formulations, and are significantly greater than AD values for all formulations except 4. Therefore, based on the tensile strength to Young's modulus ratio, the mechanical properties of MWD films are generally better than those of AD and OD50 controls, and are comparable to OD30 controls.

In conventional hot-air coating, drying rates are increased by increasing the inlet air temperature. Our results suggest that even in the relatively low 30–50 °C temperature range, temperature increases can adversely affect the mechanical properties of the film, as indicated by the fact that the tensile strength to Young's modulus ratio of the OD30 films was significantly greater than that of the OD50 films in all but one of the formulations tested. In contrast, microwave drying of free films offered a dramatic increase in the drying rate without compromising the mechanical properties. The tensile strength to Young's modulus ratio of the MWD films was comparable to that of the OD30 films, yet the MWD drying rates were 16–22 times greater than those of the OD30 controls.

In summary, microwave drying of aqueous-based tablet film coatings is a promising technique, offering dramatically increased drying rates without compromising the water vapor permeability or mechanical properties of the films. Whether or not the benefits reported here for free films will also be observed on coated tablets remains to be seen.

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