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Organic solvent residues in free ethyl cellulose films

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The properties of solvents used in film coating of tablets influence the quality of coating (Abdel-Aziz et al., 1974; Nadkarni et al., 1975; Abdel-Aziz and Anderson, 1976; Tamba Vemba and Roland, 1980). Patt and Hartman (1976) have shown that residual levels of various organic solvents in the coating films depend on the solvent, on the qualities of tablet cores, and on conditions used during coating and drying. Pure ethyl cellulose tablet coats release the test subject very slowly, but permeability can be regulated with hydrophilic additives, such as Tweens and Spans (Lindholm and Juslin, 1982).

The aim of the present study was a gas chromatographic determination of the time-course of solvent elimination from ethyl cellulose films. The film compositions used are presented in Table 1. With acetone, methanol and isopropanol as solvents, the solutions were poured on glass plates, while chromium steel and teflon plates were used with methylene chloride and chloroform, respectively. The films were allowed to dry at 22 ± 1°C.

Preparation of the test samples took place at 4°C to avoid evaporation of residual solvent. Film samples of 500 mg were extracted with 2.00 ml of methanol, while 2.00 ml of tetrahydrofurane was used in the determination of methanol residues. Isopropanol and 2-butanol were used as inner standards (0.1% v/v) in the quantification of methanol and chloroform, respectively, while 2-butanone (0.1% v/v) was used in the determination of acetone, isopropanol and methylene chloride. The capped test tubes were kept for 30 min in an ultrasonic bath at 5°C. After centrifugation, 0.1–0.3 μml of the extracts were immediately analyzed by temperature-programmed capillary column GLC. The inner glass surface of the OV-225 column (20 m, 0.32 mm i.d.) had been alkylated with pentafluorobenzyl bromide, this treatment resulting in prolonged retention of low-boiling compounds (Kari et al., 1981).

Sampling took place at 2, 4, 6, 8.5, 25 and 54 h from pouring on plates. Small methylene chloride residues (0.315 ± 0.006% m/m in unplasticized film and 0.187 ±

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TABLE 1

ANALYSIS OF VARIANCE RESULTS FROM QUANTIFICATION OF SOLVENT RESIDUES FROM UNPLASTICIZED AND PLASTICIZED ETHYL CELLULOSE FILMS

E = ethyl cellulose; TW = Tween; Sp = Span; F = variance.

Composition of film [1]	Solvents used	F	Significance [2]
E (100%)	acetone, isopropanol, chloroform	12.92	$P < 0.01$
E (70%) TW 20 (30%)	acetone, isopropanol	4.60	$P > 0.05$
E (70%) TW 81 (30%)	acetone, isopropanol, methanol, chloroform	1.01	$P > 0.05$
E (70%) Sp 20 (30%)	acetone, isopropanol, methanol, chloroform	1.35	$P > 0.05$

[1] Average film thickness was 93 ± 1 μm.

[2] Significance of differences between amounts of solvent residues. $P < 0.05$ = significant, $P > 0.05$ = not significant.

0.014% m/m with Span 20 as plasticizer) were found in the 2 h samples. In films containing Tween 20 or 81, methylene chloride was undetectable at 2 h. Methanol was undetectable from 8.5 h onwards. The results agree with those of Winkel and Hendrick (1984), the methylene chloride residues in coated tablets being lower than those of methanol. Acetone was undetectable from 8.5 h onwards, except in trace amounts in the film containing Tween 81, whereas isopropanol was still detectable in the 25 h samples of unplasticized films and in the 8.5 h samples of plasticized films. Chloroform was just detectable in the 25 h samples of unplasticized films. With Tween 81 and Span 20 as plasticizers, traces of chloroform were still detectable in the 8.5 h and 54 h samples, respectively.

According to one-way analysis of variance performed with the chromatographic data here obtained (Table 1), residual solvent amounts in unplasticized ethyl cellulose films are dependent on the type of solvent used in film preparation. On the other hand, the differences between residual solvent amounts are not significant in the films prepared by using plasticizing additives (cf. Table 1).

References

Abdel-Aziz, S.A.M., Armstrong, P.A.M. and Anderson, W., Transit in free films: casting solvent effects. J. Pharm. Pharmacol., 26 (1974) 131P–132P.

Abdel-Aziz, S.A.M. and Anderson, W., The influence of casting solvent composition on structure and permeability of acrylic-methacrylic ester copolymer films. J. Pharm. Pharmacol., 28 (1976) 801–805.

Kari, I., Huhtikangas, A., Gynther, J., Vartiainen, T. and Hiltunen, R., Modification of glass capillary gas chromatographic columns by alkylation of the glass surface with pentafluorobenzyl bromide. Chromatographia, 14 (1981) 462–464.

Lindholm, T. and Juslin, M., Controlled release tablets: ethyl cellulose coats containing surfactant and powdered matter. Pharm. Ind., 44 (1982) 937–941.

Nadkarni, P.D., Kildsig, D.O., Kraemer, P.A. and Banker, G.S., Effect of surface roughness and coating solvent on film adhesion to tablets. J. Pharm. Sci., 64 (1975) 1554–1557.

Patt, L. and Hartmann, V., Lösungsmittelreste in Filmdragees und isolierten Filmüberzügen. Pharm. Ind., 38 (1976) 902–906.

Tamba Vemba, J.G. and Roland, M., Influence of solvents and plasticizers on the permeability and the rupture force of ethylcellulose filmcoatings. Pharm. Acta Helv., 55 (1980) 65–71.

Winkel, D.R. and Hendrick, S.A., Detection limits for a GC determination of methanol and methylene chloride residues on film coated tablets. J. Pharm. Sci., 73 (1984) 115–177.