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Viscoelastic characterization of drug-loaded Eudragit E100 films for transdermal drug delivery

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Eudragit E 100 is a polymethacrylate derivative that is commonly employed as an adhesive in the formulation of transdermal patch systems. In these, therapeutic agents may be conveniently included directly in the adhesive layer. The clinical efficacy of such systems is directly dependent on the mechanical properties of the drug-containing layer, as this may affect, e.g. polymer integrity, bioadhesion and drug release. However, there is little information available concerning the effects of both processing conditions and the presence of therapeutic agents on the mechanical properties of transdermal adhesives composed of Eudragit E100. Therefore, the objective of this study was to examine the viscoelastic properties of films composed of a model drug (ibuprofen) and Eudragit E100, prepared under a range of processing conditions.

A series of Eudragit E100 films (n=24) were prepared containing Eudragit adhesive (20g), ethanol (20g) and ibuprofen base (0-50mg/cm^2 patch). Three films were prepared for each concentration of ibuprofen used. Films were cast in perspex moulds (100cm^2) backed with release liner and were dried for a period of 48 hours in incubators. Three film drying temperatures were examined; 25°C, 30°C and 40°C. Film uniformity was maintained by spirit-balancing casting moulds and by controlling solvent evaporation rates by covering moulds with glass funnels. Oscillatory properties of each film were investigated using a Carri-Med CSL^2-100 rheometer in conjunction with a parallel plate geometry. (2cm diameter, 1.0mm plate separation). Oscillatory measurements were performed at 20.0°C ± 0.2°C over a frequency range from 0.01 - 10.0Hz at a constant strain of 5.0 x 10^{-2}, selected from the linear viscoelastic region of the samples (Jones et al. 1998). Film adhesiveness was assessed by peel testing and adhesion (tensile) testing using a using a TA-XT2 texture analyser in conjunction with a Silescol® substrate (probe removal rate of 10.0mm.s^{-1}). The effects of drug content and drying temperature on the adhesive and rheological properties of films were statistically evaluated using a two-way Analysis of Variance (ANOVA).

Table 1. The effects of ibuprofen concentration and drying temperature on the storage modulus (G'), obtained at a representative frequency of 5.262Hz, and adhesion (peel) properties of a range of Eudragit films.

Temp. (°C)	Drug (mg/cm^2)	G'(Pa)	Adhesion (N.mm)
25	0	307100 ± 4222	7.39 ± 0.34
	20	92613 ± 521	9.72 ± 0.67
	50	21710 ± 2399	18.53 ± 4.0
30	0	446133 ± 4252	7.19 ±. 0.93
	20	116233 ± 1817	10.99 ± 0.76
	50	27290 ± 5641	15.79 ± 2.1
40	0	546400 ± 3477	7.89 ± 0.68
	20	275633 ± 3288	11.77 ± 0.94
	50	115800 ± 1808	17.47 ± 2.6

Rheological results indicate that as the concentration of drug in the polymer films increased, storage and loss moduli and dynamic viscosity decreased and tan (delta) increased. These results suggest that incorporated drug physicochemically interacts with the Eudragit polymer, thus decreasing the interactions between adjacent polymer chains and hence film elasticity. As the drying temperature was increased, storage and loss moduli and dynamic viscosity increased, indicative of improved film quality. Adhesiveness increased as drug concentration increased due to the increased formulation tack. However, drying temperature did not significantly affect adhesiveness.

This study has therefore shown that the formulation of drug-containing Eudragit films as transdermal drug delivery systems requires careful consideration, as the mechanical properties of such systems are clearly influenced by both formulation and processing conditions.

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