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THE EFFECT OF SEMI-PERMEABLE FILM COVERS ON THE BIOVAILABILITY OF BETAMETHASONE VALERATE DELIVERED FROM A TOPICAL CREAM VEHICLE

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Plastic "occlusive" films such as Polythene and Saran wrap are used with topical corticosteroid products to enhance their effectiveness in the treatment of recalcitrant psoriatic lesions. The prevention of moisture loss from the skin surface, leading to a hydration of the stratum corneum, results in an increase in the permeability of steroids through skin. This study was initiated to investigate the control that could be exerted on the bioavailability of a topical corticosteroid in man by the use of different covering films having a wide range of water vapour transmission rates (WVTR), and consequently likely to produce different degrees of stratum corneum hydration.

A range of extruded 2 mil thickness ethylene vinyl acetate (EVA) films (3M Specialities Division, Loughborough) containing varying proportions of vinyl acetate (VA) and an aluminium foil laminate (Scotchpak liner) with a range of WVTR to encompass the normal range of transepidermal water loss were selected for study. These were employed for a six hour period to cover 1 mg betamethasone valerate cream (0.1%) (Glaxo, U.K.), applied to discrete 7 x 7 mm square sites on the volar forearms of ten caucasian volunteers. The skin blanching assay technique (Barry & Woodford, 1974) was utilised as a means of comparing the effect of the films or laminate on topical bioavailability by reference to unoccluded treatment sites. Skin blanching of all sites was assessed under standardised lighting conditions at times of 1, 2, 3, 6, 18, 26, 42, 50, 66, 74, 90 and 90 hours after removal. Results for each treatment group were expressed for all volunteers as a percentage of the total possible score (% TPS). To compare bioavailability the areas under the blanching curve (AUC) were calculated using the trapezoidal rule.

Film	WVTR* ($mg\ cm^{-2}\ h^{-1}$)	Peak Response (% TPS)	AUC (% TPS x h^{-1})
Scotchpak liner	0.24	65.0	1611
EVA with 4.5% VA	0.89	58.7	1601
EVA with 9% VA	1.82	61.9	1554
EVA with 19% VA	4.75	45.6	1281
Unoccluded		13.1	530

* Determined by B.P. 1988 method for water vapour permeability, Appendix XX K A224

It can be seen that all four films have a marked effect of increasing the degree of skin blanching (bioavailability) of betamethasone valerate from the applied cream in comparison to the unoccluded formulation. The resultant increase was inversely related to the moisture permeability of the film. The fact that the two most permeable films still produced such a marked enhancement of blanching in comparison with the unoccluded cream was somewhat surprising, as these films have much greater moisture permeability than the normal range of forearm transepidermal water loss of 0.2-0.7 mg $cm^{-2}\ h^{-1}$ (Roskos & Guy, 1989). This is an indication that in-vivo, at least when applied over a topical cream, such films provide more of a barrier to transepidermal water loss than that predicted in-vitro. The degree of occlusion effected by a covering film (assessed as WVTR), however, is shown to be a determining factor in the degree of enhancement of topical corticosteroid bioavailability.

Barry, B.W., Woodford, R. (1974) Br.J.Dermatol., 91: 323-337
Roskos, K.V., Guy, R.H. (1989) Pharm.Res., 6: 949-953