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The effect of a hydrocolloid dermatological patch (Actiderm) in potentiating the skin blanching activity of triamcinolone acetonide

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Summary

Volunteer studies were carried out to assess the effect of a hydrocolloid containing dermatological patch (Actiderm) on the skin blanching activity of triamcinolone acetonide applied in a range of topical vehicles. Multiple blanching assessments were carried out following different application times (up to 72 h). The series of response/time profiles generated enabled the effect of different dosing regimes to be evaluated by comparing changes in peak response and cumulative area under the curve. Actiderm markedly increased the topical bioavailability of triamcinolone acetonide from creams and alcoholic solutions: similar activity to that produced by Saran Wrap occlusion was achieved. In contrast, only a slight effect on bioavailability from an ointment application was demonstrated. When using Actiderm both the concentration and quantity of steroid cream applied can be reduced considerably from that used in conventional twice daily non-occlusive therapy whilst still achieving greater activity.

Introduction

Actiderm is an adhesive dermatological patch that enhances the topical bioavailability of corticosteroids (Martin and Marriott, 1989; Fairbrother et al., 1991). It is comprised of an embossed polyethylene film to which is laminated 0.76 mm thick, pressure-sensitive adhesive. The adhesive is based on a mixture of synthetic rubbers and a block copolymer elastomer into which are dispersed equal quantities of three hydrocolloids (sodium carboxymethylcellulose, gelatin and pectin). On skin application, the hydrocolloids in the patch absorb transepidermal water and modulate skin hydration: this would be anticipated to alter steroid skin penetration rates (Hollingsbee et al., 1990).

In earlier skin blanching studies, Queen et al. (1988) and Marriott and Martin (1989) failed to show any difference in the bioavailability of proprietary corticosteroid creams applied at a single dose of 10 mg/cm^2 under Actiderm when compared with a non-absorptive occlusive plastic film (Saran Wrap$^{(R)}$). Modification of the drug con-

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TABLE 1

Summary of skin blanching study protocols and results

Study ref.	Materials	Steroid	(% w/w)	Applied quantity (mg/cm^2)	Covering film	Applied frequency	Application times (h)				Application time (h)				Application times (h)			
							6	24	48	72	6	24	48	72	6	24	48	72
							Observed peak (% TPS)				Cumulative AUC (% h)				Summed % TPS			
A	Kenalog cream	TA	0.100	2	Unoccluded	Once	14.6				554				102			
	Kenalog cream	TA	0.100	2	Actiderm	Once	47.9				1222				221			
	Kenalog cream	TA	0.100	2	Saran	Once	46.3				1137				218			
	Kenalog cream base	–	–	2	Unoccluded	Once	9.9				321				66			
	Kenalog cream base	–	–	2	Actiderm	Once	7.8				320				65			
	Kenalog cream base	–	–	2	Saran	Once	13.0				485				90			
	Kenalog ointment	TA	0.100	2	Unoccluded	Once	15.1				428				86			
	Kenalog ointment	TA	0.100	2	Actiderm	Once	17.7				589				109			
	Kenalog ointment	TA	0.100	2	Saran	Once	29.7				804				148			
	Kenalog ointment base	–	–	2	Unoccluded	Once	10.4				420				78			
	Kenalog ointment base	–	–	2	Actiderm	Once	13.0				406				73			
	Kenalog ointment base	–	–	2	Saran	Once	13.5				414				84			
B	TA in Kenalog cream base	TA	0.005	2	Actiderm	Once	24.4	31.2			642	1250			74	130		
	TA in Kenalog cream base	TA	0.010	2	Actiderm	Once	18.7	35.0			591	1186			63	129		
	TA in Kenalog cream base	TA	0.025	2	Actiderm	Once	28.1	36.2			749	1497			84	151		
	TA in Kenalog cream base	TA	0.050	2	Actiderm	Once	40.6	41.2			1036	1815			111	175		
	TA in Kenalog cream base	TA	0.100	2	Actiderm	Once	38.7	42.5			1023	1933			107	184		
	Kenalog cream base	–	–	2	Actiderm	Once	5.0	6.2			141	189			25	17		
C	TA in Kenalog cream base	TA	0.100	2	Actiderm	Once		35.0	21.2	26.2		1095	1565	2253		152	107	125
	TA in Kenalog cream base	TA	0.100	10	Actiderm	Once		41.2	23.7	28.7		976	1617	2531		164	111	142
	TA in Kenalog cream base	TA	0.025	2	Actiderm	Once		36.2	20.6	27.8		873	1268	2078		147	92	122
	TA in Kenalog cream base	TA	0.025	10	Actiderm	Once		41.9	21.9	28.1		1072	1388	2321		170	97	135
	Kenalog cream base	–	–	2	Actiderm	Once				14.2								50
	Kenalog cream base	–	–	10	Actiderm	Once				11.7								42

D	Kenalog cream	TA	0.025	2	Actiderm	Once	31.6	41.9	21.9	23.7	1402	1845	1890	2832	113	171	100	127
	Kenalog cream	TA	0.100	2	Actiderm	Once	40.0	47.5	30.3	29.4	1651	2082	3056	3403	156	183	159	149
	Kenalog cream base	–	–	2	Actiderm	Once	4.4	5.6	16.9	5.6	52	186	575	567	14	19	59	19
E	Kenalog cream	TA	0.025	2	Actiderm	Once		45.6	25.6	22.5		1447	1923	2327		189	125	111
	Kenalog cream	TA	0.100	2	Unoccluded	Twice daily		18.1	11.9	15.0		632	733	1313		67	54	77
	Kenalog cream base	–	–	2	Actiderm	Once		7.5	11.2	12.5		180	339	816		30	28	54
	Kenalog cream base	–	–	2	Unoccluded	Twice daily		2.5	7.5	7.5		43	192	447		9	20	32
F	Kenalog cream	TA	0.100	2	Actiderm	Once		47.5	23.7	25.0		1184	1803	2148		189	119	110
	Kenalog cream	TA	0.100	2	Unoccluded	Twice daily		17.5	11.2	13.7		565	751	1266		66	71	71
	Kenalog cream base	–	–	2	Actiderm	Once		8.1	9.4	11.2		153	387	559		31	37	30
	Temovate cream	CP	0.050	2	Unoccluded	Twice daily		37.5	18.7	14.4		1456	1548	1946		172	82	79
G	Kenalog cream	TA	0.100	10	Actiderm	Once	65.0	36.9	25.0	27.5	2125	2731	3124	3885	276	187	133	149
	Kenalog tincture	TA	0.100	10	Actiderm	Once	59.4	37.5	26.9	29.6	1781	2445	2984	3740	217	172	140	156
	No treatment	–	–	–	Actiderm	Once	2.5	10.0	17.5	22.9	91	603	1112	1567	11	54	85	100
H	Kenalog tincture	TA	0.100	2	Actiderm	Once	62.0	48.7	32.2		1788	2731	3173		234	226	149	
	Kenacort-T tincture	TA	0.200	2	Actiderm	Once	65.0	47.0	30.9		1942	2807	3429		250	221	158	
	Kenacort aerosol tincture	TA	0.0835	2	Actiderm	Once	49.4	48.7	31.2		1255	2171	2617		185	212	130	
	Kenalog tincture	TA	0.100	2	Unoccluded	Once	11.0				445				53			
	Kenacort-T tincture	TA	0.200	2	Unoccluded	Once	12.5				587				60			
	Kenacort aerosol tincture	TA	0.0835	2	Unoccluded	Once	16.9				409				68			
I	Kenacort-A cream	TA	0.100	10	Actiderm	Once		34.4	25.0	28.5		1135	2010	2759		150	136	145
	Drenison tape	FL	4mcg/cm^2	–	–	Once		41.3	27.8	29.4		1328	1988	2923		178	145	155
	Tokuderm tape	BV	6mcg/cm^2	–	–	Once		33.1	31.9	32.4		1323	2651	3206		157	180	167
	No treatment	–	–	–	Actiderm	Once		7.5	18.1	24.3		288	884	1543		35	78	105
J	Kenacort-A cream	TA	0.100	10	Actiderm	Once		46.2	36.1	28.9		1754	2389	2835		222	172	140
	Fluvean tape	FA	8mcg/cm^2	–	–	Once		51.9	40.1	40.4		3297	3738	5032		269	229	235
	Fluzon tape	FA	8mcg/cm^2	–	–	Once		49.3	38.9	33.9		2582	3504	3507		239	215	178
	No treatment	–	–	–	Actiderm	Once		14.4	27.6	25.0		298	1394	1521		49	118	99

TA, triamcinolone acetonide; CP, clobetasol propionate; FL, fludroxycortide; BV, betamethasone valerate; FA, fluocinolone acetonide.

centration, the quantity and composition of the vehicle applied, and the time of application of formulations beneath occlusive patches are, however, likely to alter the overall topical bioavailability. The present studies investigate the effects of dose response and vehicle characteristics on the delivery of triamcinolone acetonide applied in formulated products under Actiderm. Comparisons are also made of the intensity and drug response obtained when applied under Actiderm with those of conventional unoccluded dosing regimes or by the application of proprietary occlusive corticosteroid tapes.

The skin blanching technique used for the studies is essentially the multipoint procedure described by Barry and Woodford (1978), but is expanded to allow evaluation of a series of application times (Marriott and Martin, 1988). Data obtained using this procedure not only provide the basis for relative bioavailability estimation but also allow evaluation of the tachyphylaxis that can occur with repeated drug application (Du Vivier and Stoughton, 1975).

Materials and Methods

Actiderm dermatological patches were supplied by ConvaTec, Princeton, NJ, U.S.A. Saran Wrap(R) (Dow Chemical Co., Minneapolis, MN, U.S.A.) was purchased on the open market. Triamcinolone acetonide creams were supplied by E.R. Squibb and Sons, Princeton, NJ, U.S.A. (Kenalog 0.1 and 0.025%) or Sankyo Co., Tokyo, Japan (Kenacort A 0.1%). Triamcinolone acetonide ointment (Kenalog 0.1%) was supplied by E.R. Squibb and Sons, Princeton, NJ, U.S.A. Triamcinolone acetonide tinctures were supplied by Novo Industries A/S, Copenhagen, Denmark, (Kenalog 0.1%) and E.R. Squibb and Sons, Hounslow, U.K. (Kenacort-T comp. tincture 0.2%). The triamcinolone acetonide aerosol concentrate was manufactured by ConvaTec Product Research Laboratories, Deeside, U.K., to the formula used in Kenalog Spray (E.R. Squibb and Sons, Princeton, NJ, U.S.A.).

Clobetasol propionate cream 0.05% (Temovate, Glaxo Dermatology Products, Research Triangle Park, NC, U.S.A.); Fluzon tape (Taisho Pharmaceuticals, Tokyo, Japan), containing triamcinolone acetonide (8 $\mu g/cm^2$); Tokuderm (Taiho Pharmaceutical Co., Tokyo, Japan), containing betamethasone valerate (6 $\mu g/cm^2$); Drenison tape (Eli Lilly, Indianapolis, IN, U.S.A.); Triamcinolone acetonide creams containing 0.005, 0.01, 0.025, 0.05% were manufactured by ConvaTec Product Research Laboratories, Deeside, U.K., by sequential dilutions of Kenalog cream 0.1% with its base vehicle.

Methods

Ten separate studies were conducted and these are summarised in Table 1. In study A the effect of Actiderm applied over triamcinolone acetonide cream or ointment was compared with both an unoccluded application and an application under an occlusive plastic film (Saran wrap).

The effect of dosing level was investigated in studies B–D. In studies B and D the concentration of steroid cream applied was varied, keeping the quantity applied to the skin constant, whilst in study C both concentration and skin application quantity were varied.

In studies E and F the application of triamcinolone acetonide cream under Actiderm was compared with conventional twice daily unoccluded treatments either with triamcinolone acetonide cream itself (0.025 and 0.1%) or a highly potent steroid product containing clobetasol propionate 0.05%.

Studies G and H examined the blanching response induced by Actiderm applied over two alcoholic tinctures and an aerosol formulation. In the case of the aerosol formulation the aerosol concentrate (without propellant) was used to enable reliable and comparative dosage.

Finally, studies I and J compared the effect of a Japanese triamcinolone acetonide cream (Kenacort A) applied under Actiderm with proprietary adhesive corticosteroid tape products available in Japan.

Skin blanching methodology

10–12 Caucasian non-patient volunteers, who had not been treated with topical or systemic corticosteroids for at least 30 days, were em-

ployed in each of the studies. The nature and purpose of the study were explained to each volunteer who gave their written informed consent. The studies were performed under medical supervision.

Up to 12, 7×7 mm discrete sites were utilised on each forearm and were allocated to specific treatments according to randomisation charts. Prior to application of the treatments the sites were defined using areas punched from double-sided adhesive tape (Blenderm, 3M Health Care, Loughborough, U.K.). Creams and ointment were applied to the test sites by extrusion of a standard length from a 2 ml disposable syringe and needle, the method of application having been shown to deliver $\pm$ 20% of the target amount to the test site. Solutions were applied to the test sites using a micropipette. All treatments were spread evenly over the test site by means of a solid glass rod. Except when Saran Wrap was used to cover the test sites, the adhesive tape was then removed. The sites were then either left uncovered, or covered by 15×15 mm squares of Actiderm. Saran Wrap, being non-adhesive, was applied to the double-sided adhesive tape. In the case of studies J and K, the adhesive corticosteroid tapes were applied directly to the test site.

Covering materials and securing adhesive were left on the skin for either 6, 24, 48 and 72 h before removal and assessment of skin blanching commenced 1 h later. All test site locations were marked precisely with permanent ink.

For studies involving unoccluded treatments, volunteers were asked to leave their forearms uncovered for the first 6 h of the study so that removal of cream/ointment by clothing was minimised.

In the case of studies involving twice daily application (E and F), creams were reapplied either once at 12 h, three times at 12, 24 and 36 h or five times at 12, 24, 36, 48 and 60 h with assessment of skin blanching commencing 13 h following the last application.

Skin blanching was assessed by an experienced investigator under standardized lighting conditions, consisting of a Hancocks lightbox (fitted with 2×18 W Philips Graphica fluorescent lamps) fixed about 350 cm above the arm, at times of 1, 2, 3, 6, 26, 50, 74 and 98 h. Additional assessment times of 18, 42, 66 and 90 h were included for 6 h application times. The degree of pallor was estimated using a 0–4 scale with half point ratings based on that of Barry and Woodford (1978). All estimations of pallor were made without reference to application charts. Volunteers avoided elevated temperatures and arm contact with water during the trial.

Results and Discussion

For each test preparation the results for all volunteers were expressed as a percentage of the total possible score (% TPS) at each time point. From plots of these data as a function of time, areas under the curve (AUC) were calculated using the trapezoidal rule. For multiple application time studies where curves overlapped, the data for the longer application time (normally of higher value) were given precedence in calculations of the cumulative AUC value.

To allow direct inter- and intra-study comparisons of treatments applied for different lengths of time, summed % TPS values (Barry and Woodford, 1974) were calculated using assessment times of 1, 2, 3, 6, 26, 50, 74 and 98 h only. These values together with those for cumulative AUC and the maximum observed peak are shown for all studies in Table 1.

There has been criticism in the scientific literature (Smith et al., 1989) of the use of single point estimations of skin blanching response compared to multiple time assessments which allow estimates of AUC (or summed % TPS) to be made, particularly for the comparisons of the relative bioavailability of the same steroids from different vehicles.

Comparison of the calculated AUC values with the peak responses (generally seen at 6 h post-removal of treatment) from the present studies indicates good linear correlation between these two parameters (Fig. 1). Thus, either parameter would seem appropriate as a means of comparing the blanching response of triamcinolone acetonide in these studies.

Some variation in the results from one trial to another, where similar batches of materials and

protocols were used, was seen (e.g. as seen in studies I and J) and is not surprising in view of the use of different volunteer groups of relatively small size from trial to trial and the large difference often found in the response between volunteers. Standard errors of individual volunteer peak response or AUC results were typically 10–15% of the mean value. Such errors are of a similar level to those reported by Barry and Woodford (1978). No attempt was made to select volunteers for the studies on the basis of their ability to respond to steroid, as it was considered that a range of volunteers covering a normally wide response range was preferable for distinguishing the differences between high blanching responses anticipated from the use of occluded potent steroid creams.

As well as differences in the level of blanching response occurring between trials, there is evidence that the application time to give a peak response also can differ. For example, in study G application of 0.1% triamcinolone acetonide cream at 10 mg/cm^2 under Actiderm produced a greater peak response at 6 h than at 24 h, whilst in study B, where only 2 mg/cm^2 was applied, the situation was reversed.

The differences between studies indicates that caution is necessary in making cross-trial comparisons without the inclusion of identical control treatments in each.

A further problem when interpreting results of skin blanching studies is the significant blanching response often seen with unmedicated products (Woodford and Barry, 1973). For example, Actiderm produced significant blanching when applied to skin alone (e.g. as in studies I and J; see Fig. 8), the magnitude of which increased with application time and was similar to that typically seen with unoccluded moderately potent steroids. Such a response was reported previously by Marriott and Martin (1988). Results of study A showed very similar levels of blanching produced by both base creams and ointments applied unoccluded or occluded by Actiderm or Saran Wrap (see Fig. 2). The inclusion of control preparations in studies allows the vehicle blanching effects to be considered in the interpretation of study results and is essential for comparisons of treatments with low responses. Suitable controls were not available, unfortunately, in the case of the corticosteroid tapes used in studies I and J.

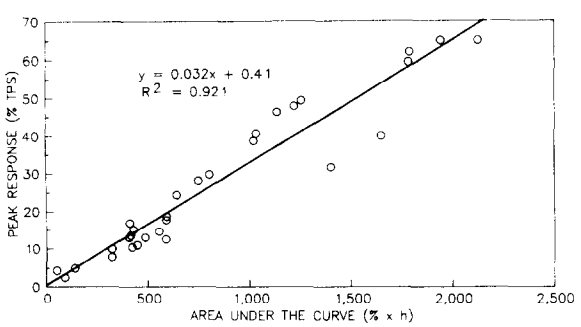

Fig. 1. Correlation of peak response with area under the curve for skin blanching profiles recorded in studies A–J.

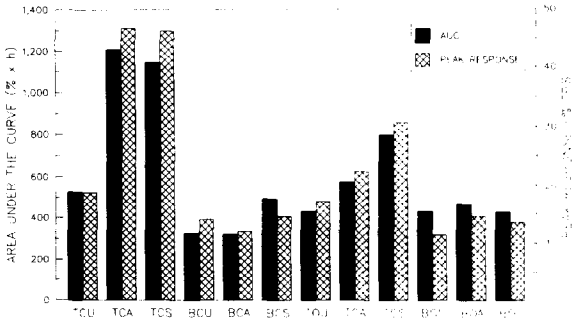

Fig. 2. The mean blanching responses for treatment groups in study A. A comparison between triamcinolone acetonide cream and ointments applied unoccluded, under Actiderm or under Saran wrap. T, triamcinolone acetonide; B, base; C, cream; O, Ointment; U, unoccluded; A, Actiderm; S, Saran Wrap.

The comparison of Actiderm with Saran Wrap occlusion. The results of study A are consistent with the increase in blanching response reported previously with a wide range of corticosteroid cream products applied under Actiderm and Saran Wrap (Marriott and Martin, 1988). The results also are in agreement with previous studies using higher skin application quantities of Kenalog cream (10 mg/cm^2) in which the blanching responses under both Actiderm and Saran Wrap were of similar magnitude following 6, 24, 48 and 72 h of application (Queen et al., 1988). The ointment blanching responses under Actiderm and Saran Wrap were, however, different

both from each other and lower than the comparative cream responses. Meyer et al. (1988) also showed availability from ointments to be less affected (and even reduced in some cases) by occlusion, the reasons for this phenomenon being unknown. The lack of response of the ointment under Actiderm (only slightly greater than the unoccluded treatment) when compared to the Saran Wrap response suggests an interaction of the triamcinolone acetonide with the patch material, effectively reducing the concentration available for skin absorption. As the hydrophobic adhesive matrix of Actiderm readily absorbs mineral oil (of which the ointment base is largely composed) this is a likely explanation for the reduced bioavailability.

The effect of applied dose on the skin blanching response of triamcinolone acetonide cream applied under Actiderm. Application of different skin application quantities of triamcinolone acetonide creams (2 and 10 mg/cm^2) produced little difference in the blanching response with the 0.1 or 0.025% creams (study C, see Fig. 3).

Application of 2 mg/cm^2 of cream at different concentrations (study B) indicates that a dose-response relationship exists (see Fig. 4) at constant

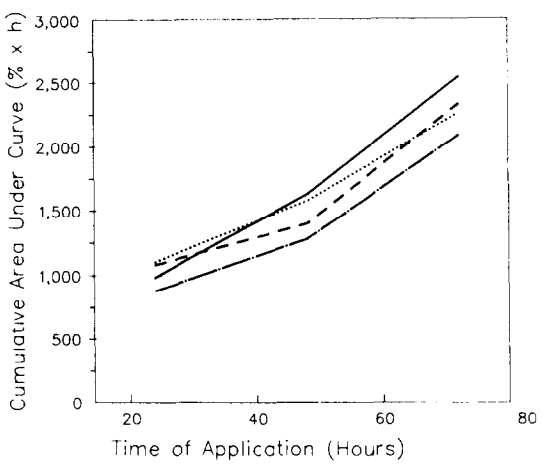

Fig. 3. The effect of the quantity of triamcinolone acetonide cream applied to the skin under Actiderm on the skin blanching response. 0.1% triamcinolone acetonide; 10 mg/cm^2 (———), 2 mg/cm^2 (·····); 0.025% triamcinolone acetonide: 10 mg/cm^2 (— — —), 2 mg/cm^2 (-·-·-).

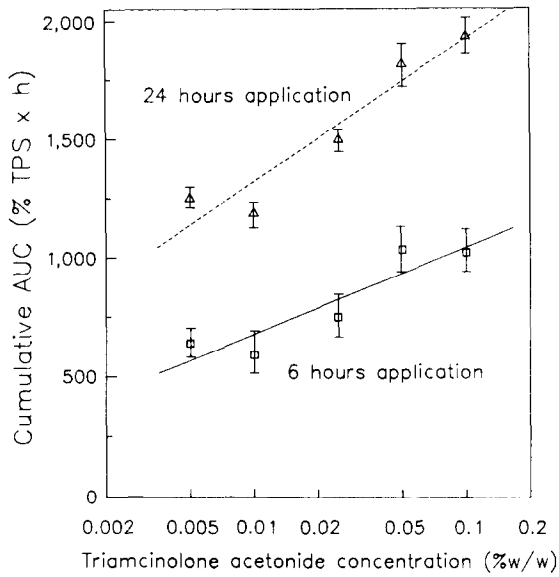

Fig. 4. The effect of concentration on the skin blanching of triamcinolone acetonide cream applied at 2 mg/cm^2 under Actiderm (values are means ± SE).

cream loadings. However, within the range of concentration of triamcinolone acetonide creams currently commercially available (0.025–0.5%), only a small difference in activity is predicted. A specific study (study D) comparing a single application of 0.025% and 0.1% proprietary creams under Actiderm confirmed this small difference over a prolonged period of application.

Although no differences have been seen previously between 0.025, 0.1 and 0.5% Kenalog cream (Stoughton and Wullich, 1989) when applied unoccluded, the effect of applied triamcinolone acetonide cream dose under occlusion has not been reported previously.

Comparison of triamcinolone acetonide cream applied under Actiderm with conventional twice daily unoccluded treatments. In study E a low clinically applied dose of Kenalog cream (0.025%, 2 mg/cm^2) produced a greater response than multiple applications of 0.1% Kenalog cream (twice daily) throughout a 72 h period (see Fig. 5) despite only 1/20th of the quantity of drug being applied to the skin.

In study F a single application of 0.1% Kenalog cream applied under Actiderm produced a

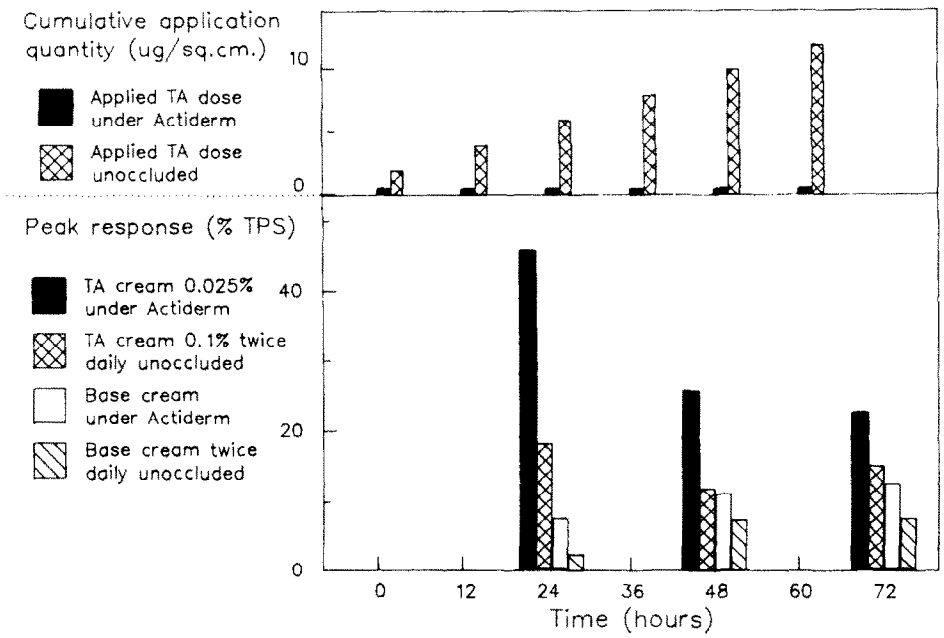

Fig. 5. A comparison of the skin blanching produced by a single application of triamcinolone acetonide (TA) cream 0.025% with twice daily application of 0.1% cream unoccluded.

markedly greater blanching response when compared to twice daily, unoccluded application of the same cream, and an equivalent response to that of unoccluded clobetasol propionate cream 0.05%, classified by Stoughton (1989) as superpotent (see Fig. 6). Tachyphylaxis of the clobeta-

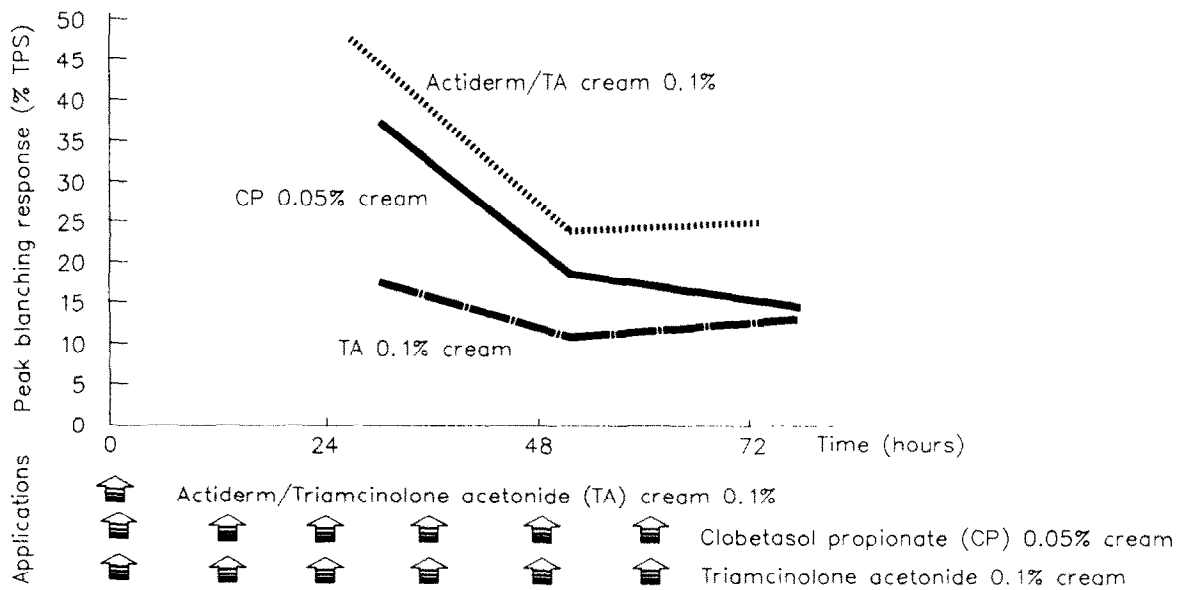

Fig. 6. The skin blanching profile of a single application of triamcinolone acetonide (TA) cream 0.1% applied under Actiderm with that of TA cream 0.1% and Clobetasol propionate cream 0.05% applied unoccluded twice daily.

sol propionate response clearly occurs over the first few days of treatment. The response of triamcinolone cream applied under Actiderm also shows a similar reduction with time. Whether or not this is due to a tachyphalyxis or merely an indication of reduced steroid absorption is not certain: the lack of any marked reduction in blanching activity with greatly reduced drug loadings under Actiderm (study B) would suggest the former is more likely.

The ability of Actiderm to enhance the activity of triamcinolone acetonide, predicted from these studies, has been confirmed in the clinic. The Actiderm Multicentre Study Group (1990) and David and Lowe (1989) both showed Actiderm applied over triamcinolone cream 0.1% (replaced once every 48 h) to be better than twice daily application of the same cream unoccluded in the treatment of psoriasis. The former study also showed increased effectiveness for betamethasone valerate and hydrocortisone cream applied under Actiderm. In another study, Bagatell (1988) showed that Actiderm applied over a moderately potent steroid (hydrocortisone valerate cream 0.2%) was more effective in treating psoriasis than twice daily application of a superpotent steroid cream product containing betamethasone diproprionate.

Use of Actiderm over other topical vehicles. Use of creams and ointments under Actiderm can be problematical in that the presence of cream excipients at the interface between the patch and skin reduces adhesion, necessitating using an oversize patch with a margin at the edge for attachment to untreated skin. The use of evaporating, non-greasy vehicles such as tinctures and aerosols has the advantage in that, subsequent to evaporation of the solvent, the patch adheres adequately to the treated skin.

Results of blanching studies with alcoholic tinctures (including the aerosol concentrate solution) under Actiderm confirmed marked enhancement of skin blanching activity (2–3 times) in all cases. Although such an enhancement was indeed anticipated following previous in vitro skin penetration studies using similar test materials (Kadir et al., 1990), no rank order correlation between the two studies was found for the various formulations.

Results for the comparative study of Kenalog

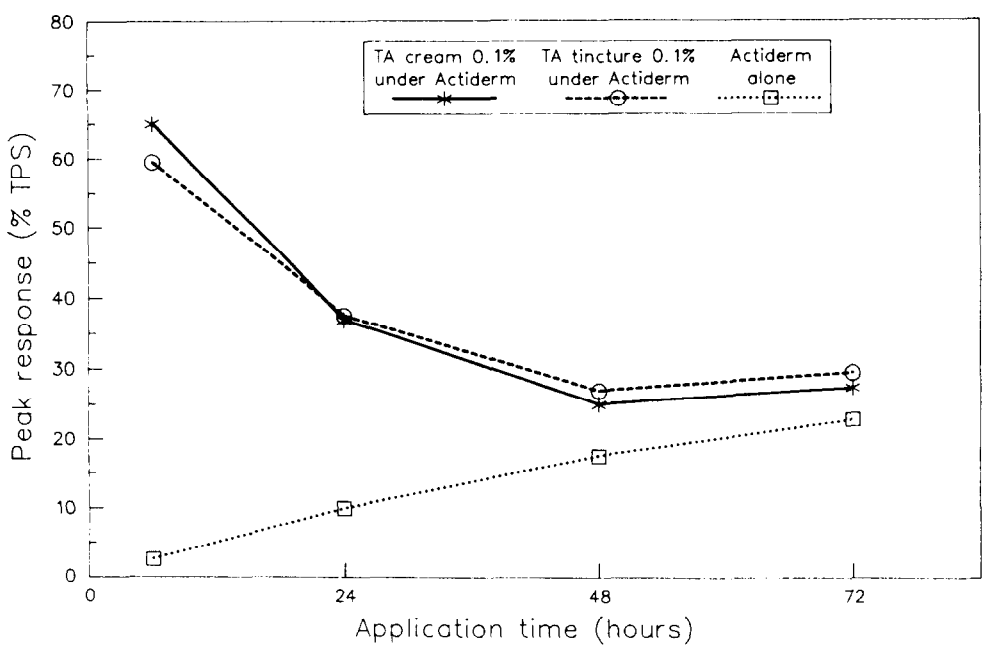

Fig. 7. A comparison between the skin blanching produced by triamcinolone acetonide 0.1% cream and tincture applied under Actiderm.

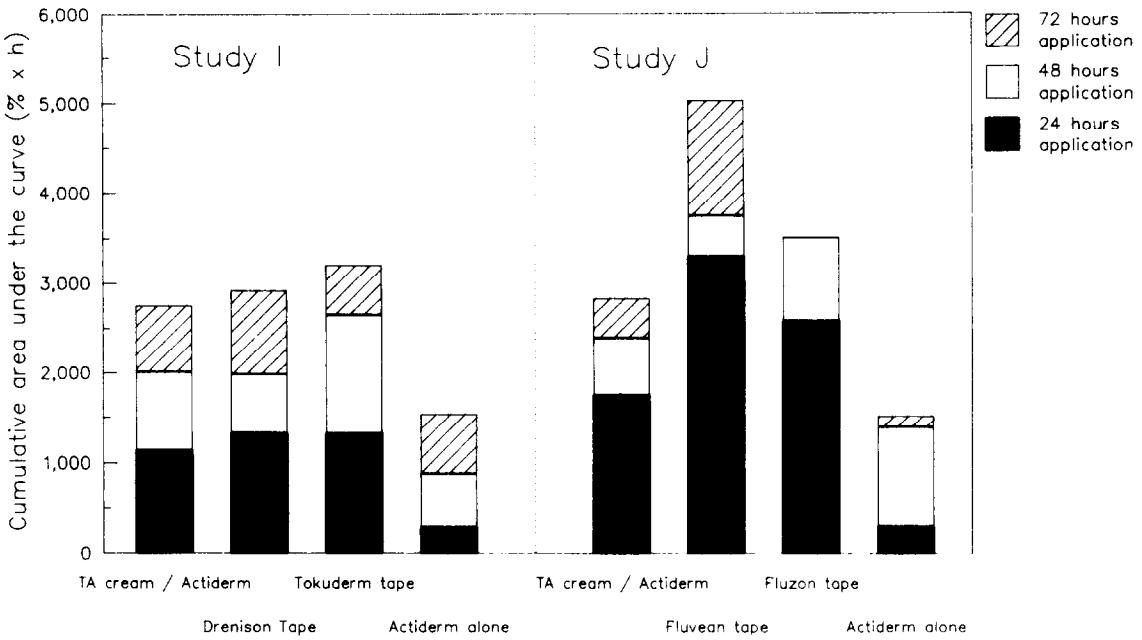

Fig. 8. A comparison between the skin blanching produced by triamcinolone acetonide cream 0.1% applied under Actiderm and four Japanese corticosteroid containing occlusive, adhesive tapes.

cream and tincture under Actiderm (study H) suggest that the use of either product under Actiderm will give an equivalent response (see Fig. 7).

Comparison with steroid-impregnated tape products. Two studies (I and J) compared Actiderm applied over Kenacort cream with four steroid impregnated, non-hydrocolloid containing patches commercially available in Japan (see Fig. 8). The absence of control (unmedicated) tape products does not allow the effect of the placebo-induced blanching typically seen with occlusive films (and clearly seen in this study with Actiderm) to be taken into account. Nevertheless, the response seen with the triamcinolone acetonide cream applied under Actiderm was similar, or only slightly less than that achieved with all the tapes. A recent clinical study (Clinical Research Group for Actiderm, 1990) showed a similar activity for Actiderm applied over hydrocortisone cream to that of Drenison (Fludroxycortide, 4 $\mu g/cm^2$) tape in psoriasis.

Conclusions

The skin blanching activity of triamcinolone acetonide has been shown to be increased by Actiderm occlusion. This effect is marked for both cream and alcoholic solution and only slight for ointments. As a good correlation exists between blanching response and clinical activity (Cornell and Stoughton, 1985) a similar increase in clinical effectiveness would be anticipated and indeed has been demonstrated in a number of clinical studies. The enhancing effect in the case of creams is similar to that achieved by use of an occlusive plastic film, Saran Wrap, or by multiple application of high potency products. The dose of steroid applied can be reduced to a small fraction of that typically applied during twice daily unoccluded application whilst still maintaining a greater activity.

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