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Assessment of the potential of a new hydrocolloid dermatological patch (Actiderm) in the treatment of steroid-responsive dermatoses

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Summary

A new hydrocolloid dermatological patch (Actiderm) has been assessed with regard to its physical properties and compared with plastic film (Saran Wrap) in its ability to enhance the blanching profile of a topical corticosteroid (triamcinolone acetonide). It was shown that the use of Actiderm was at least as effective as Saran Wrap in promoting corticosteroid activity. However, the former was found to possess a number of advantages including its relative ease of application and good adhesive properties. On the basis of in vitro moisture uptake studies it was concluded that the dressing maintains a moist microclimate adjacent to the intact stratum corneum by absorbing primarily water.

Introduction

Occlusion has been shown to be important in the promotion of drug bioavailability (Dempski et al., 1965; Barbier et al., 1979; Williamson, 1983; Azulay et al., 1985; Jaeger, 1986). For example, the use of plastic films, such as Saran Wrap, provides a microclimate which promotes the penetration of topical corticosteroids into the skin (Vickers, 1963; Dempski et al., 1965).

Saran Wrap (a copolymer of vinylidene chloride) and other plastic films have the necessary physical properties to provide an occlusive environment between the film and the skin surface. Such materials are relatively impermeable to gases (O_2/CO_2) and water vapour (Queen et al., 1987), maintaining a very moist environment beneath the film. They also provide an environment where *Staphylococcus aureus* and other bacteria can proliferate (Chan et al., 1982).

The improved efficacy of occlusive therapy is caused by the hydrating effect Saran Wrap imposes on the stratum corneum (Vickers, 1963), which is a direct result of the physical characteristics described above. Prolonged occlusion, however,

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can lead to a build-up of fluid, which could cause tissue maceration in the long term (Aly et al.,1978). In obtaining the correct occlusive microclimate it is important that intimate contact between the skin and the occlusive membrane is obtained and maintained throughout therapy. This can be provided by good adhesive qualities.

Hydrocolloid dressings are widely used in the treatment of burns and ulcers (Weston-Davies, 1986). Actiderm is a new hydrocolloid patch with potential in treating dermatological disorders. The therapeutic patch is comprised of a powder mixture (pectin, gelatin and carboxymethylcellulose) which is dispersed in a hydrophobic adhesive polymer (kraton) matrix.

Our study therefore compared the blanching profiles obtained for triamcinolone acetonide cream 0.1% (Kenalog) when occluded using the Actiderm patch or Saran Wrap. Certain physical properties were also studied to demonstrate the occlusive nature of Actiderm.

Materials and Methods

Physical properties

Moisture uptake. Bijou bottles were filled with distilled water to a level which was 1 cm from the top of the neck (Lawrence, 1986). Squares of the material (Actiderm) (2 cm × 2 cm) were preweighed and placed on top of the bottles.

In the determination of fluid uptake the bottles were placed horizontally to allow fluid/patch contact and the change in weight was determined hourly over the first 6 h and at 24 and 48 h. In the other protocol the bottles were maintained in the upright position when measuring moisture vapour uptake; the dressings were removed at predetermined time intervals (6, 24, 48, 72 and 336 h) for reweighing. Once weighed, the samples were replaced on the bottles.

The change in patch weight was recorded and the percentage weight gain calculated.

Patch adhesion. Peel tests (90°) were carried out on 5 individuals (3 male/2 female) using an Instron Tensile Tester (Instron Ltd.). Actiderm was compared to the following: Elastoplast and Micropore. Each patch of material (5 cm × 2.5 cm) was placed on the forearm of the individual and left in place for 5 h. After this period a free edge was realised and inserted between the grips on the machine cross-head. The dressing or patch was removed at a peel rate (cross-head speed) of 200 mm/min on a full scale load deflection of 0.02 kN.

The results obtained were a measurement of the force required to remove the material, giving a measurement of the material adhesive strength.

In vivo performance

Vasoconstrictor assay. Ten caucasian volunteers (5 female, 5 male who had given informed consent; age range 22–35), who had not been treated with topical or systemic corticosteroids for at least two months were employed in the trial. Twelve sites were utilised per arm and were allocated by reference to randomisation charts. Kenalog Cream (E.R. Squibb & Sons Ltd.) was applied to 6 sites per arm, the other 6 serving as untreated sites to which no corticosteroid was applied. The cream was applied to 7 × 7 mm discrete sites on the flexor surface of the forearm, defined using areas punched from Blenderm (3M Health Care Ltd.) double-sided adhesive tape. A defined quantity (5 ± 1 mg) of cream was applied by extruding a standard length from a disposable syringe, which was filled immediately prior to use. The tape was also used to define 3 of the control sites.

The Blenderm tape was removed from 3 of the sites to which Kenalog Cream had been applied and these were occluded with 15 × 15 mm squares of Actiderm (I429-068; Squibb ConvaTec). A further three 15 × 15 mm squares of Actiderm were applied to untreated sites, to serve as appropriate control areas. The remaining 6 sites per arm (3 control + 3 to which cream had been applied) were then occluded with Saran Wrap (Dow Chemical Co.). The location of all sites was marked precisely and immediately with permanent ink. One Actiderm- and one Saran Wrap-occluded area, in addition to their respective control sites, were exposed after 6, 24 and 48 h. Half an hour after the patches were removed, the sites were gently swabbed with ethanol to remove any residue which originated from the adhesives used in the patches or the tape, preventing interference in assessing

TABLE 1

Scoring scale employed in the blanching assay

Numerical value	Amount of blanching
0	Normal skin
1	Slight blanching of indistinct outline
2	More intense blanching with at least two corners outlined
3	General even blanching with a clear outline of the square
4	Marked and distinct blanching of high intensity

Half-point ratings are also employed.

the degree of vasoconstriction. Such assessment was made solely by the investigators under standardised lighting conditions.

The degree of pallor (blanching) was estimated using a 0–4 scale with half-point ratings based on that of Barry and Woodford (1978) and summarised in Table 1. Readings were taken 1, 2, 3, 6, 18, 26, 42, 50, 66, 74, 90 and 98 h after removal of the patches. Readings at 18, 42, 66 and 90 hours were precluded for the patches which remained in situ for 24 or 48 h, because of the unavailability of the volunteers at these time points.

All estimations of pallor were made without reference to the application charts.

Results

Moisture uptake (vapour and fluid)

The percentage weight gain values were calculated as follows:

$$\%\text{wt gain} = \frac{\text{wt at time } t - \text{initial wt}}{\text{initial wt}} \times \frac{100}{\text{area fraction}}$$

The area fraction is a multiplication factor to take into account the area of the patch which does not become hydrated, since in the in vivo situation a non-hydrated perimeter does not occur. It is the ratio of the unhydrated area to the hydrated area of the material under test. The results obtained are presented in Table 2.

TABLE 2

Moisture uptake by Actiderm dermatological patch

Time (h)	% Weight gain	
	Fluid uptake	Vapour uptake
1	6± 1	–
2	8± 1	–
3	8± 1	–
4	9± 1	–
5	10± 1	–
6	12± 1	1.8± 1.2
24	33± 3	5.5± 2.3
48	88±12	10.8± 4.5
72	–	15.5± 4.9
336	–	72.2±17.6

Values are mean ± 1 S.D., $n = 6$.

Material adhesion

The mean of the values obtained, along with the range of values observed are presented in Table 3. This range of values was a direct result of the differing hirsute indices of the individuals tested.

Blanching assay

Slight lifting of the Blenderm tape was observed on 10–15 of the total number of sites which were occluded with Saran Wrap for prolonged periods. When apparent these sites were covered with a detectable airstrip dressing (Smith & Nephew, Ltd.) to maintain occlusion, preventing premature exposure. All of the Actiderm patches remained in place throughout the study.

With each test preparation the results for all volunteers were expressed as a percentage of the total possible score (%TPS) at each time point. The method of calculation was as follows: maximum score per site = 4; for both arms $4 \times 2 = 8$;

TABLE 3

Dressing or patch adhesion values

Dressing material	Force required for removal (n)	Range of values
Actiderm	5.1	3.4–6.4
Elastoplast	3.7	3.1–4.5
Micropore	3.2	1.2–7.8

Values are means, $n = 5$.

TABLE 4

The percentage of the total possible score for Actiderm patch and Saran Wrap occluding control sites (postremoval)

Test preparation	Duration of application (h)	Time (h) after removal of dressing											
		1	2	3	6	18	26	42	50	66	74	90	98
Saran Wrap	6	3.1	2.5	2.5	4.4	3.1	1.9	1.9	3.1	1.3	1.9	1.9	1.3
	24	1.9	3.1	0.6	0.6		1.9		3.8		4.4		2.5
	48	8.8	6.3	5.0	2.5		1.9		1.3		1.9		0.6
Actiderm patch	6	5.0	4.4	3.1	3.8	3.1	3.8	4.4	3.8	4.4	2.5	2.5	1.9
	24	10.6	8.8	9.4	8.1		10.0		8.1		3.8		0.6
	48	11.3	9.4	9.4	10.0		9.4		7.5		2.5		1.9

for 10 volunteers $8 \times 10 = 80$. Fig. 1 and 2 show the blanching profiles obtained for Kenalog Cream occluded for different periods of time with either Actiderm or Saran Wrap. Table 4 shows the extent of blanching of control sites induced by occlusion with Actiderm and Saran Wrap alone. The areas under the curve (AUC) in Figs. 1 and 2 (which provide an indication of corticosteroid bioavailability) are shown in Table 5.

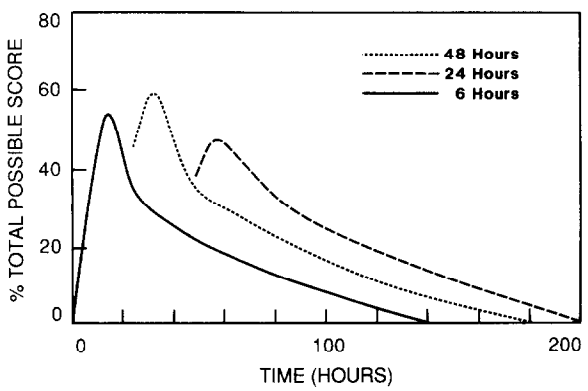

Fig. 1. Blanching induced by Kenalog Cream occluded with Actiderm.

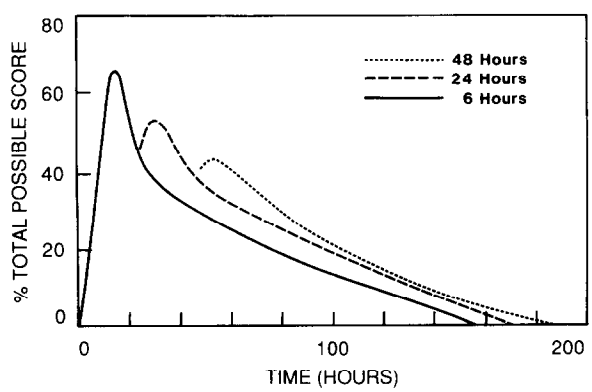

Fig. 2. Blanching induced by Kenalog Cream occluded with Saran Wrap.

Discussion

Occlusive therapy for the promotion of topical drug bioavailability has been used in clinical practice for almost 30 years. Such treatment has focussed upon the use of Saran Wrap and other plastic membranes. (Dempski et al., 1965; Barbier et al., 1979; Williamson, 1983; Azulay et al., 1985; Jaeger, 1986). However, the degree of skin hydration produced under these circumstances can be excessive.

The blanching study was carried out to assess the potential of a new dermatological patch

TABLE 5

The observed peak blanching response and cumulative area under the curve for different application times

Test dressing	Duration of application (h)	Observed peak %	Area under curve % × h
Actiderm–Kenalog	6	53.8	2345
	24	58.8	4044
	48	46.9	5000
Saran Wrap–Kenalog	6	63.8	2997
	24	53.8	4272
	48	44.4	4617

(Actiderm) in the treatment of dermatological disorders, when compared to Saran Wrap which is commonly used for this purpose.

The blanching profiles of Kenalog cream occluded with Actiderm and Saran Wrap for different time periods are shown in Table 4. The peak levels of blanching (63.8 and 53.8% respectively) induced by the cream were observed after 6 h of occlusion.

From Table 4 it can be seen that both Actiderm and Saran Wrap elicit blanching without any corticosteroid application, but this is low compared to the equivalent response on a cream-treated site. For Saran Wrap this response on control sites remained constant whereas the blanching induced by the Actiderm patch increased with time. The difference between the two responses may be attributable to the more intimate contact effected by the adhesive Actiderm by comparison with the non-adhesive Saran Wrap. Blanching is routinely observed when any adhesive dressing is removed from the skin after prolonged time periods in situ.

As can be seen from Fig. 1 and 2 the blanching profiles obtained using Kenalog Cream under occlusion with Actiderm and Saran Wrap are very similar. Also a comparison of the cumulative AUCs (Table 5) shows that the bioavailability of triamcinolone acetonide, after occlusion of the cream, is broadly independent of the covering used, although there is the suggestion that Actiderm may be slightly superior over the first 24 h. The peak response obtained using Saran Wrap is unusually low for a cream of the potency of Kenalog (Barry and Woodford, 1974) and does not compare well with the value obtained for Kenalog beneath Actiderm. Two possible reasons could account for this discrepancy:

(i) there is an interaction between the Kenalog Cream and Saran Wrap such that the corticosteroid is not completely available for absorption;

(ii) that the occlusion obtained with Saran Wrap is either incomplete or less effective than that achieved with the Actiderm patch.

Interaction between Saran Wrap and triamcinolone acetonide is the less likely explanation since the material is used clinically to produce occlusion and the blanching parameters obtained after 24 and 48 h occlusion are virtually identical to those obtained with Actiderm (Table 4).

Occlusion using Saran Wrap and double sided adhesive tape (Blenderm) was certainly more difficult to effect practically than occlusion with Actiderm. Since Saran Wrap is thinner and more pliable than other plastic films (e.g. Melinex, a polyester film) the former posed greater manipulative problems when volunteers were first entered into the trial. The Saran Wrap covering on a number of sites, although apparently well-adhered, was frequently creased and it is possible that as a consequence occlusion may have been less effective. Saran Wrap when employed clinically to produce occlusion of larger areas than the discrete 7×7 mm sites in this study, would undoubtedly be easier to handle, but many handling problems would remain and others would occur due to the increased size.

When compared to Saran Wrap, the clinical use of Actiderm is more advantageous in many ways as detailed by Queen and Marriott (1987). One important advantage is that Actiderm is adhesive and this is of particular importance in providing intimate contact between the patch and the skin surface. It is also of importance in maintaining continual effective occlusion by preventing the occlusive barrier being broken due to tearing or detachment.

From the adhesion results (Table 3) it can be seen that the hydrocolloid patch (Actiderm) is much more adhesive than the adhesive dressings generally used in occlusive therapy.

Occlusion has its effect on drug bioavailability by preventing the normal water loss from the skin, resulting in a moist environment around the treatment area. However, prolonged occlusion can result in an accumulation of moisture which will result in maceration of the treatment area. Actiderm prevents the loss of water vapour providing an occlusive environment. Maceration of the treatment area, however, is not a problem since the material absorbs the excess moisture retaining it within its structure but within the locality of the treatment area, maintaining a humid atmosphere.

The moisture uptake studies (Table 2) support this observation. When in contact with fluid the

patch will readily absorb and retain this water within its structure. However, during a previous blanching investigation (Marriott and Martin, 1986) the determination of moisture uptake in vivo showed that the levels obtained were much lower than those obtained in vitro. This is due to the skin being intact and allowing water to escape in the vapour phase.

The rate of moisture vapour uptake of Actiderm in vitro (Table 2) was similar to the low rates of moisture uptake found in vivo, when the material is placed on intact skin. The rate of direct fluid uptake when the patch is hydrated in contact with water is much faster (Table 2). The slow hydration is very important in the maintenance of the strong dry tack conditions, providing a continued strong adhesion to the skin surface.

Upon hydration the patch forms a soft gel which conforms well to the diseased skin surface, but does not abrade the surface causing descaling and bleeding. Abrasion can be a probem with plastic films due to their ability to 'slip and slide' over the skin surface causing shearing forces which may result in skin damage. During the blanching assay no irritation problems were recorded for Actiderm. This may be associated with the ability of the patch to remove excess moisture. Saran Wrap is non-absorbent and according to the volunteers in this study the accumulation of moisture causes irritation when the occlusion is prolonged.

The Actiderm dermatological patch therefore appears to provide a resilient and more substantial alternative to Saran Wrap, particularly in ambulatory individuals. Actiderm may also control the absorption of corticosteroids through the stratum corneum which would be a distinct advantage over conventional occlusive therapy.

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