A CLINICAL ASSESSMENT OF A NEW STEROIDAL CREAM FLUPREDNYLIDENE-21-ACETATE (DECODERM)

L. MARQUIS * AND C. K. JAGAVKAR †

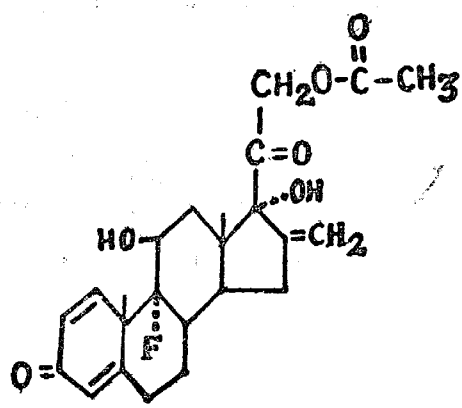
Summary

In an open clinical trial using Decoderm cream, 55 patients suffering from eczematous diseases and other corticosteroid responsive dermatoses were studied. The cream was applied twice daily for a period of 2—4 weeks. An excellent response was obtained in 16.4 %, a good response in 54 5 % and a moderate response in 23.6 % of the cases studied. The cream was well tolerated and no undesirable side effects were observed in any of these cases.

Introduction

Since the demonstration of the anti-inflammatory effect of topical preparations containing cortisone by Dougherty et al[1] in 1950, there has been tremendous progress in the development of newer and more potent steroids. Fluorinated steroids have deservedly achieved a prime position in the management of steroid responsive dermatoses, because in general, fluorinated topical corticosteroids are more effective than non-fluorinated preparations. Among the recent addition to these 16 substituted congeners, is 9-∝ - fluoro - 16-∝ - methylene - prednisolone 21 - acetate, or Fluprednylidene-21 acetate, available in many countries, under the proprietary name of Decoderm(R), which has a high potency and long acting effectiveness and is intended for external use only.[2]

Experiments on animals showed that Fluprednylidene-21-acetate is a highly effective anti-inflammatory glucocorticosteroid with pronounced anti-exudative and anti-proliferative effects. It



was remarkable that, apart from the expected glyconeogenic activity, corresponding to its anti-inflammatory action, Fluprednylidene-21-acetate was found to have no significant sodium-retaining or potassiumexcreting effect.[3,4]

One of the most important features of determining the stability of a topical corticosteroid is the way in which it

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* Hon. Dermatologist and Venereologist

† Hon. Asst. Dermatologist and Venereologist St. George's Hospital, Bombay.

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penetrates into the skin – its penetration kinetics. Using a tritium labelled preparation, Fluprednylidene - 21-acetate was shown to rapidly penetrate the outer layer of the epidermis, giving a fast onset of action.[4,5] After penetrating the outer layer of skin, it accumulated at the level of the Stratum corneum, forming a depot to give a high level of corticosteroid at the site of action. The depot forming characteristics of Fluprednylidene-21-acetate, lead to steady and sustained diffusion into the deepest epidermal layers of the skin. Clinical comparative studies have shown that as a result of this depot-effect, a once daily application produces results as good as a thrice daily application[6,7,8,9].

Because Fluprednylidene-21-acetate does not penetrate rapidly into the tissue-forming layers of the skin, its effect on collagen formation as compared with other equipotent corticosteroids is minimal. Correspondingly, the risk of skin atrophy, striae and telangiectasis is very small.[10,11].

The activity of a preparation depends in addition to its active ingredient, on its carrier, i. e. base. The base used is a novel emulsion system[12], with a uniform distribution of fat and water combining the properties of an oil-in-water and a water-in-oil emulsion, i. e. it is both an ointment and a cream. This base possesses a marked emulsifying ability for aqueous and lipoid skin secretion, and a fat content adequate for most stages of inflammatory skin diseases. It spreads easily and penetrates rapidly into the upper epidermal layer. It stimulates granulation and epithelialization and thus facilitates healing. This produces a positive balance between suppressive activity of the corticosteroid and the promotion of proliferation by application of the cream.

Method of Study

Fifty-five patients with dermatologic lesions ordinarily responsive to local corticosteroid therapy were selected without regard to age, sex or race. The age and sex distribution of the patients is shown in Table 1.

TABLE 1

Sex and Age distribution of the Patients

Age	Men	Women	Total %
10	1	1	3.63
10—19	1	6	12.72
20—29	7	3	18.18
30—39	10	1	20.20
40—49	9	3	21.81
50—59	5	2	12.72
60—69	1	2	5.47
70 & over	3	0	5.47
Total	37	18	100.00

Patients selected had not been on topical or systemic corticosteroid therapy for at least two weeks prior to enrolment in the study. Those patients with endocrine, hepatic, hematopoietic, renal or cardiovascular diseases were excluded.

The percentage area of skin involvement was recorded as per Wallace's rule of Nines (Table 2) (Fig. 1).

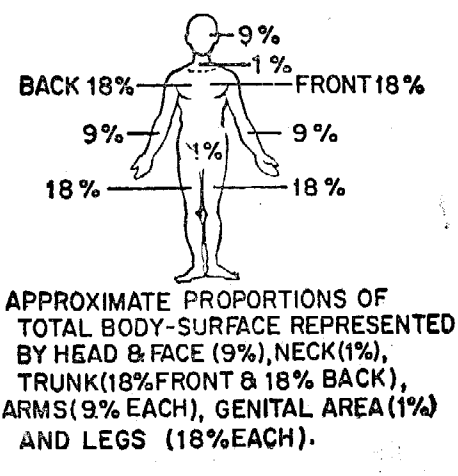


TABLE 2

Percentage area of body involvement (according to Wallace's classification)

	Percentage involvement				
	0–9	10–18	19–36	37–72	73–100
No. of cases	30	5	4	2	14

Single lesion	Multiple lesions
10 cases	45 cases

From Table No. 2, it can be seen that of the diverse eczema dermatitis cases included in the trial, 30 cases showed upto 9% involvement of skin area and 14 cases between 73 – 100% involvement. The other 11 cases showed involvement of 10 – 72%. Thus cases varied from extensive involvement to local involvement. Besides, 10 patients showed single lesions while 45 cases showed multiple lesions and extensive involvement.

A brief pretreatment clinical assessment, both topical and systemic was recorded. Details of previous therapy were also recorded. The dermatological signs and symptoms of (1) Pruritus (2) Burning (3) Erythema (4) Oedema (5) Exudation (6) Scaling (7) Vesicles (8) Crusting (9) Lichenification (10) Keratotic papules were evaluated and quantified prior to treatment.

Pruritus was the most common symptom found in all 55 patients followed by Lichenification (47), scaling (45), crusting (36), erythema (31), oedema (28), exudation (25), burning (24) vesicles (23) and keratotic papules (10).

Table 3 gives the list of the skin diseases with which the patients presented.

Patients were provided with the Decoderm cream containing Fluprednylidene-21-acetate – 0.1%. They were instructed to apply the medicament lightly over the affected area twice a day and to report weekly.

TABLE 3

Diagnoses	No of patients
Contact dermatitis	18
Seborrhoeic dermatitis	15
Neurodermatitis	6
Stasis dermatitis	2
Atopic dermatitis	7
Infectious eczematoid dermatitis	5
Exfoliative dermatitis	2
Total	55

The patients were assessed after four weeks both objectively and subjectively in four grades, viz. (1) Excellent-when both the subjective and objective symptoms showed total subsidence, i.e. there is total subsidence of initial lesions, relief of pruritus and disappearance of lichenification, relief being more than 90%. (2) Good-response being 70–90% (3) Moderate or fair-when response was 40–70% (4) Poor-when response was below 40%. Relapses if any, were recorded after cessation of therapy.

Results

Results were evaluated by studying the morphological subsidence of clinical manifestations and overall improvement of patients in each eczematous dermatitis group. Table No. 4 shows the Morphological subsidence of clinical manifestations.

From the table it can be seen that there was 85–100% improvement with regard to pruritus, scaling, crusting, erythema, oedema, exudation, vesicles and burning. Thus out of 10 morphological clinical manifestations evaluated in this trial, 85–100% improvement was obtained in 8 of them. However, for lichenification and keratotic papules improvement was only 61.7% and 50 00% respectively.

TABLE 4

Morphological subsidence of clinical manifestations

Morphology	1st wk.	2nd wk.	3rd wk.	4th wk.	Residual after 4 weeks	Percentage improvement at the end of treatment
1. Pruritus (55)*	9	12	10	16	8	85.24
2. Lichenification (47)	4	6	7	12	18	61.07
3. Scaling (45)	17	11	9	4	4	91.11
4. Crusting (36)	18	14	2	—	2	94.44
5. Erythema (31)	18	9	3	1	—	100.00
6. Oedema (28)	17	10	1	—	—	100.00
7. Exudation (25)	14	5	4	1	1	96.00
8. Burning (24)	11	8	1	1	3	87.05
9. Vesicles (23)	10	11	1	1	—	100.00
10. Keratotic papules (10)	3	2	—	—	5	50.00

* Figures in parentheses in column 1 indicate total number of patients who manifested that particular symptom. Figures in the other columns indicate the number of patients improved at the end of the 1st, 2nd, 3rd or 4th week of treatment or patients who did not improve at the end of four weeks treatment.

TABLE 5

Diagnosis	Response to treatment			
	Excellent No. %	Good No. %	Fair No. %	Poor No. %
Contact dermatitis (18)*	16.7 (3)	50.0 (9)	27.8 (5)	5.5 (1)
Seborrhoeic dermatitis (15)	26.7 (4)	53.3 (8)	13.3 (2)	6.7 (1)
Neurodermatitis (6)	—	66.7 (4)	33.3 (2)	—
Stasis dermatitis (2)	50.0 (1)	50.0 (1)	—	—
Atopic dermatitis (7)	14.3 (1)	57.1 (4)	14.3 (1)	14.3 (1)
Infectious Eczematoid Dermatitis (5)	—	60.0 (3)	40.0 (2)	—
Exfoliative dermatitis (2)	—	50.0 (1)	50.0 (1)	—
Total (55)	16.4 (9)	54.5 (30)	23.6 (13)	5.5 (3)

* Figures in parentheses indicate actual number of patients.

Table No. 5 shows the overall response to treatment in each disease entity. From this table it can be seen that in all disease entities studied, almost 71% of the patients showed excellent to good response, while poor response was obtained in less than 10% of the patients (except in the case of atopic dermatitis where 14.3% of patients showed poor response.) The remaining patients showed a fair response to treatment.

Reaction

The cream was applied over both localised areas of skin lesions and those extending in a more generalised way over the body as in the case of disseminated atopic dermatitis and seborrhoeic dermatitis. No untoward reactions were observed. The cream was found suitable in the subacute exudative phase of some of the skin diseases. No photosensitivity was observed in any case.

Discussion

Cortisol and the synthetic analogs of cortisol have the capacity to prevent or suppress the development of local heat, redness, swelling and tenderness by which inflammation is recognised at the gross level of observation. At the microscopic level, they inhibit not only the early phenomena of the inflammatory process (oedema, fibrin deposition, capillary dilatation, migration of phagocytes into the inflamed area, and phagocytic activity) but also the later manifestations (capillary proliferation, fibroblast proliferation, deposition of collagen and still later cicatarization.)

55 cases of eczema dermatitis were studied on Decoderm topical medication. As per Wallace's[13] classification (Rule of Nines), 30 cases showed involvement of upto 9% and 14 cases showed affection of 73%–100% of the body area. Hence cases varied from minor localised involvement to extensive involvement. 10 patients showed single lesions while 45 patients showed generalised involvement.

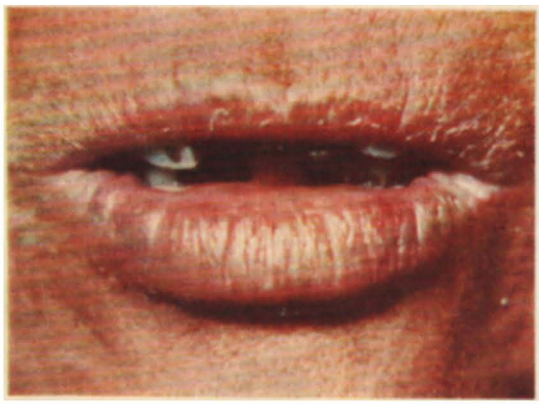
The marked anti-inflammatory activity of Decoderm was evident from the fact that it reduced erythema and oedema, the two most important signs of inflammation, by 100%. In addition, it reduced exudation, crusting, scaling and vesicle formation, which are the late manifestations of eczematisation by 90–100%. This suggests that it has very good antiproliferative action. The antiproliferative action of Decoderm was also evident in the subsidence of the lichenification in 61.7% of cases. However, 18 cases showed residual lichenification, three of which had showed a poor response to treatment. The remaining 15 showed an improvement ranging from 40 to 70%. Chronic lichenification is always difficult to tackle by topical measures only. Failure may be possibly due to difficulty of percutaneous penetration of the medicament and other extraneous contacts which may frictionise the skin and maintain the lichenification. Similarly, of the 10 cases showing keratotic papules, 5 showed complete subsidence within two weeks whereas in the other 5 they still persisted.

Decoderm also relieved the two most common symptoms, i.e. pruritus and burning. The pruritus was relieved in 85.25% of the cases who complained of this symptom. This highlights the marked anti-pruritic effect of the cream. The burning was relieved in 87.5% of the cases who complained of this. Our findings are in agreement with those of Koch and Abeille[14], who also observed that Decoderm produced pronounced anti-pruritic effects in 41 out of 44 cases giving a therapeutic success in 93% of cases.

We obtained excellent to good response in contact dermatitis, seborrhoeic dermatitis, neurodermatitis and atopic dermatitis. Capusan et al[15] while treating 48 patients with eczema observed an especially good response in contact, seborrhoeic, atopic and neurodermatitis and eczema of the legs.

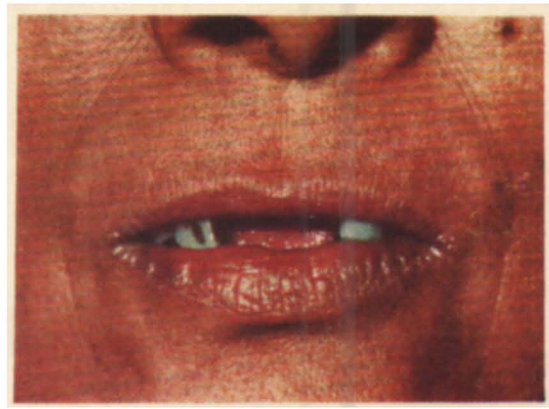
In the contact dermatitis group in this study, one patient was sensitive to tobacco powder, six had plastic and leather sensitivity, six were sensitive to various detergents and five were sensitive to rubber gloves. Only one patient in this group showed poor response. This may have been associated with the continuous maintenance of individual contact with the wearing apparel, plastic slipper (chappals).

Seborrhoeic dermatitis, basically a constitutional diathesis affecting the skin with an inborn physiological trait, can usually be controlled but not cured. The inflammatory changes showed early and good subsidence. The characteristic feature of the neurodermatitis is a severe pruritus over an underlying mosaic



BEFORE TREATMENT

CONTACT DERMATITIS



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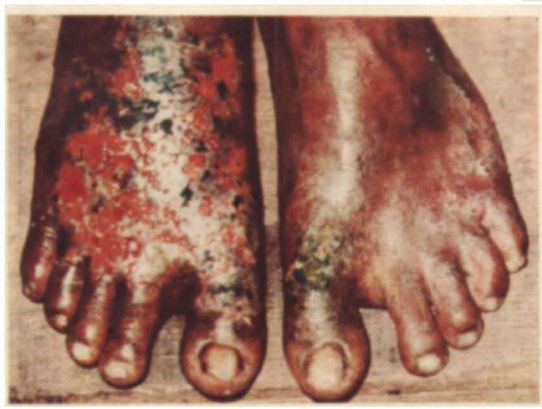

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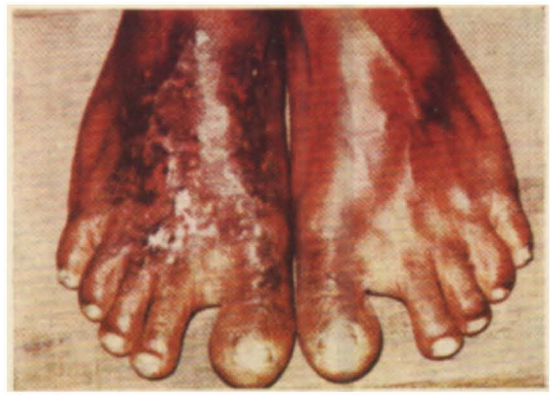
INFECTIOUS ECZEMATOID DERMATITIS



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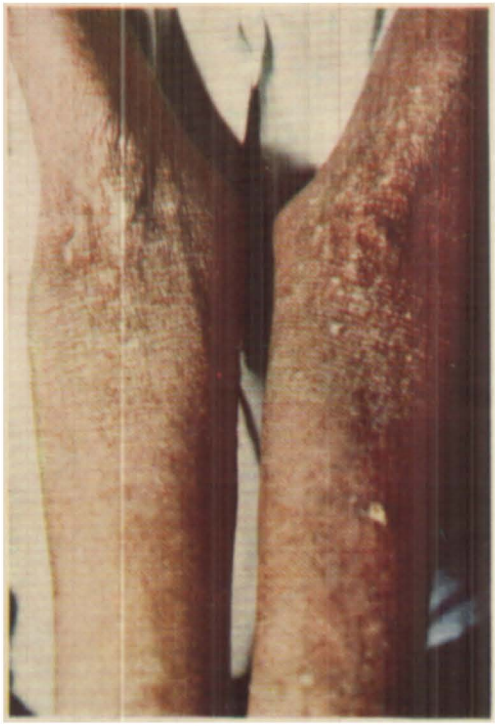
ATOPIC DERMATITIS



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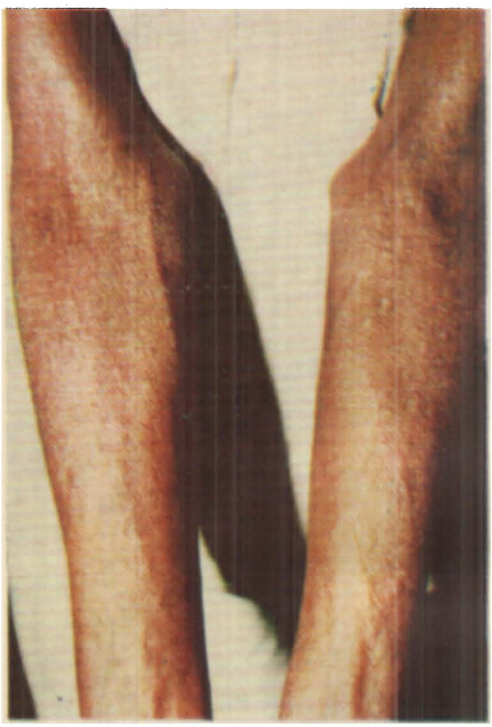

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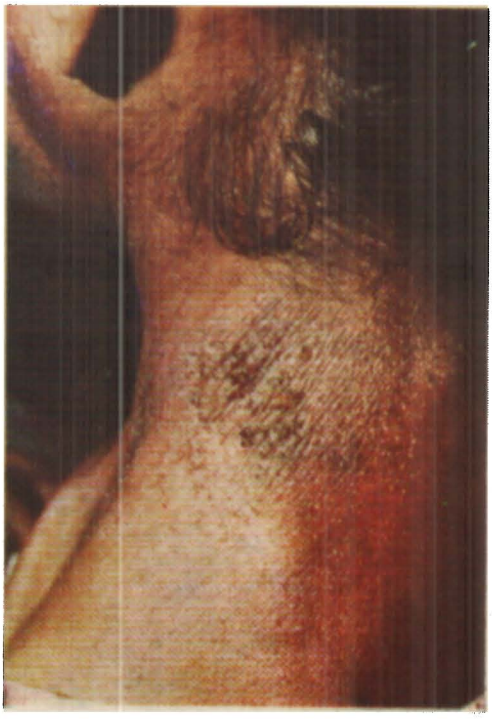
NEURODERMATITIS



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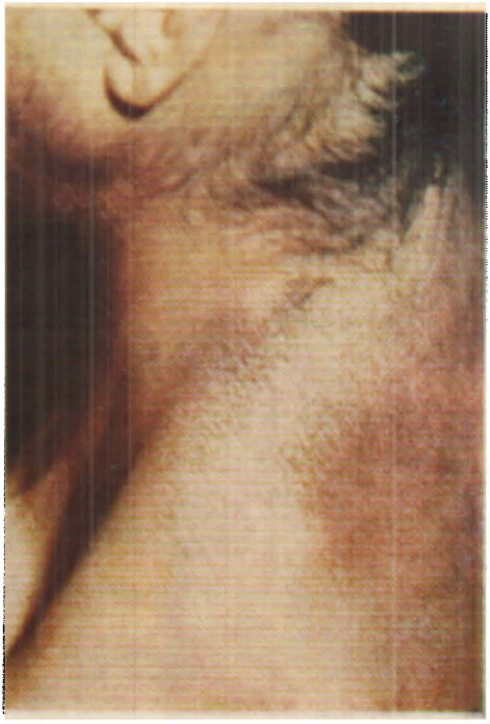

AFTER TREATMENT

pattern of lichenification associated with hyper-pigmentation. Occasionally, a few raised keratotic papules may be seen in the lesions. The topical medicament relieved pruritus with gradual subsidence of lichenification and slow disappearance of hyperpigmentation. Atopic dermatitis is a constitutional diathetic disorder generally of a recalcitrant nature. The areas of dermatitis found to be most resistant were at the usual allergenic sites, i.e. back of neck, cubital and popliteal fossae and dorsum of hands and feet. Out of the 7 cases in this group, one case showed an excellent response and 4 cases a good response. In one case response was moderate and in one poor. Lundell and Koch[16] treated 42 cases of atopic dermatitis, in a comparative double blind contralateral trial, and they observed that after two weeks of treatment where the fluprednylidene containing external preparation was used, the symptoms recorded had receded to an extent which was of greater statistical significance than where the other preparation was used.

In the infectious eczematoid dermatitis group, the pyogenic element was controlled with appropriate systemic therapy when required and the localised lesions were treated with the cream. The response was good in sub-acute phase of the disease. Rimbaud et al[17] treated 4 cases of infectious eczematous dermatitis and found very good to good response in 3 cases and average response in one case.

In the case of stasis dermatitis, the relief of pruritus and reduction of superficial inflammatory reaction was good with bed rest. Both the cases showed excellent to good response.

In exfoliative dermatitis, pruritus and dermatitis were relieved well.

Despite the small number of patients involved, the results obtained by us confirms what has been said above - the excellent therapeutic properties of the preparation, since excellent to very good response was obtained in 70.9% of the cases. We found that the preparation has very favourable anti-inflammatory, anti-exudative and anti-pruritic effects in various types of dermatitis.

Decoderm cream served very well in the dermatitis-eczema group of diseases. It is easy to apply. Neither the skin nor underclothing is soiled by it. It has a good tolerance which is an added asset. Wide-scale use of Decoderm in all the conditions mentioned above is therefore justified.

Relapses

On stopping the topical application, relapses were seen in nine cases of which 7 were seborrhoeic and one exfoliative and one stasis dermatitis.

Seborrhoeic dermatitis being a constitutional diathetic disorder can be controlled and not cured. Hence relapse of the condition following cessation of treatment is understandable. Exfoliative dermatitis being of diverse nature required prolonged steroidal medication. In stasis dermatitis the persistence of venous incompetency in the lower limb could have been an important factor in its recurrence.

Conclusions

Fluprednylidene-21-acetate, is an effective synthetic fluorinated steroid preparation and may be used in all dermatological disorders requiring corticosteroid therapy. It has a good anti-inflammatory, anti-exudative, anti-proliferative and anti-pruritic effect, and even on extensive application there is no evidence of local or systemic side effects.

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