Ind J Dermatol, Venereol Leprol 1993; 59 : 184-86

# INFLUENCE OF LIPOSOMAL DRUG ENTRAPMENT ON THE PERFROMANCE OF CORTICOSTEROID CREAMS

G U Rao, R S R Murthy, Y S Marfatia* and Rajesh Shankar*

Skin blanching and clinical efficacy of a liposomally entrapped triamcinolone acetonide (TRMA) cream was compared with that of the conventional TRMA cream in healthy human volunteers and eczema patients respectively. Both the creams showed equal efficacy in eczema patients. A significant reduction in the skin blanching response with the liposomal TRMA cream as compared to the conventional TRMA cream suggests a decrease in the systemic absorption of the corticosteroid with the former.

**Key Words : Corticosteroids, Liposomes**

## Introduction

Chronic topical application of corticosteroids in eczema, psoriasis and dermatitis is known to cause unintended systemic side effects due to the percutaneous absorption of the drug. A new approach to achieve selective drug delivery to the skin is the use of liposomes as drug localizers.[1] Liposomes are microscopic vesicles composed of phospholipid bilayers which form spontaneously when appropriate composition of phospholipids are hydrated in aqueous media.[2]

According to Mezei et al,[3] encapsulation of TRMA into liposomes favourably alters the drug disposition in rabbits with lower TRMA levels in the blood stream as compared to conventional TRMA cream.

In the present study, the liposomal TRMA cream was compared with the conventional TRMA cream with respect to its skin blanching potential in healthy human volunteers and its efficacy in eczema patients.

From the Department of Pharmacy, Faculty of Tech. and Engg., MSU, P.O.Box No. 51, Kalabhavan, Baroda-390 001, India.

* Department of Skin and VD, SSG Hospital, Jail Road, Baroda-390 001.

Address correspondence to : G U Rao

## Materials and Methods

TRMA liposomes were prepared by Bangham's lipid film rehydration method[4] using TRMA : lecithin:cholesterol in the ratio of 69μM :190μM :93μM. A 0.1 % w/w liposomal TRMA cream was prepared by incorporating the drug loaded liposomes into aqueous cream base BPC. A conventional 0.1 % w/w TRMA cream was prepared in the same base.

Selection of subjects for the skin blanching study involved the application of two dilutions of the conventional corticosteroid cream to the forearms of each volunteer under occlusion for 6 hours followed by reading the blanching responses. Only the good discriminators were taken for the present study.

A double-blind, occluded, skin blanching assay was conducted on both the forearms of 13 good discriminators using 10± 1 mg of the prepared creams. The site of application of the drug cream and the liposomal drug cream was alternated from near the wrist to near the elbow in each volunteer so as to eliminate site of application bias and intrapersonal

bias. Skin blanching score was assigned for each arm after 6 hours of application by an unbiased observer using a 0-4 scale rating based on the Barry Woodford's method.[5] The blanching scores for the two creams were subjected to a two tailed t-test to study the level of significance.

A double-blind clinical trial was conducted at the Skin and VD Department of Shri Sayaji General Hospital, Baroda, on 10 patients with dry bilateral eczema for one month, with weekly assessments by clinical experts.

## Results

Although skin blanching assays have been conventionally performed in Caucasian volunteers, Indian volunteers have shown promising results with regards to skin blanching in our laboratory. Out of the 30 volunteers screened for their blanching potential, 27 exhibited detectable blanching after 6 hours of occlusion. However, 13 volunteers were found to be very good discriminators and so the testing of the liposomal cream was restricted to these volunteers only.

The blanching scores for all the volunteers, for each formulation, were summed and expressed as the percentage of the total possible score (% TPS). Fig. 1 shows a statistically significant ($p<0.001$) decrease in the % TPS with the liposomal TRMA cream as compared to the conventional TRMA cream suggesting a decrease in the skin blanching response elicited by the former.

Table I shows the results of the clinical trials. No statistically significant difference was observed in the clinical efficacy of the two creams in eczema patients.

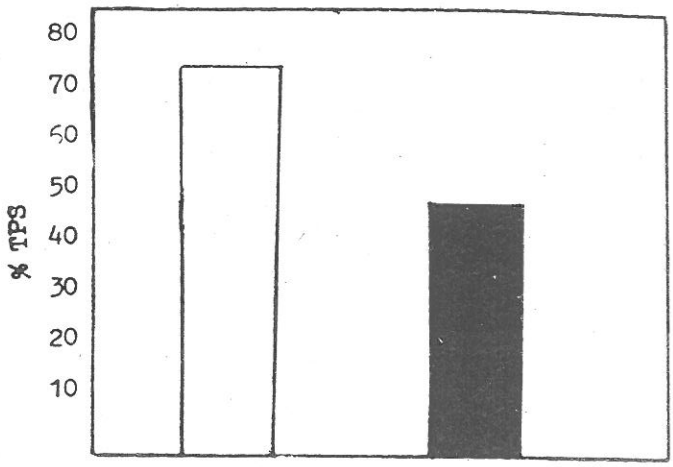


Fig.1. Comparative skin blanching responses for the liposomal TRMA cream (■) and the conventional TRMA cream (□). ($p<0.001$, n=13)

**Table I.** Results of clinical trials

| Symptoms | % of patients responding to | |
|---|---|---|
| | liposomal TRMA cream | conventional TRMA cream |
| Exfoliation/ Hyperpigmentation | 20 | 20 |
| Lichenification/ Fissuring | 40 | 40 |
| Pruritus | 50 | 50 |
| Erythema/ Itching/Burning | 60 | 60 |

## Comments

The human skin blanching assay is an excellent model in evaluating the efficacy of topical corticosteroids prior to clinical trials.[6] When corticosteroids from topically applied dosage forms penetrate to the blood vessels of the skin, they cause vasoconstriction of the same and hence the skin gets blanched.

Reduction in skin blanching without adverse effects on the efficacy by the liposomal TRMA cream suggests the following: (1) incorporation of drug into liposomes limits the drug from reaching the blood stream. The lecithin of the liposomes probably increases the total lipid content of the stratum corneum which leads to formation of a steroid

depot in this region from where a controlled delivery of the steroid to the lower skin layers where blanching takes place occurs. Hence the use of liposomal cream may reduce the systemic side effects. (ii) Liposomally entrapped drug, localizes in the epidermis-dermis. Hence the dose of the drug can be reduced making the therapy cost effective.

## References


1. Mezei M. Liposomes as a skin drug delivery system. Topics in Pharmaceutical Sciences (Breimer DD, Speiser P, eds) New York : Elsevier Science Publishers, 1985 ; 345-58.
2. Tyrrell DA, Heath JD, Colley CM, et al. New aspects of Liposomes. Biochim Biophys Acta 1976 ; 457 : 259-302.
3. Mezei M, Gulasekharan V. Liposomes-a selective drug delivery system for the topical route of administration. Life Sci 1980; 26 : 1473-7.
4. Bangham AD, Hill MW, Miller NGA. Methods in Membrane Biology (Korn ED ed). New York : Plenum Press, 1974; 1-68.
5. Barry BW, Woodford R. Comparative bioavailability of proprietary topical corticosteroid preparations. Br J Dermatol 1974; 91 : 323-38.
6. Haigh JM, Kanfer I. Assessment of topical corticosteroid preparations : the human skin blanching assay. Int J Pharmacol 1984; 19 : 245-62.