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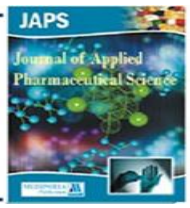

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Effect of Clobetasol Propionate and Clobetasol Butyrate with Biopolymer on Skin Inflammatory Model in Wistar Rats

Bairy KL, Pawan kumar A.V, Chandrashekar BR, Avinash M Holla, Rockson Christopher, Purnima Sirigiri and Satish Kumar MC

Bairy KL
Kasturba Medical College,
Manipal University,
Manipal, Karnataka- 576104, India.

Satish Kumar MC
Kasturba Medical College,
Manipal University, Manipal,
Karnataka- 576104, India.

Pawan kumar A.V., Chandrashekar BR, Avinash M Holla, Rockson Christopher, Purnima Sirigiri
Kasturba Medical College, Manipal University, Manipal, Karnataka- 576104, India.

For Correspondence
Dr. K. L. Bairy
Professor and Head
Department of Pharmacology
Kasturba Medical College
Manipal-576104, India.

ABSTRACT

The treatment of chronic inflammatory skin conditions are not satisfactory. There is a need for better antiflammatory drugs for these conditions. This study was done to compare the efficacy of biopolymer based formulations of clobetasol propionate and clobetasol butyrate with commercially available Preparations of clobetasol in animal models of superficial skin inflammation in rats. The croton oil ear edema in rats was the chronic inflammatory model used in this study. In this model, the animals treated with clobetasol propionate and clobetasol butyrate with biopolymer showed a significant decrease in inflammation as compared to commercially available preparations of clobetasol(Tenovate and Eumosone).

Keywords: Atopic dermatitis, biopolymer, clobetasol propionate, clobetasol.

INTRODUCTION

Atopic dermatitis affects up to 20% of children and 3% of adults (Larsen and Hanifin., 2002). In recent decades, there has been an increase in the global prevalence of the disease, particularly among young children (Williams *et al.*, 1999) Exposure to chemicals, irritants and allergens leads to various inflammatory disorders such as atopic dermatitis, eczema etc. The treatment for such disorders include avoidance of allergens, irritants, adequate cutaneous hydration and judicious use of low to moderate potency corticosteroids. Since the outcome of such treatment is not satisfactory there is need for more efficacious preparations. Clobetasol propionate and clobetasol butyrate are moderately potent glucocorticoids with anti-inflammatory and immunosuppressive properties. These drugs are available in various forms and one of them is clobetasol propionate marketed as tenovate and clobetasol butyrate marketed as eumosone. There are reports that biopolymer based preparations are more efficacious in terms of better penetration and hence the outcome.

Hence, in this study we are comparing the anti-inflammatory activity of tenovate with a new formulation of clobetasol propionate and eumosone with a new formulation of clobetasol butyrate with biopolymer on superficial skin inflammation in rats.

MATERIALS AND METHODS

Animals

Four months old male Wistar rats (weighing between 150-200g) were used in this study. Animals were acclimatized to the laboratory environment for 5-7 days before entering in the study. They were maintained on standard rat diet under laboratory conditions and water *ad libitum*. Twelve hour light/dark cycle was maintained. All procedures were carried with approval of Institutional Animal Ethics Committee (IAEC).

Drugs

Tenovate (clobetasol propionate)**,** Eumosone (clobetasol butyrate), clobetasol propionate and clobetasol butyrate with biopolymer (Apex Labs Chennai).

Antiinflammatory studies

Croton oil ear edema in rats

The study was conducted in male Wistar rats. The irritant croton oil was prepared by dissolving 4 parts of croton oil, 10 parts of ethanol, 20 parts of pyridine and 66 parts of ethyl Ketamine. The test compounds were dissolved (5mg/ml strength) in the croton oil. The animals were divided into twelve groups of 10 animals each. The control and the test animals were anaesthetized with ether and then received the drugs in following doses.

Group I - 0.02ml of croton oil solution.

Group II - 0.02ml of croton oil solution containing dissolved Tenovate (5mg/ml).

Group III - 0.02ml of croton oil solution containing clobetasol propionate A with biopolymer (5mg/ml).

Group IV - 0.02ml of croton oil solution containing clobetasol propionate B with biopolymer (5mg/ml).

Group V - 0.02ml of croton oil solution containing clobetasol propionate C with biopolymer (5mg/ml).

Group VI - 0.02ml of croton oil solution containing clobetasol propionate D with biopolymer (5mg/ml).

Group VII - 0.02ml of croton oil solution containing clobetasol propionate E with biopolymer (5mg/ml).

Group VIII - 0.02ml of croton oil solution containing clobetasol propionate F with biopolymer (5mg/ml).

Group IX - 0.02ml of croton oil solution containing Eumosone(5mg/ml).

Group X - 0.02ml of croton oil solution containing clobetasol butyrate A with biopolymer (5mg/ml).

Group XI - 0.02ml of croton oil solution containing clobetasol butyrate B with biopolymer (5mg/ml).

Group XII - 0.02ml of croton oil solution containing clobetasol butyrate C with biopolymer (5mg/ml). The drug was applied externally to the outer surface of right ear of each rat. The animals were sacrificed by cervical dislocation after four hours and discs of 8mm punches were made with a cork borer. Each ear disc was weighed and compared with control.

Statistical analysis

Results are expressed as mean ± SEM and were analyzed statistically by analysis of variance (ANOVA). P values of less than 0.05 were considered significant.

RESULTS

Croton oil edema in rats

Topical application of croton oil induced cutaneous inflammation which caused a significant increase in ear plug weight. The eleven treatment groups were compared with control. The difference in weight between two plugs was taken as a measure of edematous response. Drug effects were calculated as percent inhibition of edema using the equation(Paula., 2003).

$$\frac{\text{Weight of control ear - Weight of test ear}}{\text{Weight of control ear}} \times 100$$

Table.1: The percentage of edema in twelve groups is shown.

Groups (n=10)	Mean ± SEM
Control	70.84 ± 3.41
Tenovate	39.12 ± 11.15*
Clobetasol propionate A	22.44 ± 2.59*
Clobetasol propionate B	13.20 ± 2.84*
Clobetasol propionate C	19.07 ± 4.18*
Clobetasol propionate D	28.20 ± 8.12*
Clobetasol propionate E	31.43 ± 7.86*
Clobetasol propionate F	18.90 ± 4.94*
Eumosone	26.69 ± 4.31*
Clobetasol butyrate A	31.83 ± 6.47*
Clobetasol butyrate B	53.11 ± 8.67
Clobetasol butyrate C	34.53 ± 2.34*

* Significant $p < 0.05$.

DISCUSSION

Chronic inflammatory conditions of skin require treatment with corticosteroids. Various corticosteroid preparations are available in the market and being used with variable result. In this study, new biopolymer based steroid preparations of clobetasol propionate and clobetasol butyrate is compared with available standard market preparation on croton oil induced inflammation in male Wistar rats. It has been established that inflammation induced by croton oil is related to the activation of phopholipase A2, which releases arachidonic acid from the cell membrane. Arachidonic acid, in turn, is metabolized to prostaglandins (PG's) and leukotrienes. Substances able to inhibit edema could be inhibitors of cyclooxygenase (COX) and/or 5-lipoxygenase (Benito, 1998). The anti-inflammatory action of glucocorticoids is mediated mainly by lipocortin 1, which inhibits phospholipase A2 on the arachidonic acid cascade(Goulding and Guyre., 1993) resulting in decreased synthesis of PG's. It is clear from the data generated that there is a significant decrease in edema in rats treated with clobetasol propionate A, clobetasol propionate B**,** clobetasol propionate C, clobetasol propionate D, clobetasol

propionate E, clobetasol propionate F with biopolymer as compared to Tenovate and clobetasol butyrate A, clobetasol butyrate C with biopolymer as compared to eumosone. Many drugs have limited efficacy because of sub-optimal pharmacokinetics and advances in drug delivery are needed to improve the pharmacokinetics of such drug (Chow *et al.*, 2008). Biopolymers are generally nontoxic and biocompatible. Biopolymer based drugs play an important role in development of drug formulations as they have specific advantages (Sinha and Kumria., 2001). It is most probably the better pharmacokinetics of the biopolymers that gives them an advantage over the conventional preparations. In conclusion, a biopolymer based corticosteroid preparation of clobetasol is superior to commercially available preparations in its anti-inflammatory effect. This may be due to better pharmacokinetics of new formulations. Biopolymer based formulations can be promising candidates for various types of inflammation including atopic dermatitis in which conventional preparations have shown less efficacy.

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