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Effect of Halobetasol Propionate with Biopolymer on Skin Inflammatory Model in Wistar Rats

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ABSTRACT

Various glucocorticoid preparations are used in atopic dermatitis to reduce inflammation. Halobetasol propionate is one such steroid used in atopic dermatitis. There is always a need for better anti-inflammatory drugs for conditions like atopic dermatitis. A newer formulation is biopolymer based halobetasol propionate. This study was done to compare the efficacy of halobetasol propionate with biopolymer with halobetasol propionate (Halovate) in croton oil ear edema model. In this model, the animals treated with halobetasol propionate with biopolymer showed a significant decrease in inflammation as compared to halobetasol propionate (Halovate).

Keywords: Inflammation, halobetasol propionate and halobetasol propionate with biopolymer.

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INTRODUCTION

Skin conditions like atopic dermatitis is associated with varying degrees of inflammation. Though inflammation is a protective mechanism, in some situations if untreated can lead to serious complications. Inflammation is a complex biological response of vascular tissues to harmful stimuli, pathogens or irritants [1]. Exposure to chemicals, irritants and allergens leads to various inflammatory disorders. The treatment for such disorder includes avoidance of allergens, irritants, adequate cutaneous hydration and judicious use of low to moderate potency corticosteroids. Halobetasol propionate is a moderately potent glucocorticoid with anti-inflammatory and immunosuppressive properties. This drug is available in various forms and one of them is halobetasol propionate marketed as halovate.

Biopolymers are obtained from living organisms and generally nontoxic and biocompatible. Biopolymer based drugs play an important role in development of drug formulations as they have specific advantages [2]. In this study we compared the anti-inflammatory activity of halovate with a new formulation halobetasol propionate with biopolymer on superficial skin inflammation in rats

MATERIALS AND METHODS

Animals

Male Wistar rats weighing between 150-200g were used. Animals were acclimatized to the laboratory environment for 5-7 days before entering in the study. They were allowed free access to water and were maintained on standard rat diet under laboratory conditions. Twelve hour light/dark cycle was maintained. The experimental protocol was approved by the Institutional Animal Ethics Committee and experiments were conducted according to the ethical norms approved by Ministry of Social Justices and Empowerment, Government of India and Committee for the purpose of control and supervision on experiments on animals (CPCSEA) guidelines on the use and care of experimental animals.

Drugs

Halovate (halobetasol propionate), halobetasol propionate with biopolymer (Apex Labs Chennai).

Anti-inflammatory studies

Croton oil ear edema in rats [3]:

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 ether. The test compounds were dissolved (5mg/ml strength) in the croton oil. The animals

were divided into five 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 Halovate(5mg/ml)

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

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

Group V - 0.02ml of croton oil solution containing halobetasol propionate 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. Drug effects were calculated as percent inhibition of edema using the equation

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

Statistical analysis

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

RESULTS

All the drug treated groups have reduced the croton oil induced edema significantly. The maximum reduction was seen with halobetasol propionate A and C. Both halobetasol propionate A and C are more effective in edema reduction when compared to halovate and halobetasol propionate B.

Table 1. Percentage of Edema in Croton Oil Edema Model.

Groups (n=10)	Mean \pm SEM
Control	70.84 \pm 3.41
Halovate	24.80 \pm 2.09*
Halobetasol propionate A	16.95 \pm 2.95*
Halobetasol propionate B	51.18 \pm 9.17*
Halobetasol propionate C	17.45 \pm 1.68*

* Significant $p < 0.05$

DISCUSSION

Croton oil induced inflammation is due to the activation of phospholipase 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 [4]. The anti-inflammatory action of glucocorticoids is mediated mainly by lipocortin 1, which inhibits phospholipase A2 on the arachidonic acid cascade [5] resulting in decreased synthesis of PG's.

In this study there was a significant decrease in edema in rats treated with Halobetasol propionate A and Halobetasol propionate C with biopolymer as compared to Halovate and Halobetasol propionate B with biopolymer. Many drugs have limited efficacy because of sub-optimal pharmacokinetics and advances in drug delivery are needed to improve the pharmacokinetics of such drug [6]. Hence biopolymer based drugs may play an important role in development of drug formulations as they have specific advantages [2]. It is most probably the better pharmacokinetics of the biopolymers that gives them an advantage over the conventional preparations. In conclusion, advances in drug delivery improve the pharmacokinetics of promising drugs for many diseases and biopolymers have great potential for delivery of pharmaceuticals. Biopolymer based formulations can be promising candidates for various types of inflammation in which conventional preparations have shown less efficacy.

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