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

Bairy KL*, Bharti C, and Veena N.

Department of Pharmacology, Kasturba Medical College, Manipal University, Manipal, Karnataka- 576104, India.

ABSTRACT

There is always a need for better antiflammatory drugs for conditions like atopic dermatitis. A newer formulation is biopolymer based fluticasone propionate .This study was done to compare the efficacy of fluticasone propionate with biopolymer with fluticasone propionate (Flutivate) in animal models of superficial skin inflammation in rats. The inflammatory model croton oil ear edema in rats was used. In this model, the animals treated with fluticasone propionate with biopolymer showed a significant decrease in inflammation as compared to control group.

Keywords: Inflammation, fluticasone propionate and fluticasone propionate with biopolymer

Corresponding author

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INTRODUCTION

The skin [1] is one of the largest organs in the body in surface area and weight. The skin consists of two layers: the epidermis and the dermis. Beneath the dermis lies the hypodermis or subcutaneous fatty tissueThe skin interfaces with the environment and is the first line of defense from external factors. For example, the skin plays a key role in protecting the body against pathogens [2] and excessive water loss [3]. Inflammation is a protective immunovascular response that involves immune cells, blood vessels, and molecular mediators. The purpose of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and to initiate tissue repair [4]. Various animal models can be used to study the efficacy of anti-inflammatory drugs. Various inflammatory disorders can result from exposure to chemicals, irritants and allergens. The management of such disorder includes avoidance of allergens, irritants, adequate cutaneous hydration and judicious use of low to moderate potency corticosteroids. Attempts have been made to look for more efficacious preparations. Fluticasone propionate is a moderately potent glucocorticoid with anti-inflammatory and immunosuppressive properties. This drug is available in various forms and one of them is fluticasone propionate marketed as Flutivate. Biopolymer based drugs play an important role in development of drug formulations as they have specific advantages such as relieve irritation, have antibacterial property, smooth pain and adsorb odour etc [5]. A new formulation of Fluticasone with is one such preparation.In this study, the anti-inflammatory activity of fluticasone with biopolymer is compared with flutivtae on superficial skin inflammation in rats.

MATERIALS AND METHODS

Animals

Wistar rats (150-200g) bred in the central animal facility of the University were used in this study. They had free access to water and were maintained on standard rat diet (obtained from VRK Nutritional Solutions, Pune) under laboratory conditions with 22-24◦ C room temperature, 12- hour light/dark cycle and relative humidity 40-60%. Approval of Institutional Animal Ethics Committee (IAEC) was obtained before starting the experiment.

Drugs

Flutivate (fluticasone propionate), fluticasone propionate with biopolymer were obtained from Apex Laboratories Private Limited, Chennai (India) (Apex Labs Chennai).

Croton oil ear edema in rats [6]

A total of 30 Wistar rats were used in the study. They were divided in to five groups of six animals each. The edema was induced by croton oil which was prepared by dissolving four 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 control and the test animals were anaesthetized with ether. Animals received the drugs in the following doses.

Group I - 0.02ml of croton oil solution
Group II - 0.02ml of croton oil solution containing dissolved Flutivate(5mg/ml)
Group III - 0.02ml of croton oil solution containing fluticasone propionate A with biopolymer (5mg/ml)
Group IV - 0.02ml of croton oil solution containing fluticasone propionate B with biopolymer (5mg/ml)
Group V - 0.02ml of croton oil solution containing fluticasone propionate C with biopolymer (5mg/ml)

The drug was applied once externally to the outer surface of right ear of each rat and the left ear was kept as control. The animals were sacrificed after four hours by excess dose of ketamine and discs of 8mm punches were made with a cork borer and each ear disc was weighed. The ear disc of test was compared with control and the difference in weight between the treated and the untreated ear indicated the degree protection of inflammatory edema. The percentage increase in the edema was calculated by the formula:

$$\% \text{ of ear edema} = \frac{\text{Weight of right ear disc - Weight of left ear disc X 100}}{\text{Weight of left ear disc}}$$

Statistical analysis

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

RESULTS

Application of croton oil locally in to rat ear induced cutaneous inflammation which caused a significant increase in ear plug weight. The difference in weight between two plugs was taken as a measure of edematous response. There was significant decrease in in edema of all drug treated groups when compared to control group ($p<0.05$). There was no difference among the drug treated groups. However, among the drug treated groups maximum decrease in edema was seen with Fluticasone propionate C.

Table 1: Showing percentage inhibition of ear edema

Groups (n=10)	Mean ± SEM
control	70.84 ± 3.41
Flutivate	29.39 ± 6.16*
Fluticasone propionate A	30.04 ± 4.14*
Fluticasone propionate B	29.53 ± 3.25*
Fluticasone propionate C	22.93 ± 6.68*

* Significant $p< 0.05$

DISCUSSION

Croton oil induces inflammatory changes by activation of phopholipase A_2, which releases arachidonic acid from the cell membrane. Arachidonic acid, in turn, is metabolized to prostaglandins (PGs) and leukotrienes. Substances able to inhibit edema could be inhibitors of cyclooxygenase (COX) and/or 5-lipoxygenase [7]. The anti-inflammatory action of glucocorticoids is mediated mainly by lipocortin 1, which inhibits phospholipase A2 on the arachidonic acid cascade resulting in decreased synthesis of PGs [8]. In this study there was a significant decrease in edema in rats treated with Flutivate, Fluticasone propionate A, Fluticasone propionate B and Fluticasone propionate C with biopolymer as compared to control. Among the four drug treated grupos the maximum reduction in edema was seen with Fluticasone propionate C suggesting that this formulation may be more useful in reducing the skin inflammation. Many drugs have limited efficacy because of sub-optimal pharmacokinetics and advances in drug delivery are needed to improve the pharmacokinetics of such drug [9]. Biopolymer based drugs play an important role in development of drug formulations as they have specific advantages [5]. Biopolymers are generally nontoxic and biocompatible. 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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