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Heterocyclic Indane-1,3-Dione Derivatives as Topical Anti-Inflammatory Agents

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Abstract:
An attempt was made to develop a topical ointment of the most active compound among the synthesized series which has a potent anti-inflammatory activity. The optimum concentration of the drug was determined by comparing the anti-inflammatory effect of ointment preparations at different concentrations. The anti-inflammatory effects were studied by using carrageenan-induced paw edema method in rats. Good effect was observed with ointment containing 4% and 5% of the drug concentration. Based on the results, ointment containing 5% of drug was adopted as the suitable drug. The results showed that the drug had an obvious anti-inflammatory effect as an external preparation and the activity is comparable to that of the standard ointment.
Keywords: anti-inflammatory, formulation, indane-1,3-dione, ointment

INTRODUCTION:

Application of the drug on the diseased site or the nearby area is reasonable, since drugs produce effects after they reach the affected site. Topical non-steroidal anti-inflammatory drugs (NSAIDs) are applied in the skin in the form of ointment, gel, cream or spray in the region where pain is experienced [1]. They have to penetrate the skin, enter tissues or joints, and at high concentration to have an effect on the inflammation process causing pain. The inhibitory activities of NSAID ointment on inflammatory responses were almost the same as those obtained by oral administration of such NSAID and more potent that those of steroidal ointment [2]. Drug must be transported through skin layers like the stratum corneum, viable epidermis, the basement membrane and the dermis [3]. Absorption into systemic circulation or penetration into deeper tissues occurs from this point [4,5].

Indane-1,3-dione derivatives possess good analgesic, anti-inflammatory, antimicrobial, anticoagulant activities. Several thiopyrimidine derivatives of indane-1,3-dione derivatives were synthesized and evaluated for its analgesic, anti-inflammatory, antimicrobial [6], anticoagulant [7], antihistamine [8,9] anti-tumor [10] activities. The synthesized compounds then docked into COX-2 receptor and the activity was compared. It was found that compound 2-[6-(1*H*-indol-2-yl)-2-thioxo-1,2,5,6-tetrahydro pyrimidin-4-yl]-indane-1,3-dione was the most potent one among the synthesized series. So it was planned to formulate the same derivative in the form of ointment. To find the most suitable concentration for the ointment, five different concentrations like 1%, 2%, 3%, 4% and 5% were selected for the study. The formulated ointments were then evaluated for anti-inflammatory activity.

MATERIALS AND METHODS:

Carrageenan (Hi-Media Laboratories Pvt Ltd, Mumbai), Polyethylene Glycol, Propylene Glycol, Petrolatum (S.D.fine- Chem Ltd, Mumbai) were used in the present study

Method of preparation of ointment:

Ointment was prepared by melting together petrolatum, polyethylene glycol 3000, propylene glycol and menthol on a hot plate (70 ºC). The drug was dissolved in it under stirring and cooled. Various compositions of ointment formulations were mentioned in the Table 1.

Anti-inflammatory activity:

Anti-inflammatory activity was carried out using carrageenan-induced rat paw edema [11]. The rats weighing between 150-200 g were selected randomly excluding pregnant female rats for the test. Animals were divided into

Table 1: Composition used in the study to prepare ointments

Ingredients (in g)	*F1*	*F2*	*F3*	*F4*	*F5*
Drug	0.1	0.2	0.3	0.4	0.5
Polyethylene glycol-3000	0.6	0.6	0.6	0.6	0.6
Propylene glycol	0.4	0.4	0.4	0.4	0.4
Menthol	0.5	0.5	0.5	0.5	0.5
Petrolatum	q.s to10	q.s to10	q.s to10	q.s to10	q.s to10

Table 2: Effect of topical administration of formulation on carrageenan induced paw edema in rats

Compound	*Change in paw volume (in ml) after drug administration (Mean ± SEM)*				*Percentage inhibition of oedema volume after*			
	1 h	*2 h*	*3 h*	*4 h*	*1 h*	*2 h*	*3 h*	*4 h*
Control	0.71 ± 0.02	0.77 ± 0.03	0.71 ± 0.02	0.60 ± 0.02	-	-	-	-
Standard	0.42 ± 0.03**	0.43 ± 0.04**	0.44 ± 0.04**	0.40 ± 0.03**	40	44	38	33
F1	0.58± 0.04	0.60 ± 0.01	0.57 ± 0.05	0.49 ± 0.03	19	22	21	19
F2	0.54± 0.02*	0.57± 0.01*	0.53± 0.04	0.48± 0.04	24	26	26	20
F3	0.52± 0.01*	0.55± 0.01*	0.51± 0.04*	0.48± 0.04	27	28	29	20
F4	0.49± 0.02**	0.53± 0.02**	0.48± 0.04**	0.47± 0.04	30	31	33	22
F5	0.47± 0.04**	0.50± 0.04**	0.47± 0.04**	0.46± 0.04	34	35	34	24

SEM- Standard Error Mean , *P<0.05; **P<0.01.

different groups with six animals in each group. One group of rats were treated with ointment base which served as control, other group was administered with standard ointment. Remaining groups were treated with formulated ointment (F1-F5). 0.2 g of ointment was applied to the plantar surface of the hind paw by gentle rubbing 50 times with index finger. After 30 min 0.1 ml of 1% w/v of carrageenan was injected in the plantar region of the left paw of rats. The paw volumes were noted for 1, 2, 3 and 4 h after carrageenan challenge. The results were tabulated in Table 2. The percentage edema inhibition by the drug was calculated by the formula

$$\left[1 - \frac{Vt}{Vc}\right] \times 100$$

Where

Vt: - is edema volume in drug treated group.

Vc: - is edema volume in the control group

Statistical analysis:

The results were expressed in mean± SEM. The data from experiments were analyzed separately using one-way Anova followed by Dunnett test was used to determine significant difference between the groups and $p<0.05$ was considered significant.

RESULTS AND DISCUSSION:

Different formulations (**F1-F5**) were prepared by keeping the ointment base constant and changing the drug ratio (1-5%). All the formulations were stable for evaluation of anti-inflammatory activity. Anti-inflammatory activity was carried out for the formulated compounds using carrageenan-induced rat paw edema method in rats. Statistical analysis showed that, the edema inhibition was significantly different from control group at all the tested concentrations. The results showed that the anti-inflammatory effect was more for the formulation containing 5% of the drug. F4 and F5 were statistically significant till third hour. But on comparing with all the formulations, F5 was the most active formulation.

CONCLUSION:

From this result, we conclude that topical preparation containing 5% possesses good anti-inflammatory activity which can be used for the treatment of topical inflammation.

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REFERENCE:

[1] Kyuki, K., Shibuya, T., Tsurumi, K., Fujimura, H., *Japan J. Pharmacol.* 1983, *33*, 121-132.

[2] Kyuki,K., *Nippon. Yakurigaku. Zasshi.* 1982, *79*(6), 461-485.

[3] Vaile, J. H., Davis, P., *Drugs* 1998, *56*(5), 783-799.

[4] Singh, P., Robert, M., *J. Pharm. Exp. Ther*. 1994, *268*,144-151.

[5] Wang, J., Jinlan, Ruan., Cai, Y., Wu, Y., *Pak. J. Pharm. Sci.* 2008, *21*(2), 89-91.

[6] Giles, D., Prakash, M., Ramsesu, K., *E-J. Chem.* 2007 *4*(3), 428-433.

[7] Shapiro, S. L., Geiger, K., Freedman, L., *J. Org. Chem.* 1960, *25*, 1860-1865.

[8] Buckle, D., Smith, H., *U.S. Patent* 3,925,557, 1975, Nov 18.

[9] Buckle, D., Smith, H., *U.S. Patent* 3,978,231. 1976, Aug 31.

[10] Inayama, S., Mamoto, K., Shibata, T., Hirose, M., *J. Med. Chem.* 1976, *19*(3), 433-436.

[11] Morteza-Semnania, K., Saeedib, M., Hamidiana, M., *Fitoterapia.* 2004, *75*,123-129.