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Research Article

DRUG NEOMYCIN RELEASE FROM *CORDIA DICHOTOMA* TRANSDERMAL FILM AND ANTIINFLAMMATORY ACTIVITY

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ABSTRACT
Transdermal Films were prepared using 10 % w/v natural polymer (fruit gum) of *Cordia dichotoma* with different percentage of plasticizer (glycerin 0.10, 0.20 and 0.25 % w/v), same percentage of preservative (methyl paraben 0.1 % w/v) and drug (neomycin 0.2 % w/v). The films were casted on glass plates and dried under controlled evaporation. Films prepared with 0.20 % w/v of glycerin showed satisfactory drying after 24 h. They were evaluated by the various parameters like thickness, tensile strength, water uptake, folding endurance, piercing load and skin irritation test. In the present study *Cordia dichotoma* Transdermal film was investigated for Anti-Inflammatory activity in carrageenan-induced rat paw edema. It was compared to control group and with that of standard drug,diclofenac sodium. The neomycin film with 0.20% plasticizer showed significant result.
KEYWORDS: *Cordia dichotoma* Transdermal Film, Neomycin, Anti-Inflammatory Activities.

INTRODUCTION

Herbal gums are being widely used in the process of development of new pharmaceutical formulations. When the gum mucilage is mixed with water, a protective soothing preparation results, which when applied externally will protect lesion or ulcer, from environmental contamination, infection, and sepsis[1]. There are several reports about the successful use of natural gums in various pharmaceutical preparations[2-6] was found through literature search. The gum in the present study is exudates from ripen fruits of *Cordia dichotoma*, this plant belonging to family Boraginaceae is medium sized tree with a short, usually crooked trunk 3-4 ft. in girth[7] . The fruits are globose, yellowish-brown, pink or black and pulpy. The plant grows in India and other warmer regions. The fruits of the plant are used as cooling, astringent, emollient, expectorant, anthelmintic, purgative and diuretic. A number of pharmacological properties such as analgesic, anti-inflammatory and hepatoprotective have been reported[7,8,9]. The gum is initially white in color but changes to brownish black on exposure to atmosphere. It is sparingly soluble in water but swells in contact with water, giving a highly viscous solution. It is a polyuronide consisting of arabinose, galactose, and glucoronic acid in the proportion of 10:7:2 moles; rhamnose is present in traces[8]. The neomycin drug in the form of Transdermal film was reported to possess potent wound healing activity[10]. In the present study the neomycin Transdermal film is used to study anti-inflammatory activity in carrageenan-induced rat paw odema. Literature survey reveals no scientific investigation reported so far, hence the present study is taken up.

MATERIALS AND METHODS

Preparation of Natural Gum Films

Glycerin, methyl paraben and drug neomycin were obtained from Kem Well House, Bangalore.

Gum was collected from the authenticated fruits of *Cordia dichotoma*, dried, grounded and passed through sieve no 80. Gum powder (10 g) was stirred in distilled water (250 ml) for 6-8 h at room temperature. The supernatant was obtained by centrifugation. The residue was washed with water and the washings were added to the separated supernatant. Finally the supernatant was made up to 500 ml and treated with twice the volume of acetone by continuous stirring. The precipitated material was washed with distilled water and dried at 50-60°C under vacuum. The gum (10 % w/v) mucilage was prepared by dispersing in distilled water; it was allowed to equilibrate for a period of 24 h. The 5 ml mucilage was mixed with drug (neomycin 0.2 % w/v), plasticizer (glycerin 0.10, 0.20 and 0.25 % w/v) and preservative (methyl paraben 0.1 % w/v) by stirring for a period of 15 min. The films were prepared on glass plate of an area 10 sq.cm (Table 1). They were placed in a dry chamber for evaporation. After 24 h the films (F2 and F3) were observed satisfactory and were subjected for various evaluations.

Evaluation of Films

The prepared satisfactory films F2 and F3 were evaluated for various parameters. The water uptake was determined by drying the films at 60°C with a current of air, after which the films were subjected to desiccation over calcium chloride at 40°C for 24h. These samples were weighed and exposed to 70% relative humidity at room temperature and percentage of water uptake was calculated. Thickness of polymeric film was measured by using a dial gauge having least count of 0.002 mm. The films were conditioned at 55 % relative humidity at 25°C to 30°C for 48 h before testing tensile strength. In order to determine the elongation for calculating tensile strength, the polymeric film was pulled by means of a pulley system[11]. The folding endurance was determined using a simple instrument as reported[12], to evaluate the ability of the films to withstand folding. Water vapor transmission rates were determined using pre-weighed glass vials of 5 ml containing 1 g of fused calcium chloride. Prepared films were fixed on the brim of the vials with an adhesive and stored in a humidity chamber at relative humidity of 70% and temperature of 25°C for 24 h; and the weight gained was determined.

Anti-Inflammatory Study

Anti-inflammatory activity was assessed using the carrageenan-induced rat paw oedema method [11]. The ethical clearance was obtained by the Institutional Animal Ethics committee (Registration number IAEC/NCP/12/09 before the experiment. Rats were kept in polypropylene cages and fed on standard laboratory diet with water *ad libitum*. The animals were exposed to 12 h of darkness and light each. Animals were divided into six groups of 6 animals each and were given the following treatments. Group 1 (control) received 1 ml 0f 5%v/v solution of Tween 80 in distilled water orally; group 2 received 15 mg/kg of diclofenac sodium orally; groups 3, 4 and 5 were applied neomycin Transdermal film with three different percentage of plasticizer(0.10, 0.20 and 0.25 % w/v) . After 1 h, subcutaneous injections of 0.1ml of 1% w/v solution of carrageenan into the subplanter side of the left hind paw. The paw was marked with ink at the level of lateral malleolus and immersed in mercury up to this mark. The paw volume was measured plethysmographically immediately after injection (0 h) and followed

by every hour for 6 h after injection of carrageenan to each group. The difference between the initial and subsequent reading gave the actual oedema volume.

RESULTS AND DISCUSSION

Films were successfully formed by the method adopted in this research[13] details are mentioned in the Table 1. Various physicochemical properties of the films are presented in Table 2. Results indicate that as the thickness of the film increases the tensile strength also increases, where as % water uptake decreases as the thickness increases. The folding endurance and piercing load did show any trend with increase in the film thickness. In anti-inflammatory activity percentage inhibition of inflammation was calculated using the formula, % inhibition = 100 (1- vt/vc) where Vt represents oedema volume in test compounds and Vc represent oedema volume in control. The data was analyzed using student's t-test. Level of significance was set at $p < 0.001$. The results obtained as mean increase in paw volume (ml) and % inhibition are represented in Table 1. The highest percentage inhibition of oedema is observed with at 0.20% w/v glycerin. i.e. 67.36 at 6 h as compared to standard. i.e. 69.47.

Carrageenan-induced inflammation is a biphasic phenomenon[14,15]. The first phase of oedema is attributed to release of histamine and 5-hydroxytryptamine. Plateau phase is maintained by kinin like substances and second accelerating phase of swelling is attributed to prostaglandin like substances[16]. The knowledge of these mediators involved in different phases is important for interpreting mode of drug action.

Neomycin is absorbed from the peritoneum, respiratory tract, bladder, wounds and inflamed skin; little is absorbed when applied topically. It interferes with bacterial protein synthesis by binding primarily to the 30s subunit of bacterial ribosomes. Neomycin sulfate is active against many strains of gram-positive and gram-negative bacteria.

The results obtained indicate that Neomycin, a cationic aminoglycoside antibiotic that interacts with polyphosphoinositides resulting in blockade of phosphoinositide breakdown results decrease in the Rat paw[17]oedema at 0.20%w/v plastizer neomycin *Cordia dichotoma* Transdermal film applied to the paw was found to have statistically significant anti-inflammatory activity ($P > 0.001$). While standard drug, Diclofenac sodium showed significant activity ($P < 0.001$). The neomycin has been reported to possess anti-inflammatory activity [17]. The principle objection to incorporating antibiotics is the inability to remove the drug in case of allergic reaction. While it is apparent that only minute amount would be released into systemic circulation, it is also certain that only molecular quantities are needed to produce a true hypersensitivity reaction. The risk of such sensitivity is reduced in Transdermal film although not completely eliminated[18].

CONCLUSION

It was concluded that, neomycin *Cordia dichotoma* Transdermal film with 0.20% plasticizer showed significant anti-inflammatory activity.

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Table 1: Composition of *Cordia dichotoma* film casting solution

Film No.	Polymer (*C.dichotoma*) (10 %w/w)	Plasticizer (Glycerine) (%w/v)	Drug (Neomycin) (%w/v)	Preservative (Metyl paraben) (%w/v)	Distilled Water (Q.S)	Observation after 24 h
F1	5 ml	0.05	0.2	**0.1**	10 ml	Dried
F2	5 ml	0.15	0.2	0.1	10 ml	Dried
F3	5 ml	0.25	0.2	**0.1**	10 ml	**wet**

Table 2: Evaluation of *Cordia dichotoma* Films

Film No	Mean Thickness (mm)	Tensile strength (kg/cm2)	Water Uptake (%)	Folding endurance (No. of counts)	Piercing load (kg)
F2	0.475 ± 0.25	4.853 ± 0.025	7.82 ± 0.38	238 ± 0.37	0.269 ± 0.23
F3	0.487 ± 0.14	3.982 ± 0.032	5.86 ± 0.54	246 ± 0.28	0.288 ± 0.34

Table 3: Results of Medicated *Cordia dichotoma* Film *on* Carrageenan-induced paw Oedema in rats.

Treatment	Mean increase in paw volume ± S.E (ml) at different time intervals			
	0 h	2 h	4 h	6 h
Control (Vehicle)	0.29± 0.003	0.43 ± 0.004	0.89 ±0.005	0.95±0.005
Diclofenac Sodium (1 (5 mg / kg, p.o)	0.16 ±0.002 (44.80)	0.18 ±0.005* (58.10)	0.30± 0.004* (66.29)	0.29 ±0.006* (69.47)
F1 film (0.05% plasticizer)	0.17 ±0.005 (41.40)	0.19 ±0.005* (55.81)	0.29±0.008* (67.41)	0.31 ±0.008* (67.36)
F2 film (0.15% plasticizer)	0.29 ±0.006	0.40 ±0.015 (6.97)	0.87 ±0.008 (2.24)	0.92 ±0.009 (3.15)
F3 film (0.25% plasticizer)	0.29 ±0.004	0.40 ±0.005 (6.98)	0.84 ±0.001 (5.61)	0.95 ±0.001 (0.03)

**Indicates satisfactory,*

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