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RELEASE OF DRUG NEOMYCIN FROM *CORDIA DICHOTOMA* TRANSDERMAL FILM

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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 0.05, 0.10, 0.15, 0.20 and 0.25 % w/v), same percentage of preservative (methyl paraben 0.2 % 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. The wound healing results obtained are comparable with marketed product framycetin tulle® and neomycin loaded films showed significant wound healing activity. Hence, Cordia dichotoma film gum can be used as natural polymeric drug delivery system.

KEYWORDS

Cordia dichotoma Film, Neomycin, Wound Healing 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, 3, 4, 5, 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 [8]. A number of pharmacological properties such as analgesic, antiinflammatory and hepatoprotective have been reported [9,10,11]. 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[7].

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 0.05, 0.10, 0.15, 0.20 and 0.25 % w/v) and preservative (methyl paraben 0.2 % 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 (F_3 and F_4) were observed satisfactory and were subjected for various evaluations.

Evaluation of Films:

The prepared satisfactory films F_3 and F_4 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 24 h. 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[12]. The folding endurance was determined using a simple instrument as reported[13-15], 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[16].

Wound Healing Study:

Healthy albino rats of either sex weighing between 150-200 gm were used for study. Animals were grouped into 3 groups of 6 animals each in both incision and excision models. They were housed individually with food and water. The animals were starved for 12 h prior to wounding under light anesthetic ether. For group 1, 2 and 3 applied plan film, medicated film (0.2 % neomycin) and Framycetin tulle® respectively. The test materials were applied daily for 10

consecutive days on incision and 17 days on the excision wound model.

RESULTS AND DISCUSSION

Films were successfully formed by the method adopted in this research[17] 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. Results of excision wound closure of various films are presented in Table 3. It was observed that around 90 % wound closer was observed at 16th day for both test as well as Framycetin tulle treated where as only 69 % observed for control group. Results of time of epithelization in days are presented in Table 3. The fast epithelization was observed for test and standard treated group. Results of size of scar area in % sq. mm are presented in Table 3. Results indicated that scar sizes were comparatively lower in test as well as standard treated group

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.
F-1	5 ml	0.05	0.2	0.2	10 ml	Dried
F-2	5 ml	0.10	0.2	0.2	10 ml	Dried
F-3	5 ml	0.15	0.2	0.2	10 ml	*
F-4	5 ml	0.20	0.2	0.2	10 ml	**
F-5	5 ml	0.25	0.2	0.2	10 ml	Wet

**Indicates satisfactory, **Indicates very satisfactory means films are not so brittle / 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)
F-3	0.475 ± 0.25	4.853 ± 0.025	7.82 ± 0.38	238 ± 0.37	0.269 ± 0.23
F-4	0.487 ± 0.14	3.982 ± 0.032	5.86 ± 0.54	246 ± 0.28	0.288 ± 0.34

Values are expressed as mean ±S.E.

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Table 3

Results of Medicated Cordia dichotoma on Excision Wound Parameters.

Groups	% (Sq.mm) Wound Contraction on					Period of Epithelization (days)	Mean size of scar area (mm^2)
	4th Day	8th Day	12th Day	16th Day	18th Day		
Control	10.88 ± 1.05	26.53 ± 1.20	48.15 ± 1.89	70.86 ± 2.34	79.53 ± 1.00	21.00 ± 0.35	16.55 ± 0.86
Medicated C.dichotoma **film**	18.39 ± 1.23*	39.06 ± 1.51**	65.27 ± 1.25*	89.80 ± 1.25**	97.48 ± 2.13**	17.50 ± 0.24**	11.75 ± 0.28**
Framycetin tulle	24.15 ± 0.45**	46.75 ± 1.34**	68.65 ± 1.36**	92.82 ± 2.15**	98.85 ± 0.28**	17.25 ±0.26 **	10.82 ± 0.34**

*Values are expressed as mean ± S.E; n= 06; **p<0.01 and ***p<0.001.*

CONCLUSION

It was concluded that, stem gum of *Cordia dichotoma*has enormous potential for use in the preparation of polymeric films as drug delivery systems. The various *in vitro* tests have been performed. *In vivo* studies were conducted in rats and results showed significant wound healing activity property.

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