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ANTI INFLAMMATORY ACTIVITY OF DICLOFENAC SODIUM GEL

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ABSTRACT

Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID), is frequently prescribed for the long term treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Gastrointestinal side effects such as bleeding, ulceration or perforation of intestinal wall are commonly seen when the drug is administered orally. In view, of adverse drug reaction associated with oral formulations, diclofenac sodium is increasingly administered by topical route. In present study anti inflammatory activity of diclofenac sodium gel containing linseed oil and ginger oleoresin was checked by using Albino rats (Strain Wistar). It was found that diclofanac sodium gel containing 3% linseed oil, 1.5% ginger oleoresin and 10% methyl salicylate shows 81.18% edema inhibition in 3rd hour as compare to marketed Divon gel which shows 79.74% edema inhibition.

INTRODUCTION

Inflammation can be defined as defensive but exaggerated local tissue reaction in response to exogenous or endogenous insult. It is complex phenomenon, comprising of biochemical as well as immunological factors [1, 2] .Inflammation is the process which may be due to release of histamine, kinins, serotonins and prostaglandin. Anti-inflammatory are the agents which normally inhibit the release of these inflammatory mediators[3].

Diclofenac sodium is the non-steroidal anti-inflammatory drug (NSAID) [4,5, 6], which is chemically, 2-(2-(2,6-dichlorophenylamino)phenyl)acetic acid [7]. Diclofenac sodium is used for musculoskeletal complaints, especially arthritis, rheumatoid arthritis [8], polymyositis, dermatomyositis, osteoarthritis, dental pain [9], spondylarthritis, ankylosing spondylitis, gout attacks, and pain management in cases of kidney stones and gallstones. An additional indication is the treatment of acute migraines [10]. Diclofenac sodium is used commonly to treat mild to moderate post-operative or post-traumatic pain, particularly when inflammation is also present, and is effective against menstrual pain and endometriosis .Mechanism responsible for its anti-inflammatory, antipyretic, and analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis[11] . Ginger (*Zingiber officinale*) contains oleoresin, which contain gingerol and shagaol. These active principles are responsible for anti-inflammatory activity of ginger. It has ability to inhibit thromboxane synthetase and acts as prostacyclin agonist[12]. This may be indicated for rheumatoid arthritis, muscular cramps, and other musculoskeletal disorders [13]. Linseed oil contains essential fatty acids viz α-linoleic acid and γ-linoleic acid both of them are used in the treatment of musculoskeletal system disorders like rheumatoid arthritis, painful breast (mastalgia) and also reduces the inflammation within body [12].

The aim of the present study is to perform antiinflammatory activity of diclofenac sodium gel containing linseed oil and ginger oleoresin by using Albino rats (Strain Wistar) and to compare it with marketed Divon gel.

MATERIAL AND METHODS

Diclofenac sodium was a kind gift from Medley Pharmaceutical Ltd., Daman, India. All other ingredients were of analytical grade and were supplied by S. D. Fine chemical Ltd. Mumbai. Divon gel of Micro Eros Pvt. Ltd. Bangalore, was purchased from market. Carrageenan was borrowed from Hi-media Laboratories Pvt. Ltd., Mumbai.

Animals [14]

Wister Albino rats of either sex, weighing between 150-225 g were acclimatized for 10 days before and during study approved by institutional ethical committee, Chikhli, Dist: Buldana. Animals were kept under standard husbandry conditions at room temperature of 24± 2°C, relative humidity 45-55% and 12:12 light/dark cycle. The animals were fed with standard rodent pellet (Sai Durga feeds & food, Bangalore, Pranava Agro Industries Ltd., Sangali, India).Water was supplied ad-libitum under strict hygienic conditions. The protocol of the study were approved by Institutional Animal Ethics Committee,

Anuradha College of Pharmacy, Chikhli and conducted according to the Indian National Science Academy guidelines for the use and care of experimental animals.

Methods of preparation of Diclofenac sodium gel

Table 01: Preparation of hydrogels

Ingredients (% w/w)	Gels 100 gm							
	F1	F2	F3	F4	F5	F6	F7	F8
Diclofenac sodium	1	1	1	1	1	1	1	1
Linseed oil	3	3	3	3	3	3	3	3
Ginger oleoresin	0.5	1	1.5	2	0.5	1	1.5	2
Methyl salicylate	10	10	10	10	10	10	10	10
Carbopol 974 P	1	1.25	1.5	1.75	-	-	-	-
HPMC	-	-	-	-	1	1.5	2	2.5
Menthol	5	5	5	5	5	5	5	5
Triethanolamine	2	2	2	2	-	-	-	-
Methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Propyl paraben	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Chremophore Rh 40	4	4	4	4	-	-	-	-
Tween 60	1	1	1	1	-	-	-	-
Isopropyl alcohol	7	7	7	7	7	7	7	7
Propylene glycol	15	15	15	15	5	5	5	5
Distilled Water Up to	100	100	100	100	100	100	100	100

1) Gel with carbopol base

Heat propylene glycol at 65^0C and dissolve in it methyl paraben and propyl paraben, add water and carbopol, and keep it for 8 hours for adequate swelling of polymer. Add triethanolamine to neutralize the carbopol and adjust the pH 6.7 – 6.9. Take another vessel and heat propylene glycols at 65^0C, add diclofenac sodium, cool at room temperature and add in carbopol base. Take IPA and dissolve menthol in it till the clear solution is obtained, add it in above gel. Oil phase was prepared by dissolving tween 60,chremophore Rh 40, methyl salicylate, linseed oil and ginger oleoresin, mix till the clear solution is obtained. Oil phase is slowly added in the above aqueous carbopol gel while constantly stirring to get emulgel and adjust the pH 7.0 – 7.5.

Gel was packed in aluminium collapsible tube. (Table: 01)

2) Gel with hydroxy propyl methyl cellulose

Diclofenac sodium was dissolved in propylene glycol. Menthol was dissolved in Isopropyl alcohol. The whole amount of HPMC was sprinkled on drug solution with slow stirring then methyl paraben and propyl paraben was added. The mixture of drug solution and polymer was kept aside for six hour to seven hour, for adequate swelling of polymer. The oil phase consisting of linseed oil, ginger oleoresin and methyl salicylate was added slowly in above aqueous gel with continuous stirring with overhead stirrer. The gel was packed in aluminium collapsible tube. (Table: 01)

***In Vivo* study** [15,16, 17,]

Acute edema was induced in the right hind paw of rats by injecting 0.1 ml of freshly prepared 1 % aqueous solution of carrageenan in the plantar region of the right hind paw. The volumes of the hind paw were measured using plethysmometer at 60, 120 and 180 min after carrageenan challenge. Inflammation was expressed as the percentage change in paw volume.

Statistical Analysis [18,19]

The anti-inflammatory effect was expressed as percent edema inhibition. The formula for the same is as below.

$$\% \text{ Edema inhibition} = \frac{\text{mean paw edema of control} - \text{mean paw edema of test}}{\text{mean paw edema of control}} \times 100$$

RESULT AND DISCUSION

According to statistical analysis carried out by using student's unpaired 't' test, a significant inhibitory effect was observed for each of the formulations tested versus the control. After 3rd hour of study, batch F3 showes maximum anti-inflammatory response (Table: 03). Addition of propylene glycol to these formulations as a permission enhancer responsible for the easy diffusion or fast diffusion. Though the ingredients of all formulations are same, polymer concentration affects the diffusion of drug. Thus F3 batch shows better release and good anti inflammatory activity as compare to other formulations.

Table 02: Comparative studies of Anti-inflammatory activity of various formulations

Formulation No.	1st hour % Edema Inhibition	2nd hour % Edema Inhibition	3rd hour % Edema Inhibition
F1	37.61	65.35	75.60
F2	31.65	64.68	79.66
F3	45.14	71.60	81.18
F4	48.54	74.67	80.08
F5	28.71	61.33	69.76
F6	34.68	52.12	61.68
F7	38.65	61.33	80.85
F8	14.87	57.33	62.79
Divon gel (M1)	42.65	65.33	79.74

Graph01: Graphical representation of various formulations with marketed preparation

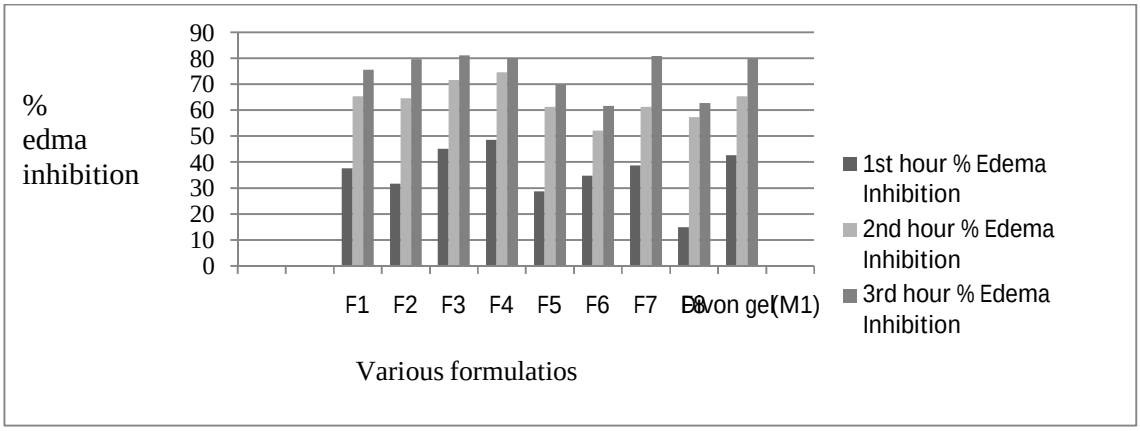

Table 03: Comparative study of anti inflammatory activity of optimized formulation with marketed preparation

Formulations	1st hour	2nd hour	3rd hour
Divon gel (M1)	42.65	65.33	79.74
F3	45.14	71.60	81.18

CONCLUSION

From the above results it can be concluded that the batch F3 containing 1% diclofenac sodium, 3% linseed oil, 1.5% ginger oleoresin and 10% methyl salicylate was suitable for topical application and it shows good anti inflammatory activity with that of marketed Divon gel (M1).

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