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RESEARCH ARTICLE

In Vivo Efficacy Study of Aceclofenac Gel Containing Linseed Oil and Ginger Oleoresin

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ABSTRACT:
Aceclofenac is a Non-Steroidal Anti-Inflammatory Drug (NSAID), used in the treatment of inflammation and degenerative disorder of the musculoskeletal system. It is widely prescribed for the treatment of osteoarthritis, rheumatoid arthritis, dysmenorrheal, acute lumbago, musculoskeletal trauma and gonalgia (Knee pain). Aceclofenac is well tolerated, with most adverse events being minor and reversible and affecting mainly the G.I system. Most common events include dyspepsia, abdominal pain, nausea, ulcerative stomatitis and pancreatitis. In present study anti inflammatory activity of aceclofanac gel containing linseed oil and ginger oleoresin was checked by using Albino rats (Strain Wistar). It was found that aceclofanac gel containing 3% linseed oil, 1.5% ginger oleoresin and 10% methyl salicylate shows 81.16% edema inhibition in 3rd hour as compare to marketed Nusaid gel which shows 76.74% edema inhibition.

KEYWORDS: Aceclofenac gel, Anti inflammatory, linseed oil, ginger oleoresin, In vivo

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 agents are the agents which normally inhibit the release of these inflammatory mediators[3].

Aceclofenac is a diclofenac derivative of the Non Steroidal Anti-Inflammatory drug[4,5,6] (NSAID), which is chemically, (2-[2-[2-(2,6-dichlorophenyl) aminophenyl]acetyl] oxyacetic acid)[7,8]. Aceclofenac is used in treatment of osteoarthritis, rheumatoid arthritis, acute lumbago, and dental pain condition[9,10,11]. However like other NSAIDs, oral administration of this drug is also associated with severe gastrointestinal side effects like- ulceration and gastro intestinal bleeding.

Aceclofenac has dual action i.e. it blocks the prostaglandin (PGE2) Secretion and also inhibits the release of Cytokines (substances produced by inflammatory cells: IL, TNF), which are involved in the inflammation[12].

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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. This may be indicated for rheumatoid arthritis, muscular cramps, and other musculoskeletal disorders[13,14]. 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 [13,14].

The aim of the present study is to perform anti inflammatory activity of aceclofenac gel containing linseed oil and ginger oleoresin by using Albino rats (Strain Wistar) and to compare it with marketed Nusaid gel**.**

MATERIAL AND METHODS:
Aceclofenac 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. Nusaid gel (M1) of Molekule Pharmaceuticals Pvt. Ltd. was purchased from market. Carrageenan was borrowed from Hi-media Laboratories Pvt. Ltd., Mumbai.

Animals [15]
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, Pusad.

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 protocols of the study were approved by Institutional Animal Ethics Committee, S.N. Institute of Pharmacy, Pusad and conducted according to the Indian National Science Academy guidelines for the use and care of experimental animals.

Methods of preparation of aceclofenac gel:

1) Gel with carbopol base:

Heat propylene glycol at 65ºC 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°C, add aceclofenac, 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:

Aceclofenac 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)

3) Gel with Sodium CMC base:

Aqueous gel base was prepared by dissolving of sodium CMC in water and with continuous stirring add propylene glycol. Dissolved drug was added. The SLS was charged slowly and with continuous stirring. Take IPA and dissolve menthol in it till the clear solution is obtained add it in above gel. Oil phase was prepared by dissolving, methyl salicylate, linseed oil and ginger oleoresin mix till the clear solution is obtained, oil phase is slowly added in the above aqueous gel while constantly stirring and lastly, methyl paraben was added to the gel. Gel was packed in aluminium collapsible tube. (Table: 01)

Table 01: Preparation of hydrogels

Ingredients (% w/w)	**Gels 100 gm**								
	A1a	**A1b**	**A1c**	**A2a**	**A2b**	**A2c**	**A3a**	**A3b**	**A3c**
Aceclofenac	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
Linseed oil	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**
Ginger oleoresin	**0.5**	**1**	**1.5**	**0.5**	**1**	**1.5**	**0.5**	**1**	**1.5**
Methyl salicylate	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Carbopol 974 P	**1**	**1.25**	1.5	-	-	-	-	-	-
HPMC	**-**	**-**		1	1.5	2	-	-	-
Sodium CMC	**-**	**-**	-	-	-	-	3	4	5
Menthol	**5**	**5**		**5**	**5**	**5**	**5**	**5**	**5**
Triethanolamine	2	2	2	-	-	-	-	-	-
Methyl paraben	**0.1**	**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**	**-**	**-**	**-**
Chremophore Rh 40	**4**	**4**	**4**	**-**	**-**	**-**	**-**	**-**	**-**
Sodium lauryl sulphate	**-**	**-**	**-**	**-**	**-**	**-**	**0.03**	**0.03**	**0.03**
Tween 60	1	1	1	-	-	-	-	-	-
Isopropyl alcohol	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
Propylene glycol	15	15	15	5	5	5	5	5	5
Distilled Water Up to	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

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**
A1a	37.62	65.33	75.58
A1b	31.68	64.66	79.65
A1c	45.14	71.60	81.16
A2a	48.50	74.66	80.04
A2b	28.71	61.33	69.76
A2c	34.65	52.00	61.62
A3a	38.61	61.33	80.81
A3b	14.85	57.33	62.79
A3c	22.77	45.33	61.62
Nusaid gel (M1)	42.57	65.33	76.74

Table 03: Comparative studies of anti inflammatory activity of optimized formulations with marketed preparation

Formulations	1st hour	2nd hour	3rd hour
Nusaid gel (M1)	42.57	65.33	76.74
A1c	45.14	71.60	81.16

In Vivo Efficacy Study:[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:

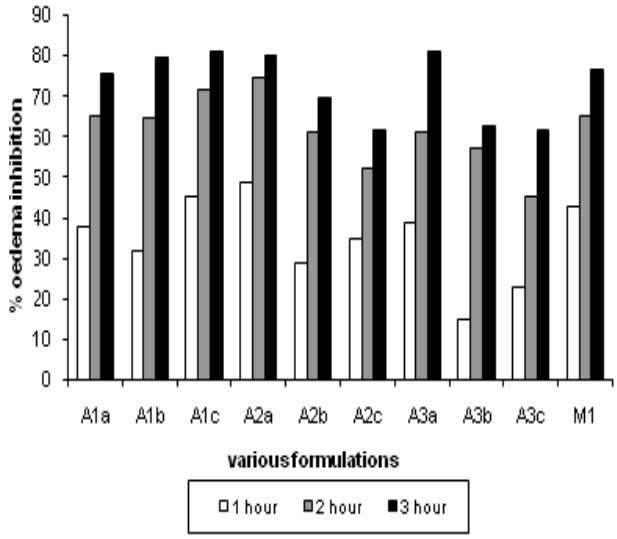
The anti-inflammatory effect was expressed as percent edema inhibition. The formula for the same is as below.

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

RESULT AND DISCUSION:

According to statistical analysis carried out by using student's unpaired't' test the obtained results shows a significant inhibitory effect was observed for each of the formulations tested versus the control (Table-2). After 3rd hour of carrageenan administration, batch A1c (Aceclofenac 1.5% gel) showed maximum anti-inflammatory response [18] (Table: 03). Addition of propylene glycol to these formulations as a permission enhancer responsible for the easy diffusion or fast diffusion[19]. Though the ingredients of all formulations are same, polymer concentration affects the diffusion of drug. Thus A1c shows better release and good anti inflammatory activity as compare to other formulations.

Graph01: Graphical representation of various formulations with marketed preparation



CONCLUSION:

From the above results it can be concluded that the aceclofanac gel formulation A1c containing 3% linseed oil, 1.5% ginger oleoresin and 10% methyl salicylate was suitable for topical application and it shows good results with that of marketed Nusaid gel (M1).

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