



Pre-Clinical Evaluation of Anti-Arthritic, Anti-Inflammatory and Analgesic Activities of The Polyherbal Formulation Freemodex

Dr. Kunal Gupta	Shree Devi College of Pharmacy, Airport Road, Kenjar, Mangalore. Dept. of Pharmacology, Shree Devi College of Pharmacy Airport Road, Kenjar, Mangalore.
Swati M	Shree Devi College of Pharmacy, Airport Road, Kenjar, Mangalore.
Vijayalaxmi	Shree Devi College of Pharmacy, Airport Road, Kenjar, Mangalore.
JV Kamath	Shree Devi College of Pharmacy, Airport Road, Kenjar, Mangalore.

ABSTRACT

The present study was carried out to evaluate the anti-arthritic, anti-inflammatory and analgesic activity of the polyherbal formulation freemodex. Models used in this study were acetic acid induced writhing in mice, formaldehyde induced arthritis in rats and carrageenan induced paw edema in rats. Both doses of freemodex showed significant improvement in the measuring parameters (number of writhings and paw volume) when compared with diseased ones.

KEYWORDS

anti-arthritic, anti-inflammatory, analgesic, freemodex

Introduction

Rheumatoid arthritis is a disorder of joint involving its inflammation and pain. Inflammation is biological response of [vascular](#) tissues to a variety of harmful stimuli, such as damaged cells, or irritants. Pain is an untoward feeling, generally caused by damaging stimulus such as inflammation. About 1% of the world's population suffers from this disease and women three times more than men¹. In India, more than 20% of total population suffers from arthritis². In America, around forty six million people report that they have arthritis or other rheumatics. Different forms of arthritis are osteoarthritis, rheumatoid arthritis etc. Here there is synovial proliferation and articular cartilage destruction. Various mediators of inflammation such as prostaglandins, macrophages, leukotrienes, cytokines gets released by the generated inflammatory cells. These in turn cause pain, damage cartilage and erode bones. Various drugs used in the treatment of arthritis are methotrexate, azathioprine, cyclosporine, leflunomide etc. But these drugs have numerous side effects such as oral ulceration, diarrhea, headache, nausea, hair loss etc³. Hence there's need for exploring other better alternatives, such as herbs for the treatment. Herbal medicines are much safer and so becoming popular due to the toxicity, side effects of allopathic counterparts⁴. Freemodex (Jaffman Pharmaceuticals, Jaffman Marg, Kumta, Karnataka) is a polyherbal formulation which contains Dwipantaravacha, Musta, Mahayogaraj guggul, Guggul purified, Sallaki, Shunti, Lasuna, Ashwagandha, Rasna, Ballataka purified, Kuchala purified, Haridra, Amrita, Shatavari, Shilajit, Amalaki, Haritaki, Vibhitaki, Katukaronini, Sameerapannaga ras Mahavatvidwans ras Ela, Twak, Patra, Maricha, Nirgundi, Neelanirgundi, Gandhaprasarini, Rasna Ashwagandha, Amrit, Musta, Bala, Shigru indravalli, Erand, Lajalu, Shatavari, Arjuna, Haridra. No scientific report is available for its combined anti-arthritic, analgesic, anti-inflammatory potential. Hence, the present study is aimed to investigate the anti-arthritic, analgesic, anti-inflammatory activity of polyherbal formulation freemodex.

Materials and methods

Experimental animals

Wistar rats and Swiss albino mice of either sex was housed in standard conditions at 25±5°C, relative humidity 50±5% in well ventilated animal house under 12 hour day and night cycle. CPCSEA guidelines were followed. Institutional animal ethics committee approved the experiment.

Drug, dosage and group

The dose of standard drug, diclofenac sodium [Pfizer (India) Ltd.] was 10 mg/kg. The dose of freemodex was calculated from human dose by using dose conversion formula⁵. Accordingly low and high doses were found out to be 80 mg/kg and 160 mg/kg. Freemodex solution was prepared using distilled water and was orally administered to animals with the help of a feeding needle. Diclofenac was also administered the same way orally. Rest of the chemicals and reagent used were of analytical/reagent laboratory pure grade. Animals were divided into four groups of six animals each. Group 1 was control group, group 2 was the standard group i.e diclofenac sodium, group 3 was treatment group i.e low dose of freemodex, group 4 was treatment group i.e high dose of freemodex.

Experimental protocol

Acetic acid induced writhing in mice

Drug treatment on mice were done accordingly. First test drugs and vehicle were administered. 30 mins later intraperitoneal injection of acetic acid 0.7% v/v (0.1 ml/10 g) was administered to mice (overnight fasting). For diclofenac sodium it was 15 minutes. Animals were then observed individually for counting the number of writhing made by them in 15 minutes from 5 minutes after acetic acid injection⁶.

Formaldehyde induced arthritis in rats

Basal paw volume of hind paw of rats were measured on day zero using plethysmometer. On day one and day three in the sub-plantar region of left hind paw, 0.1ml 2% v/v formaldehyde in normal saline was injected. Respective drug treat-

ments were started on the same day and were continued for 10 days. Paw volume was measured daily⁷.

Carrageenan induced paw edema in rats

Initial paw volume of rats was noted. Then the animals were given respective treatments. After sixty minutes, 0.1ml of 1% sterile carrageenan in saline was administered into right hind paw. Then after 0, 1, 2, 3 and 4 hours of carrageenan injection, volume displaced by the paw was measured using plethysmometer. Paw volume difference and percentage inhibition of edema were calculated accordingly⁸.

Statistical analysis

Statistical analysis was done using Graph Pad Prism version 4 software (Graph Pad Inc, USA). ANOVA followed by Dunnett's Multiple Comparison test (all columns) was applied. Data was presented as MEAN±SEM. Confidence level was taken as 95%.

Results

Acetic acid induced writhing in mice

Both doses of freemodex showed moderately significant reduction in number of writhings when compared with control. Diclofenac also showed a similar activity profile. See table no.-1.

Formaldehyde induced arthritis in rats

Both doses of freemodex and standard showed moderately significant reduction in paw volume when compared with control at 10 day. See table no.-2.

Carrageenan induced paw edema in rats

Both doses of freemodex and standard showed moderately significant reduction in paw edema when compared with control at 3 hour. Both doses of freemodex and standard showed significant reduction in paw edema when compared with control at 4 hour. See table no.-3.

Discussion

In the present study, arthritis was induced in the experimental animals by formaldehyde. Both doses of freemodex, statistically significantly, reduced the increased paw volume. This reduction may be associated with inhibition of neutrophil infiltration, pannus formation and bone erosion⁹. Pain was introduced in the experimental animals by introducing acetic acid. This initiated a noxious stimuli. Both doses of freemodex, statistically significantly, reduced the pain by releasing endogenous substances. Carrageenan was used to induce inflammation in the experimental animals. Inflammation occurred due to release of histamine, serotonin, bradykinin, protease, lysozymes. Both doses of freemodex, statistically significantly, reduced the inflammation of the paw. This may be due to suppression of the above mentioned various chemical mediators of inflammation³.

Conclusion

From the findings of the present study, it can be concluded that freemodex has anti-arthritis, anti-inflammatory and analgesic activity.

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Tables

Table no.- 1: Acetic acid induced writhing in mice

Treatment	Number of writhing	% Inhibition
Control	65.5±1.34	-
Diclofenac sodium	13.83±0.70**	78.89
Freemodex low	24.41±0.58**	62.74
Freemodex high	20.14±0.32**	69.26

Writhing values are MEAN ± SEM. N=6. * p< 0.05, **p< 0.01, ***P<0.001 when compared with control.

Table no.- 2: Formaldehyde induced arthritis in rats

Paw volume (ml)				
Days	Control	Standard	Freemodex low	Freemodex high
0	0.8±0.03	0.79±0.03	0.79±0.07	0.8±0.05
10	2.5±0.08	1.1±0.06**	1.5±0.08**	1.4±0.02**
% inhibition 10 th day		56	40	44

All values are MEAN ± SEM. N=6. * p< 0.05, **p< 0.01, ***P<0.001 when compared with control.

Table no.- 3: Carrageenan induced paw edema in rats

Paw volume (ml)				
Time (hours)	Control	Standard	Freemodex low	Freemodex high
0	0.5±0.037	0.5±0.03	0.5±0.52	0.5±0.39
1	1.4±0.058	0.6±0.04	0.9±0.48	0.8±0.27
2	2.0±0.16	0.9±0.07	1.4±0.05	1.2±0.86
3	2.5±0.06			
4	2.9±0.06	1.4±0.05*	1.6±0.67*	1.5±0.07*

All values are MEAN ± SEM. N=6. * p< 0.05, **p< 0.01, ***P<0.001 when compared with control.

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