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Formulation and Evaluation of Etoricoxib Herbal Gel for Analgesic Activity

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ABSTRACT

Medicinal plants play an imperative function in the development of potent therapeutic agents. The existing study has been undertaken with the plan to formulate and evaluate the etoricoxib herbal gel containing *Buchanania lanzan* extract for the management and treatment of pain. The etoricoxib herbal gel formulation was intended by using etoricoxib, menthol, linseed oil with different polymers and additives in the composition of gel. Formulated gel was evaluated in terms of various evaluation parameters as physicochemical assessment, pH, viscosity and spreadibility. Further, formulated etoricoxib herbal gel was investigated for analgesic activity by using hot-plate and acetic acid induced writhing methods. The obtained findings conclude that formulated etoricoxib herbal gel is the appropriate option for the treatment of pain and such other indications.

Keywords: Pain, Analgesic, Etoricoxib, *Buchanania lanzan*

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INTRODUCTION

Medicinal herbs as possible source of therapeutics aids has attained a significant role in health system all over the world for both humans not only in the diseased condition but also as potential material for maintaining proper health. Herbal drug is a chief constituent in traditional medicine and a common constituent in ayurvedic, homeopathic, naturopathic and other medicine systems. Herbs are usually considered as safe since they belong to natural sources.[1] Pain can be defined as an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage. It is often described in terms of a penetrating or tissue-destructive process. Furthermore, any pain of moderate or high intensity is accompanied by anxiety and an urge to escape or terminate the feeling. When acute, pain is characteristically associated with behavioral arousal and a stress response consisting of increased blood pressure, heart rate, pupil diameter and plasma cortisol levels. In addition, local muscle contraction (limb flexion, abdominal wall rigidity) is often presented. Pain is a pervasive public health problem, and analgesic drugs play a central role in its treatment. Pain is also a pervasive public health problem, and analgesic drugs play a central role in its treatment.[2] Topical application of gel overcomes the problems to be associates with other dosage forms.Etoricoxib is a synthetic, nonsteroidal anti-inflammatory drug (NSAID) with antipyretic, analgesic and potential antineoplastic properties. Etoricoxib specifically binds to and inhibits the enzyme cyclooxygenase-2 (COX-2), resulting in inhibition of the conversion of arachidonic acid into prostaglandins. *Buchanania lanzan* is an evergreen moderate-sized tree, with straight, cylindrical trunk, upto 10-15 m height. The plant is used as expectorant, aphrodisiac, purgative, blood purifier and wound healer.[3, 4] Determining the biological properties of plants used in traditional medicine is helpful. Hence a study on formulation and evaluation of herbal gel with a potential drug etoricoxib with plant extract was selected as the principle object of current investigation.

MATERIALS AND METHODS

Collection of Etoricoxib and other drug samples

The drugs etoricoxib, menthol and linseed oil were received from Rouzel Pharma, Chandigarh as gift sample.

Collection of plant drug

Leaves of *Buchanania lanzan* were identified and collected from the local area of Sehore district. The specimen was identified at the Department of Pharmacognosy RKDF COP and a herbarium was submitted.

Preparation of aqueous extract of *Buchanania lanzan*

The collected leaves parts were washed with tap water. The leaves were organized in to small pieces and air-dried carefully under shade for 15 days. The shade dried materials were converted into moderately coarse powder. 50g of powdered material of *Buchanania lanzan* was taken in beaker having 2 L capacities and 500 ml of distilled water was added, soaked for 48 h with occasional shaking and stirring. The soaked material of plant was filtered through several layers of muslin cloth one by one for coarse filtration. The filtered extracts were concentrated under reduced pressure. Obtained semi-solid mass was stored in a refrigerator until use.

Formulation of etoricoxib herbal gel

Etoricoxib herbal gel was prepared by cold mechanical method. Required quantity of polymer (HPMC) was weighed and it was sprinkled slowly on surface of purified water for 2 hrs. After which it was continuously stirred by mechanical stirrer, till the polymer soaked in the water. Triethanolamine was added with continuous stirring to neutralize the gel and it maintains the pH of the gel. Then the appropriate quantity of DMSO (Dimethyl sulfoxide) was added to the gel, which behaves as the penetration enhancer, followed by the required quantity of methyl paraben as a preservative. Finally the drug etoricoxib, menthol, linseed oil and aqueous extract of *Buchanania lanzan* were added to the gel with continuous stirring till all the ingredients get dispersed in gel completely. [5] The formula of herbal gel is given in table

Table 1 Composition of Etoricoxib Herbal Gel (EHG)

S.N.	Ingredients	Qty
1	Etoricoxib	1%
2	Menthol	1%
3	Linseed oil	1%
4	Standardized Extract of *Buchanania lanzan*	1%
5	HPMC	2%
6	DMSO	2%
7	Triethanolamine	1.5%
8	Methyl Paraben	0.5%
9	Methanol-Water mixture	Q.S.

Evaluation of formulated etoricoxib herbal gel [6, 7]

Physicochemical parameters

All the formulated herbal gels for inflammation were tested for the physiochemical parameters like appearance, consistency and homogeneity by visual inspection and the findings were calculated and recorded.

Measurement of pH

The pH of developed gel formulations was determined using digital pH meter. 1 gm of gel was dissolved in 100 ml distilled water and kept aside for two hours. The measurement of pH of each formulation was done in triplicate and average values are calculated.

Determination of viscosity

The measurement of viscosity of the prepared gel was done with a Brookfield Viscometer. The viscosity of the gel was obtained by multiplication of the dial reading with factor given in the Brookfield Viscometer catalogues. All the findings were calculated and recorded.

Extrudability

The gel formulations were filled in standard capped collapsible aluminum tubes and sealed by crimping to the end. The weights of the tubes were recorded. The tubes were placed between two glass slides and were clamped. Formulation was placed over the slides and then the cap was removed. The amount of the extruded gel was collected and weighed. The percent of the extruded gel was calculated.

Spreadibility

Spreadibility was measured on the basis on slip and drag characteristics of gels. It was calculated using the following formula**:**

$S = M \times L / T$

Where, S= Spreadibility, M= weight in the pan, L= Length moved by the slide, T= Time (in sec.)

Experimental animals

Albinos Wister rats (100-150g) of either sex and of approximate same age are used in the present studies were procured from listed suppliers of Bhopal M.P. India. The animals were fed with standard pellet diet and water ad libitum. All the animals were housed in polypropylene cages. The animals were kept under alternate cycle of 12 hours of darkness and light. The animals were acclimatized to the laboratory condition for 1 week before starting the experiment. The animals were fasted for at least 12 hours before the onset of each activity. The animals received the drug treatments by oral gavages tube. The experimental protocol was approved by Institutional Animal Ethical Committee.

Animals and treatment protocol

The grouping of animals was done as per the following;

Group I: Control (Received gel base only)

Group II: Standard Drug (Piroxicam gel)

Group III: Formulated etoricoxib herbal gel

Determination of analgesic activity by hot-plate method [8]

Evaluation of analgesic activity of the formulated etoricoxib herbal gel was carried out using hot plate method. All animals were lowered onto the surface of a hot plate (55 ± 0.5°C) enclosed with cylindrical glass and the time for the animal to jump or lick the forelimb was noted as the reaction time. A cutoff period of 30 seconds was observed to avoid damage to the paw. The observations were made before and after administration of respective drugs at 30 min, 60 min, and at the end of 90 min. The reaction time of the test and standard groups were compared with the control.

Determination of analgesic activity by acetic acid induced writhing test [9, 10]

The analgesic activity of the formulated herbal gel was evaluated using acetic acid induced writhing method. Acetic acid is administered intraperitoneally to the experimental animals to create pain sensation. Writhing in animals was produced by i.p. administration of 300 mg/kg acetic acid solution (3%). The control, standard and treated group were topically applied with gel base, standard gel and formulated etoricoxib herbal gel 2% respectively. The writhing movements were observed and counted for every 30 min

after acetic acid administration. The number of writhes of test groups at different dose levels along with standard was compared with the control. The percent inhibition of writhing count of the treated group was calculated from the mean writhing count of the control group. Percentage inhibition was calculated using the following formula:

% inhibition= { (Wc- Wt) × 100 } / Wc

Where, Wc = No. of writhes in control group, Wt = No. of writhes in test group

RESULTS AND DISCUSSION

Formulated etoricoxib herbal gel was found light brown colour with smooth consistency. The pH of formulated herbal gel was found 5.8 and maintained throughout the study. Viscosity and spreadibility were also found 23800 cps and 18.8 g/sec respectively. All the results were shown in table 1.

Table 1 Evaluation Parameters of Formulated Herbal Gel

Colour	Light brown
Consistency	Smooth
pH	5.8
Viscosity (cps)	23800
Spreadibility g/sec	18.8

Hot-plate test

At 90 minutes, the maximum reaction time of 3.88 ± 0.40 for control group, 13.20 ± 0.20 for standard group and 11.20 ± 0.30 for group III (formulated etoricoxib herbal gel) respectively. The results indicated that the gel significantly ($p < 0.001$) reduced pain threshold as compared to control and the activity was constant throughout the entire observation period. The reaction time following the topical administration of different doses of formulated etoricoxib herbal gel and standard drug were shown in fig 1. Hot-plate test is a widely used model for neurologic pain and centrally acting analgesic agents can increase reaction time in hot-plate test through their action at the spinal cord level. The results of hot plate test indicate that the formulated etoricoxib herbal gel possesses the ability to reduce pain and such other conditions.

Acetic acid induced writhing test

Effect of formulated etoricoxib herbal gel in acetic acid induced writhing test was found in rats 28.00 ± 0.42, 12.10 ± 0.35, 18.20 ± 0.40 in 30 minutes for control, standard and treated group respectively. The percent inhibition of standard and treated group was also determined and found 84% and 72% respectively. The findings were shown in fig 2. In acetic acid induced method pain is generated indirectly via endogenous mediators like prostaglandin, which stimulates peripheral nociceptive neurons. Analgesic activity of the test compound is inferred from decrease in the frequency of writhings.

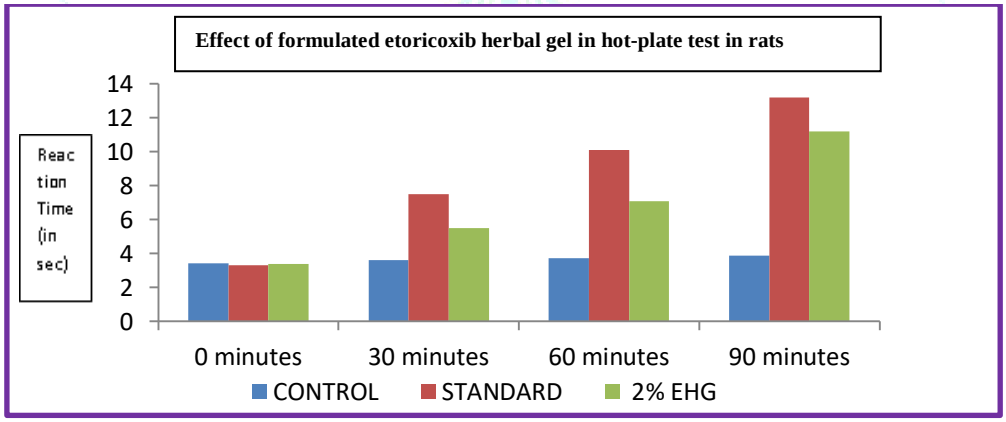

Fig 1 Effect of formulated etoricoxib herbal gel in hot-plate test in rats

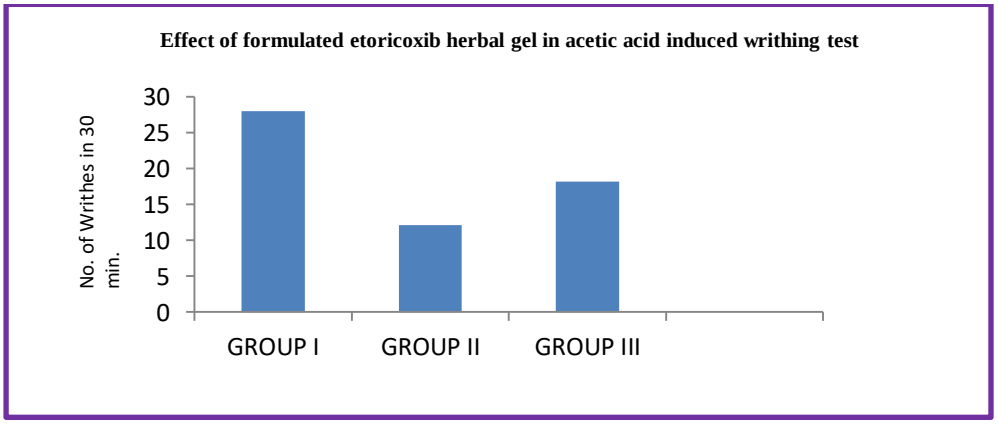

Fig 2 Effect of formulated etoricoxib herbal gel in acetic acid induced writhing test

CONCLUSION

This study demonstrates that formulated etoricoxib herbal gel was found to normalize pain. Thus this formulation should be the potential source for the treatment and management of pain and such other related conditions.

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