WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 9, 1333-1342. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF POLY HERBAL ANTI-INFLAMMATORY GEL

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Article Received on
17 May 2022,

Revised on 07 June 2022,
Accepted on 27 June 2022

DOI: 10.20959/wjpr20229-24765

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ABSTRACT

In ancient days majority of the diseases or illness can be cured by using the herbal- drugs because when compared to the synthetic drugs, herbal drugs show least side effects. Herbal medicines consist of plant or its part to treat illness or ailments and promotes health. In modern days herbal drugs, which are obtained from plant sources are used in various dosage forms to treat various diseased conditions. To avoid the side effects caused by synthetic medicine we have formulated and evaluated poly-herbal anti-inflammatory gel using clove oil. Eucalyptus oil, and turmeric using Carbapol-934 and HPMC polymers as gel base. The combination of Carbapol-934 and HPMC gel-based preparations are proved to be very effective in the treatment of inflammatory diseases with no side effects they showed considerable range of penetration property and stability. They are easily miscible with the skin secretions and shows effective activity. Since the treatment of inflammation is not a multidimensional therapeutic approach to inflammation with the help of herbal medicine and modification in lifestyle.

KEYWORDS: Herbal anti-inflammatory gel, Syzygium aromaticum, Eucalyptus globulus, Homogeneity, Viscosity.

INTRODUCTION

Inflammation

Inflammation is a complex process which is frequently associated with pain and involves occurrences such as; increase the vascular permeability, increase of protein denaturation and membrane alteration.

Classification of inflammation

1. Acute inflammation
2. Chronic inflammation
3. Miscellaneous

Gels

Pharmaceutical gels are defined as semi solid system in which there is interaction between within a liquid vehicle the vehicle is continuous and interacts with the colloidal particles within the three-dimensional structure.

Types of gels

Gels can be classified on basis on colloidal phases nature of solvent used, physiological nature and rheological properties.

1. Based on colloidal phases:

1) Inorganic (Single phase system)
2) Organic (Two phase system)

2. Based on nature of solvent

Hydrogels: They contain water as continuous phase.

Organic gels: They contain nonaqueous solvents as continuous phase.

Xerogels: They are the gels with lowest solvent concentration.

MATERIALS AND METHODS

Oils of Syzygies aromatic, that is a common spice and Eucalyptus globulus are collected from the ayurvedic market for the preparation of anti-inflammatory gel.

Preparation of aqueous extract of turmeric

One gram of turmeric is diluted in 100 ml of distilled water to obtain a clear aqueous solution of turmeric.

Preparation of gel base

Carbopol-934 and HPMC (1, 1.5, 2,% w/w) and purified water were taken in a beaker and allowed to soak for 24 h. To this required amount of drug was dispersed in water and then Carbopol 934p was then neutralized with sufficient quantity of Triethanolamine. Glycerine as

moistening agent, methyl paraben and Propyl paraben as preservatives were added slowly with contineous gently stirring untill the homogenous gel was formed.

Formulation of topical gel

Herbal gel was prepared using gelling agent Carbapol-934 in 1% W/W concentration with deionized water using mechanical stirrer. Then, skin pH (6.8-7) was maintained by dropwise addition of tri-ethanolamine with continuous stirring. various concentrations 1ml, 2ml of both oils are added to the gel bases along with 2 ml of aqueous turmeric extract and stir red for sufficient time for homogenous mixing of extract in gel base. collapsible tubes are used for filling of prepared gel. These formulations were stored at a cool and dry place. Formulation was evaluated.

Organoleptic evaluation

Physical parameters such as color and appearance were recorded.

Viscosity

Viscosity of gel was measured using Brookfield viscometer with spindle number 7.

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. 500 g 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 (>90% extrudability: Excellent, >80% extrudability: Good, and >70% extrudability: Fair)

Spreadability

Spreadability was determined by the apparatus which consists of a wooden block, which was provided by a pulley at one end. By this method, spreadability was measured on the basis of slip and drag characteristics of gels. An excess of gel (about 2 g) under study was placed on the ground slide. The gel was then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with a hook. A 1 kg weight was placed at the top of the two slides for 5 min to expel air and to provide a uniform film of the gel between the slides. Excess of the gel was scrapped off from the edges. The top plate was then subjected to pull of 80 g with the help of string attached to the hook, and the time (in

seconds) required by the top slide to cover a distance of 7.5 cm was noted. A shorter interval indicated better spreadability. Spreadability was calculated using the following formula

$S = M \times L / T$

Where, S = Spreadability

M = Weight in the pan (tied to the upper slide)

L = Length moved by the glass slide

T = Time (in sec.) taken to separate the upper slide from the ground slide.

Measurement of pH

The pH of developed gel formulations was determined using digital pH meter. 1 g of gel was dissolved in 100 ml distilled water and kept aside for 2 h. The measurement of pH of formulation was done in triplicate, and average values are calculated.

Table 1: Composition of various formulations containing clove oil, eucalyptus Oil and Turmeric.

Ingredients	F1	F2	F3	F4	F5
Eucalyptus oil	1.5ml	1.5ml	1.5ml	1.5ml	1.5ml
Clove oil	1ml	1ml	1ml	1ml	1ml
Turmeric aqueous extract	1ml	1ml	1ml	1ml	1ml
Carbapol-934	1	2	-	-	1
HPMC	-	-	1	2	1
Methyl paraben (0.5%)	0.02ml	0.02ml	0.02ml	0.02ml	0.02ml
Propyl paraben (0.2%)	0.01ml	0.01ml	0.01ml	0.01ml	0.01ml
Glycerine (5%)	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml
Triethanolamine	q.s	q.s	q.s	q.s	q.s

Homogeneity

All developed gels were packed in containers and then tested for homogeneity by visual inspection. They were tested for their appearance and presence of any aggregates.

Grittiness

All the formulation were evaluated microscopically for the presence of any appreciable particulate matter which was seen under light microscope. Hence, obviously the gel preparation fulfils the requirement of freedom from particular matter and form grittiness as desired for any topical preparation.

Stability study

ICH guidelines were followed for stability study. The formulated gel was filled in collapsible tubes and stored at different temperatures and humidity conditions, namely 25±2°C/60±5% RH, 30±2°C/65±5% RH, and 40±2°C/75±5% RH for a period of 3 months and studied for appearance, pH, and spreadability.

Skin irritation studies

The intact skin of Wistar rats of either sex with average weight 150– 200 g was used. The hairs were removed from the rat 3 days before the experiment. Prepared gel formulations were used on the test animal and gel base on control group. The animals were treated daily for 7 days, and erythema and edema on the treated skin were examined.

Evaluation of anti-inflammatory activity

Animals

Albino Wistar rats of either sex with average weight 150–200 g was used. All animals used in the study were housed in standard environmental conditions and fed with standard rodent diet with water ad libitum. All animal procedures were followed in three groups, namely control, test, and standard of six animals each. The Institutional Animal Ethical Committee approved protocol of experiment (CPCSEA/1093), and all the animals used in this work were treated according to the norms established by CPCSEA.

Carrageenan-induced rat paw edema

Animals were fasted for 24 h before the experiment with water ad libitum. Edema was induced by injecting 0.1 ml of 1% w/v carrageenan in saline into the plantar side of right hind paw of rat 1 h before each experiment. Herbal gel 0.2 g was applied to the plantar surface of the hind paw by gentle rubbing 50 times with the index finger. Rats of the control groups received the plain gel base. 1% valdecoxib gel 0.2 g was applied in the same way as a standard. Drugs or placebo was applied 1 h before the carrageenan injection. Paw volume was measured immediately after carrageenan injection and at 1, 2, 3, and 4 h intervals after the administration of the noxious agent using a Plethysmometer. Percentage inhibition in paw volume is calculated using the formula.

%Inhibition = [Paw volume (Control) - Paw volume (Test)] *100 + Paw volume (Control).

Statistical analysis

Data were reported as the mean ± standard error of the mean. Data analysis was done by one-way analysis of variance followed by Dunnett's test using GraphPad version 7. Probability values of 0.05 ($p<0.05$) or less were considered statistically significant.

RESULTS

Physical evaluations of ointment formulation

The herbal gel was prepared using Carbopol 934, various concentrations of clove oil, eucalyptus oil, glycerine, methylparaben, propylparaben, distilled water, and triethanolamine. Prepared gels were subjected for appearance, viscosity, spreadability, pH, and homogeneity, and results are shown in Table 2. All gel formulations have pale yellow colour with a translucent appearance and have smooth feel on application which was remain same on stability testing period. All these formulations have shown optimum viscosity. The pH values of all prepared formulations ranged from 6 to 7 which is considered acceptable to avoid the risk of irritation on application to the skin. All formulations when prepared and after 3 months remain homogeneous without any gritty particle. Furthermore, the stability study's results revealed that the preparation was stable under normal storage conditions.

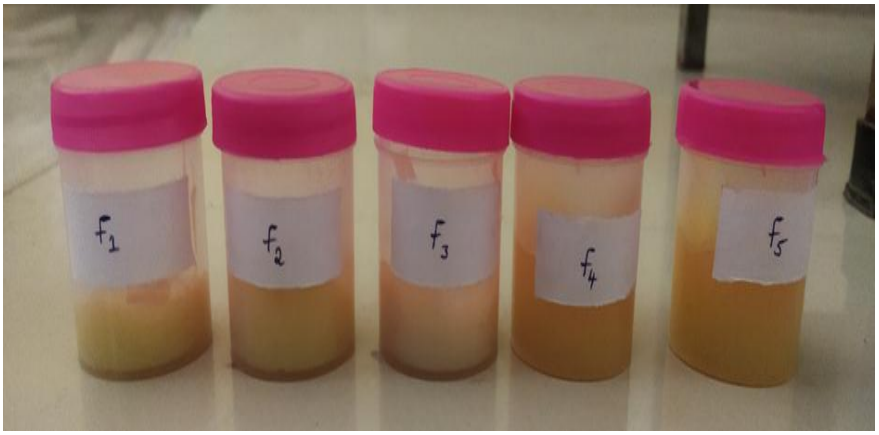

Fig. 1: Gels of five different formulations F1, F2, F3, F4, F5.

Extrusion of the gel

The extrusion of the gel from the tube is an important during its application and in patient acceptance. Gels with high consistency may not extrude from tube, whereas low viscous gels may flow quickly, and hence, suitable consistency is required to extrude the gel from the tube. Extrudability of all gel formulations was found to be good.

Acute skin irritation study

Results of skin irritation test indicate that prepared gels were not produce irritation, redness, or edema on application and free from dermatological reaction.

Table 2: Physical evaluation of various gel formulations.

Formulation	Appearance	Viscosity	spreadability	pH	Homogeneity
F1	Pale yellow	4520	24.36	6.3	Homogenous
F2	Pale yellow	4260	22.35	6.5	Homogenous
F3	Pale yellow	4300	24.83	6.8	Homogenous
F4	Pale yellow	4500	19.32	6.1	Homogenous
F5	Pale yellow	4800	19.14	7	Homogenous

Table 3: Extrudability study of various gel formulations.

Formulation	Weight of formulation	Weight of gel extruded	Extrudability amount	Grade
F1	15.2	13.1	86.18	Good
F2	15.64	12.9	82.48	Good
F3	15.95	13.42	84.13	Good
F4	15.26	13.15	86.17	Good
F5	15.23	12.7	86.38	Good

Investigation of anti-inflammatory activity of various gel formulations

Anti-inflammatory activity of various gel formulations was investigated by carrageenan-induced paw edema method, and results obtained. Edema inhibition in carrageenan-induced rat paw edema by various formulations and standard 1% valdecoxib. Formulations with 5% and 10% extract did not show significant percent inhibition of rat paw edema, whereas formulations containing 15%, 20%, and 25% have shown significant percent inhibition. Formulation F5 significantly inhibited the inflammation to the extent of 56.66%, 61.66% at 3 h and 59.21%, 63.15% 4 h, respectively, while the reference drug reduced the inflammation by 66.66% at 3 h and 76.31% at 4 h. The anti-inflammatory effect of F5 was comparable to that of valdecoxib at respective time point.

DISCUSSION

Five different concentrations of Carbapol and HPMC were used for preparation of topical gel formulation, and they were stable during the period of stability testing. All formulations were subjected for investigations of anti-inflammatory activity using carrageenan-induced rat paw edema. Carrageenan-induced paw edema in rat has known as a sensitive method for studying of non-steroidal anti-inflammatory agents and shows a biphasic event which is attributed to the different mediators. At the first phase means at about 2 h after carrageenan injection,

hyperemia mainly induces because of the release of histamine and serotonin, whereas prostaglandins and bradykinin potentiate the second phase of edema by mobilization of leukocytes. The edema was reached its highest thickness 4 h after the application of the stimulus. Investigation anti-inflammatory efficacy of the topical gel preparations of clove oil and Eucalyptus oil was best demonstrated when concentrations of used were above 2% and F5 formulation shown same results means that concentration range of extracts required for effective use. Phytochemical analysis of clove oil and eucalyptus oil showed the presence of alkaloids, terpenoids. clove oil contains tannins, phenolic compounds, saponins, terpenoids, ascorbic acids, carbohydrates, and many other compounds like Eugenol used in tooth ache. Syzygium aromaticum and Eucalyptus globulus were reported to have anti-inflammatory activity, and rational behind incorporation of Eucalyptus oil is its potent antioxidant effect thus potentiation of anti-inflammatory activity of prepared topical gel.

CONCLUSION

Results shown that gel formulations are good in appearance, homogeneity, extrudability, and spreadability. Formulation F5 with clove oil and eucalyptus oil and turmeric aqueous extract has shown significant anti-inflammatory activity in carrageenan-induced rat paw edema model.

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