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FORMULATION AND EVALUATION OF ANALGESIC ANTI INFLAMMATORY POLYHERBAL GEL

Rutika Nikam*, Mayuri Lad, Sakshi Panari, Rutuja Pandhare, Amruta Pashte and Pratibha Adnaik

Anandi B Pharmacy College, Kalambe tarf Kale, Kolhapur.

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***Corresponding Author**
Rutika Nikam
Anandi B Pharmacy College, Kalambe tarf Kale, Kolhapur.

ABSTRACT

Cucurbita maxima (pumpkin) and Lagenaria siceraria (bottle gourd) have long been used as analgesics and anti-inflammatory herbs. Not only are both seeds eaten as a delicacy in many parts of the world, but they also have several nutritional and medicinal benefits. In this study, the potential analgesic and anti-inflammatory qualities of these seeds are examined. The present study aimed to formulate and evaluate an analgesic anti-inflammatory gel using oils of Cucurbita maxima and Lagenaria sicereria. The gel was prepared using a combination of the two oils, which have been traditionally used to treat pain and inflammation. The extraction of oils took place by Soxhlet extraction process. The physicochemical characteristics of oils were found by standardization tests such as acid value and saponification value. The formulated gel was evaluated for its physicochemical properties, pH, spreadability, viscosity and stability. The results showed that the gel had a pH range of 6 -6.2, suitable for topical application. The study suggests that the formulated gel has potential as a natural, topical analgesic and anti-inflammatory agent, offering an alternative to synthetic drugs.

KEYWORD: Analgesic, anti-inflammatory, Polyherbal gel formulation, Standardization of oil, Soxhlet extraction n hexane.

INTRODUCTION

Discomfort, redness, immobility, oedema, and heat are immunological reactions brought on by damage, irritants, or pathogens. These immune responses are accompanied by inflammation and discomfort. The body uses immunity as a natural defence against viruses

and shocks from the outside world. It requires interactions between different cell types and chemical mediators to restore equilibrium. Adhesion atoms, lipid-derived mediators, peptide facilitators, and enzymes are examples of these mediators, depending on the kind of cell involved and the type of detrimental stimulation. However, if they proliferate out of control, they might damage host tissues and cause disease. Oral medicine prescriptions are routinely written to relieve acute pain. For chronic pain, several antidepressants and anticonvulsants are also used in addition to these drugs. Oral pharmaceutical distribution is effective at relieving pain, but it frequently results in systemic Adverse Drug Reactions (ADRs), which can make it difficult to continue taking the medicine and necessitate stopping it. Herbal treatments are gaining popularity among those with rheumatoid arthritis, persistent pain, inflammation, and other illnesses.[1]

Topical drug delivery systems are dosage forms administered topically to treat skin problems or other illnesses when other techniques of medication administration are not successful. One advantage of the topical drug administration method is its ability to negotiate the first pass metabolism. Additionally, the danger and discomfort related to the IV route hypothesis are reduced. Topical medicines come in a range of viscosities, from liquid to semi-solid to solid. One example of a mixture of formulations that may be utilised to enhance medicine distribution in specific circumstances is Emulgel. Gels consist of a dispersed phase and a dispersed medium in a semisolid system. The dispersed phase's macromolecules or three-dimensional particle network limit or constrain the dispersed media between the particles.[2]

Advantages of Gel

1.Gels can be used for controlled release drug delivery system.
2.It has good adherence property on the application site.
3.Gels are biodegradable and biocompatible in nature.
4.They have better retention time than the other formulations.
5.Gels have long term stability.
6.Gels are easily to wash and non-toxic in nature property.
7.They have good spread ability.
8.They can be used for both polar and non-polar drugs.
9.They have cooling effect on the administration site due to solvent evaporation.

Anaesthetic and anti-inflammatory properties have been used to Cucurbita maxima (pumpkin). The seeds of this plant are used as a delicacy in many parts of the world and have

several nutritional and medicinal benefits. Elevated levels of magnesium in C. maxima seeds block the NMDA receptor, which effectively reduces acute and chronic pain, especially nerve pain. Similar to this, bottle gourds, or Lagenaria siceraria, have long been utilised as analgesics and anti-inflammatory drugs. Long recognised for its therapeutic benefits, the fruit has been utilised as an antipyretic, nutritive agent, diuretic, cardiotonic, and cardioprotective.[3]

Role Of Herbal Ingredients

1. Pumpkin seeds

Fig. 1: Pumpkin seeds.

Synonyms: Cucurbita pepo var. maxima (Duchesne) Delile.

Biological Source: It is the seed oil obtained by Soxhlet extraction of *Cucurbita maxima Duchesne,* belonging to family Cucurbitaceae.

Geographical Source: It is mainly found in northern Argentina near the ands or in certain Andean valleys.

Uses: It is used to reduce risk of chronic diseases, such as cancer. It acts as antioxidant and reduce inflammation.

2. Bottle Gourd Seeds

Fig. 2: Bottle gourd seeds.

Synonym: *Lagenaria Siceraria.*

Biological source: It is cold pressed from the seeds of the fruits of *Lagenaria Sicerari.*

Geographical source: It considered to be native to tropical Africa. It is cultivated in India, Japan, Srilanka, China and Thailand.

Uses: It is used as Emetic, Purgative, Cooling, Sedative, Diuretic.

3. Mentha

Fig. 3: Mentha leaves.

Synonym: Brady Mint.

Botanical Source: It is the oil obtained by the distillation of Mentha piperata, belonging to family Labiatae.

Geographical source: It is mainly found in Europe, United States, and also in damp places of England.

Uses: It is used to treat headache, muscle ache, joint pain and itching. It is also used for treating cough and colds, reducing stress and improving mental functions.

4. Camphor

Fig. 4: Camphor.

Synonym: Gum Camphor, Japan Camphor.

Biological Source: It is solid ketone, obtained from the volatile oil of Cinnamomum Camphora.

Geographical Source: It is mainly found in Sri Lanka, Egypt, South Africa, Sumatra, Brazil.

Uses: It is mainly used in pain relief medication, including topical analgesic. It can also help to reduce chronic muscle and joint pain.

5. Turpentine Oil

Fig. 5: Turpentine oil.

Synonyms: OleumTerbinthae, rectified oil of turpentine.

Biological Source: It is obtained by the distillation of oleoresin from PinusLongifoliaRoxb belonging to family Pinaceae.

Geographical Source: It is cultivated in India, Pakistan, United State, France, Europe and Russia.

Uses: It is used as counterirritant, rubefacient, in swelling and neuralgia. It is mild antiseptic and used chronic bronchitis as expectorant. It is used in the preparation of disinfectants, insecticides, paints, varnishes and pine oil.

6. Eucalyptus oil

Fig. 6: Eucalyptus leaves.

Synonym: Stringy bark tree, Blue gum, Blue gum tree.

Biological Source: It is an essential oil obtained by the distillation of fresh leaves pf Eucalyptus globulus belonging to family Myrtaceae.

Geographical Source: It is found in Australia, Tasmania, United State, Spain, Portugal, Brazil, North and South Africa, India, France and Southern Europe.

Uses: It is used as antiseptic, flavouring agent, deodorant, antimicrobial, and used in treatment of lung diseases, sore throat and vapour bath for asthma.

7. Clove

Fig. 7: Clove.

Synonym: Clove buds, Caryophyllum.

Biological Source: It consist of dried flower bud of Eugenia caryophyllata belonging to Myrtaceae.

Geographical Source: It is indigenous to Amboyna and Molucca islands, also cultivated in Zanzibar, Pemba, Penang, Madagascar, Caribbean islands, Sri Lanka and India.

Uses: It is used as carminative, antiseptic, local anaesthetic. It is also used as flavouring agent.

Fig. 8: Analgesic and anti-inflammatory poly herbal gel.

MATERIAL AND METHOD

1. Extraction of Cucurbita oil

1. The Cucurbita seeds were gathered from the vicinity of APCK.
2. They spent two weeks being sun dried after being cleaned with distilled water.
3. The seeds' outer layer was removed by hand.
4. The dried seeds were ground in a mortar and pestle to create the powder, which was then sieved and kept in a sealed plastic container for later use. n Hexane from a special laboratory.
5. Every chemical utilised was pure to 95–98% and of analytical grade.[4]

2. Extracting Oil

1. The method of Soxhlet extraction was used to obtain Cucurbita oil.
2. 30g of powdered Cucurbita seeds were extracted using a Soxhlet extractor and 250ml of hexane solvent over the course of six hours at 30 to 40O C.
3. Following extraction, it was filtered, and all of the hexane evaporated.[5]

Fig. 9: Extraction of Cucurbita oil.

Fig.10: Cucurbita oil.

2. Bottle gourd oil extraction

Materials

1. The seeds for bottle gourds were gathered from the vicinity of APCK.
2. After two weeks of sun drying, they were cleaned with distilled water.
3. To make the powder, dried seeds were ground in a mortar and pestle, sieved, and then kept in a closed plastic container for later use. Hexane from a special laboratory was acquired.
4. Analytical grade compounds with purity levels between 95% and 98% were all utilised.[6]

Oil Extraction

1. The Soxhlet extraction process was used to obtain bottle gourd oil.
2. 30g of bottle gourd seed powder was extracted using a Soxhlet extractor at 30 to 40 degrees Celsius for six hours using 250ml of hexane solvent.
3. It was filtered after extraction, and all of the hexane was evaporated.[7]

Fig.11: Extraction of Bottle gourd oil.

Fig.12: Bottle gourd oil.

Cucurbita maxima and Lagenaria siceraria oils' physicochemical characteristics are as follows

1. Calculating the acid value

A 100 mL conical flask was filled with weighed 0.5 g of oil samples. Next, 0.5 mL of neutralised ethanol (heated to 60–65 o C) and 1 mL of 1% phenolphthalein were added. The mixture was then titrated with an ethanolic KOH 0.1 M until a pale pink colour was reached.[36] The acid value was utilised to compute the AV (mg KOH/g oil).[36]

The acid value of the sample was calculated using the following equation: M KOH × 56.1 × V KOH (mL).

$$\text{Acid value (mg/g)} = \frac{\text{V KOH (mL)} \times \text{M KOH} \times 56.1}{\text{Mass of the sample (g)}}$$

where, V = volume of KOH, and M (molarity) = concentration of KOH solution.

2. Determination of saponification value

2.5 mL of a 0.5 M ethanolic potassium hydroxide solution and 0.2 g of oil were heated under reflux for 30 minutes in a conical flask. After adding 1 mL of 0.05% phenolphthalein to the saponified liquid, it was titrated with 0.5 M HCl. The end point is achieved when the pink colour turns colourless.[35] The blank solution was also used for the titration. The following formula was used to determine the saponification value.

$$\text{Saponification value (mg KOH/g)} = \frac{\text{V HCl (mL)} \times \text{M KOH} \times 56.1}{\text{Mass of the sample (g)}}$$

where, V is the volume of HCl used for titration, M is concentration in molarity of HCL and calculated by subtracting the total volume needed for titration of the blank solution and the sample (V HCl for blank - sample).[8]

Physicochemical Test Results

Table No. 2: Physicochemical Tests.

Sr. No.	Test	Cucurbita maxima oil	Lagenaria siceraria oil
1	Acid value	1.1 mg KOH/g	3.3 mg KOH/g
2	Saponification value	182.325 mg KOH/g	28.05 mg KOH/g

Gel preparation

Material

1. Plant material

Cucurbita oil, Lagenaria siceraria, camphor, clove oil, eucalyptus oil, and peppermint oil.

2. Chemicals

Carbopol 934, tween 80, triethanolamine, E.D.T.A., and methyl paraben.

Method of preparation of thick gel

Water is taken and Carbopol was added to it. It was dissolved and kept aside for 1 hr to swell. After an hour Methyl paraben was added as a preservative, E.D.T.A was added as chelating agent, and tween 80 was added as cross polymer to it. They were mixed properly to prepare thick gel.

Method of preparation of herbal pain gel

All the herbal ingredients were mixed first and then added to thick gel. They were stirred continuously to form homogenous mixture. Then triethanolamine was added drop wise to the formulation for adjustment of pH (6.8 to 7.2) and finally herbal pain gel was prepared.[9]

Formulations

From the method mentioned above three formulations were prepared F1, F2 and F3 having different quantities of ingredients as tabulated in Table 1.

Table No. 3: Formulation of herbal pain gel three batches (F1, F2 and F3)

Ingredients	Formulation 1	Formulation 2	Formulation 3
Cucurbita oil	2.0%	2.4%	2.2%
Bottle gourd oil	2.5%	2.1%	2.3%
Peppermint oil	6.0%	6.2%	5.5%
Eucalyptus oil	2.5%	2.1%	2.3%
Camphor	3.2%	2.4%	2.4%
Clove oil	0.4%	0.3%	0.4%
Turpentine oil	0.17%	0.27%	0.25%
Tween 80	1.0%	0.5%	0.3%
Methyl paraben	0.15%	0.14%	0.13%
E.D.T.A.	0.05%	0.05%	0.07%
Triethanolamine	0.5%	0.4%	0.6%
Water	Q.S.	Q.S.	Q.S.

Evaluation tests for Polyherbal gel

1. Physical Appearance

The colour, homogeneity, consistency, and phase separation of the produced polyherbal gel are examined visually.

2. pH Evaluation

This is a crucial factor, particularly when it comes to topical formulation. To replicate the skin's state, the produced gel's pH should be between 6.62 and 7.08. The patient may become irritated if the produced gel has an acidic or basic pH. Using a digital pH metre, the produced gel's pH was determined by dipping a glass electrode into the gel. Each formulation's pH was measured three times, and the average results were determined.[10]

3. Spreadability

The diameter of the gel circle that forms when gel is sandwiched between two glass plates of a certain weight is used to quantify the spreadability of the gel. One glass plate is filled with a weighted quantity of gel (350 mg), and another glass plate is dropped from a distance of 5 cm. Next, the spread gel circle's diameter is measured. It is computed using the formula.[11]

$S = M.L/T$

Where, S - spreadability

M - weight tied to upper slide L - length of glass slide

T - time taken to separate the slide completely.

4. Stability studies

For the most suitable formulation, a stability study was conducted. For a duration of one month, they were kept at room temperature while enclosed in the collapsible tubes. Following the previously described protocol, the samples were examined at the end of the month to determine their physical characteristics, spreadability, pH, drug content, drug release, and analgesic activity.

5. Washability

After applying formulations to the skin, the degree and ease of washing with water were physically assessed. Because none of the formulas were oily, they were all very washable and did not leave any residue on the skin when water was used to wash them.[12]

6. Viscosity

Using a Brookfield viscometer set at 25 C and rotating at 12 rpm on its spindle, the viscometer's viscosity was determined for the gel.

RESULT AND DISCUSSION

The herbal gel had a pleasing scent and a white hue. When applied on site, it also provided a smooth feel that lasted after a tested stability study. Following the stability research, the pH of all three formulations was found to be maintained, ranging from 6.8 to 7.2. The three formulations' viscosities. There was little change from the original formulation in the spread ability test conducted following the stability investigation. The herbal gel was discovered to be non-irritating.

Table No. 4: Analgesic Anti-inflammatory Gel Results.

Sr. No.	Test	Result
1	Colour	White
2	Homogeneity	Homogenous
3	Consistency	Good
4	Odour	Pleasant
5	pH	6.2
6	Spreadability	Excellent
7	Viscosity	High

CONCLUSION

Comparing the herbal pain gel to the other synthetic semisolids, it is better. Herbal gels have several advantages over synthetic gels, including greater bioadhesion, less irritation, increased viscosity, longer residence duration, and several other characteristics. Following a

thorough examination of every formulation, it was determined that formulation F2 outperformed formulations F1 and F3. Despite this, none of the three formulations caused irritation or shown any harmful side effects. Ultimately, it was discovered that the F2 formulation had more stability than the F1 and F3 formulations.

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