Formulation and Evaluation of Polyherbal Gel

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***Abstract*: Polyherbal gels, topical formulations incorporating multiple herbs, offer a promising approach to achieving diverse therapeutic effects, particularly for pain relief. Herbal remedies are increasingly favored due to the perception of greater safety and fewer side effects compared to synthetic drugs, increasing market demand for natural formulations. Medicinal plants play a crucial role in developing treatments for pain and inflammation; however, conventional analgesic drugs often present undesirable side effects. This necessitates the search for novel analgesics with reduced or absent adverse reactions. This study focused on formulating and evaluating a polyherbal analgesic gel. The analgesic gel was prepared using ethanolic extracts of Vitex negundo leaves, Azadirachta indica leaves and Aloe vera gel. The formulation included excipients such as carbopol 934, propylene glycol, peppermint oil, triethanolamine, propyl paraben, methyl paraben, and distilled water. Formulations were created with varying extract concentrations. The resulting gel was evaluated for color, odor, appearance, feel, pH, spreadability, washability, and skin irritancy. The prepared gel met the desired criteria for a topical formulation. The study concludes that this herbal analgesic gel formulation demonstrates significant potential, exhibiting satisfactory topical formulation characteristics, ease of use, and minimal skin irritation.**

***Keywords*: Polyherbal gels, Herbal remedies, Medicinal plants, polyherbal analgesic gel.**

1. Introduction

A. Herbal Medicine

Herbal medicine, also referred to as Herbalism, Phytomedicine, or Phytotherapy, stands as a cornerstone of complementary and alternative medicine, focusing on the botanical study and application of medicinal plants. This field includes more than just biologically active natural herbs; it incorporates herbal materials, preparations, and finished products containing plant-derived active ingredients, along with fungal and bee products, minerals like kaolin and bentonite, ash, shells, insects, and animal parts. These diverse natural resources are employed to maintain health and manage various diseases through herbal medicines. Herbal remedies often utilize whole plants or unpurified extracts, and are increasingly subjected to modern effectiveness testing standards. The appeal of herbal medicine lies in its perceived low toxicity, effectiveness in addressing certain challenging diseases, accessibility, ease of preparation, and safe usage. The therapeutic benefits are attributed to complex chemical compounds within the plants, which contribute to both pharmacological activities and prophylactic effects for health maintenance. The specific dosage form of herbal medicine is determined by factors such as the disease being treated, the method of administration, the patient's cultural background, and their personal beliefs. Common preparations include infusions, decoctions, poultices, and powders derived from fresh or dried herbs.

Commercially available dosage forms range from pills, capsules, and tablets to powders, granules, creams, ointments, syrups, elixirs, and tinctures. Herbalists often favour liquid extracts for their freshness, potency, superior absorption, and ease of formulation. Many finished herbal products are based on traditional recipes and incorporate multiple herbs, where the combined components synergistically enhance biological activities, such as the absorption, distribution, metabolism, and elimination of bioactive compounds, ultimately leading to improved health outcomes. Consequently, the quality of herbal products depends on the safety and efficacy of the herbal material, taking into account its chemical composition, potential contaminants and adulterants, and production processes, all of which must be properly controlled through standardization and regulation. Driven by public preference, perceived fewer side effects, easy accessibility, affirmed efficiency, and economic considerations, the demand for herbal medicines is experiencing significant growth in the global market.[1]

B. Analgesics

Algesia (Pain) is an unpleasant sensation, a form of suffering, triggered by harmful stimuli, whether originating externally or within the body.

Analgesics: These are medications specifically designed to alleviate pain without significantly affecting a consciousness. They achieve this by acting on the central nervous system (CNS) or peripheral pain pathways.

Pain serves as a crucial warning signal, primarily protective. However, it can cause considerable discomfort and suffering, sometimes becoming unbearable and debilitating. It's often the primary reason individuals seek medical attention. Intense pain can manifest in numerous ways, including feelings of faintness, anxiety, sweating, nausea, palpitations, blood pressure fluctuations and rapid breathing. Analgesics work by masking pain as a symptom, rather than addressing its underlying cause. They are valuable when the source of pain cannot be eliminated

or as supplementary treatments alongside approaches that target the root cause.[2]

Cyclooxygenase (COX), Also known as prostaglandin-endoperoxide synthase (PTGS), COX is an enzyme instrumental in the production of prostanoids, such as thromboxane and prostaglandins (including prostacyclin), from arachidonic acid. This enzyme, belonging to the heme peroxidase family, catalyzes the conversion of arachidonic acid to prostaglandin H2 via prostaglandin G2. Inhibiting COX through pharmaceutical means can alleviate inflammation and pain.[3]

Pain significantly impacts an individual's life, making pain management and prevention vital in healthcare. Systemic analgesic drugs can cause side effects, such as ulcers and liver damage. Topical applications can minimize these adverse effects. Considering that many topical analgesic forms are greasy and herbal remedies are generally safer than allopathic drugs, this study focuses on developing and evaluating a non-greasy herbal analgesic gel.[4]

C. GEL

Gels are semisolid systems characterized by the dispersion of small or large molecules within a liquid medium. This liquid is rendered jelly-like through the action of a gelling agent, also known as a gelator. Common gelling agents include proteins, starches, gelatin, cellulose derivatives (like carboxymethyl cellulose), and even certain low molecular weight molecules.

Definition: Gels are defined as semi-rigid systems where the movement of the dispersing medium is restricted by a three-dimensional network. This network is formed by either interlacing particles or solvated macromolecules of the dispersed phase.

Gels are sometimes classified as colloidal dispersions due to the presence of particles in the size range of 1 nm to 0.5 µm. Structurally, gels feature a liquid phase constrained within a polymeric matrix. This matrix exhibits a high degree of chemical or physical cross-linking, and twisted, matted strands are often bound together by strong van der Waals forces, creating crystalline or amorphous regions throughout the system. Examples include gels made with tragacanth or carboxymethylcellulose (CMC).

The rigidity of a gel originates from the network created by the interlinking of particles, facilitated by the gelling agent. The nature of these particles and the forces responsible for the linkages dictate the network's structure and the gel's properties. During gel formation, swelling occurs as the solvent penetrates, causing the polymer network to stretch and hold its shape, effectively entrapping any incorporated drug particles. Viscosity is crucial in the gel formation process.[5]

D. Classification of Gels

Gels are primarily classified into two categories based on their colloidal phases:

- Single-Phase Systems (Organic)
- Two-Phase Systems (Inorganic)

1) Single-Phase Systems (Organic)

These gels consist of organic macromolecules that are uniformly distributed through- out the liquid. Consequently, no distinct boundaries are visible between the dispersed macromolecules and the liquid medium. Examples include gels made with carbomers or tragacanth as gelling agents.

2) Two-Phase Systems (Inorganic)

In these systems, the particle size of the dispersed phase is relatively large, and these particles form a three-dimensional structure throughout the gel. The system comprises floccules of small particles rather than larger molecules. These gels are not always stable and are often thixotropic, meaning they exist as a semisolid when standing but become liquid upon agitation. Examples include aluminum hydroxide gel and bentonite magma.

E. Characteristics

i. Swelling
ii. Swelling is taking up of a liquid by a gel with in the volume. Only liquids that solvate a gel can cause swelling. Gels can swell, absorbing liquid with an increase in volume. This can be looked on as the initial phase of dissolution.
iii. Syneresis:
iv. Many gel systems undergo contraction upon the interstitial liquid is expressed, collecting at the surface of the gel. This process, referred to as syneresis.
v. Ageing:
vi. Colloidal systems usually exhibit slow spontaneous aggregation. This process is referred to as ageing. In gels, gelling agent, ageing results in the gradual formation of a dense network.
vii. Thisotropy:
viii. Thisotropy is a reversible gel-sol formation with no change in volume or temperature, a type of non-Newtonian flow.

F. Ideal Properties of Gel Formulation

i. Ideally, the gelling agent must be inert, safe and cannot react with other formulation constituents.
ii. The gelling agent should produce a sensible solid-like nature at the time of storage which is easily broken when exposed to shear forces produced squeezing the tube, trembling the bottle or at the time of topical application.
iii. It should have suitable anti-microbial agent.
iv. The topical gel must not be sticky.
v. The Ophthalmic gel must be sterile.
vi. The viscosity or gel strength increases with an increase in the effective crosslink density of the gel.
vii. Each component is continuous throughout the system.
viii. The gels remain equally uniform upon standing and doesn't freely settle.[6]

G. Advantages

1. *Synergistic effects*: Combining multiple herbs can enhance their individual benefits and create

synergistic effects.

2. *Multi-targeted approach*: Polyherbal gels can target multiple skin concerns or conditions simultaneously.
3. *Natural and holistic*: Herbal ingredients can provide a natural and holistic approach to skin care.
4. *Potential for improved efficacy*: Combining herbs with complementary mechanisms of action may improve overall efficacy.
5. *Customization*: Polyherbal gels can be formulated to address specific skin types or concerns.

H. Disadvantages

1. *Complexity*: Polyherbal gels can be complex formulations, making it challenging to predict interactions between ingredients.
2. *Potential interactions*: Herbs can interact with each other, pharmaceuticals, or other products, leading to adverse effects.
3. *Standardization*: Ensuring consistent quality and potency of herbal ingredients can be difficult.
4. Allergic reactions: Some individuals may be allergic to one or more herbs in the formulation.
5. *Regulatory challenges*: Polyherbal gels may face regulatory challenges due to the complexity of herbal ingredients and potential interactions.
6. *Stability and shelf-life*: Polyherbal gels may have stability and shelf-life concerns due to the natural ingredients.[7][8]

2. Aim and Objectives

A. Aim

To Formulate and Evaluate a safe effective and stable polyherbal gel by using Vitex negundo, Neem and aloe vera extract which gives analgesics effect**.**

B. Objectives

- The main objective is to formulate and evaluate Polyherbal gel with analgesic activity.
- To develop a safe and effective topical formulation for pain relief and anti-inflammation.
- To optimize the formulation for desired properties like spreadability and extrudability, and ensuring the gel's stability and efficacy through various evaluation tests.
- To assess the physical properties of the gel such as pH, viscosity, and spreadability.
- To evaluate the stability of the gel formulation under various conditions, such as temperature and humidity.

C. Herbs Prfile

1) Nirgudi (Vitex Negunda) [9]

Family:- Lamiaceae

Synonym:- Agnus-castus negundo (L.) Carriere

Biological Source:- Vitex negundo, commonly known as the five-leaved chaste tree or Lagundi, is the plant itself. All parts of the plant, including the roots, bark, leaves, flowers, and fruits are utilized for medicinal purposes. It is a shrub or small tree belongs to the family Lamiaceae.

Fig. 1. Vitex negunda

Chemical Constituents:

1. Flavonoid (Luteolin and Casticin)

Structure:-

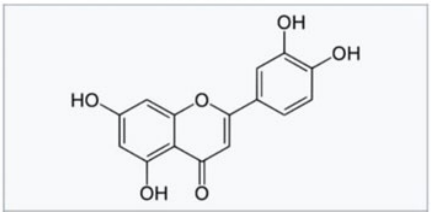

Fig. 2. Luteolin Structure

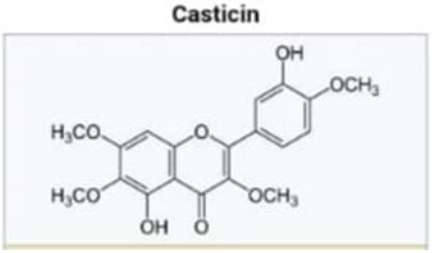

Fig. 3. Casticin Structure

Table 1
Herbs profile

Sr.No	Botanical Name	Family	Part Used	Chemical Constituents	Activity
1)	Vitex Negunda (Nirgudi)	*Lamiaceae*	Leaves	Flavonoid (Luteolin and Castin)	Analgesics
2)	Azadirachta Indica (Neem)	*Meliaceae*	Leaves	Triterpenoid (Nimbin, Nimbolides), Amino acids	Anti - Inflametry
3)	Aloe barbadensis Miller (Aloe vera)	*Asphodelaceae (Liliaceoe)*	Aloe vera Leaves	Anthraquinones (Aloin, Emodin)	Analgesics Anti - Inflametry

Part Used: Leaves

Activity: Analgesic

2) Neem (Azadirachta Indica) [10]

Family:- Meliaceae

Synonym:-Margosa, nim tree or Indian lilac

Biological Source:- Neem consists of the fresh or dried leaves and seed oil of Azadirachta Indica belong to family Meliaceae.

Chemical Constitutes:

1. Triterpenoid (Nimbin and Nimbolide)
2. Amino acids

Fig. 4. Azadirachta indica

Structure:

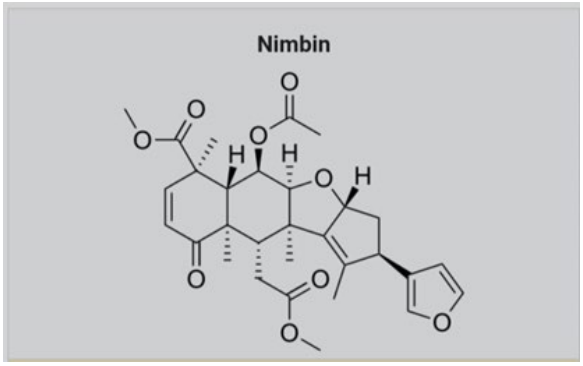

Fig. 5. Nimbin Structure

Part Used: -Leaves

Activity: Anti-Inflammatory

3) Aloe Vera (Aloe barbadensis Miller)[11]

Fig. 6. Aloe barbadensis miller

Biological Source:-Aloe is obtained from the dried juice of the leaves of aloe barbadensis Miller

Chemical Constituents:

1. Anthraquinones (Aloin and Emodin)

Structure:-

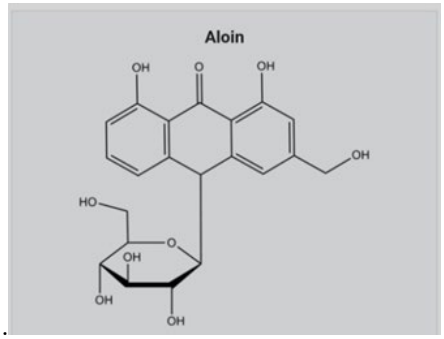

Fig. 7. Aloin Structure

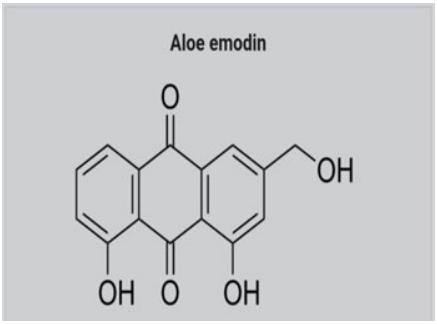

Fig. 8. Aloe emodin Structure

Part Used: Aloe vera whole plant

Activity: Anti-Inflammatry

D. Excipient Profile

Table 2
Excipient profile

Sr.no	Excipients	Use
1.	Carbopol 934	Gelling Agent
2.	Alcohol	Solvent
3.	Methyl paraben	Preservative
4.	Propyl paraben	Preservative
5.	Propylene glycol	Humectants and thickener
6.	Peppermint Oil	Fragrance and cooling agent
7.	Triethanolamine	pH adjuster
8.	Distilled Water	Solvent

3. Materials and Methods

A. Materials

The Raw material used for preparation of polyherbal formulation were Extract of leaves of Vitex Negunda, Azadirachta Indica , Aloe barbadensis miller , Carbopol 934,Alcohol , Methyl Paraben , Propyl Paraben , Propylene glycol ,Peppermint Oil, Distill Water.

B. Collection and Authentication of Crude drug

The required plant leaves of crude drug were collected from the local garden. The plant material were authenticated by Dr. S.P. Giri and verified by Dr.A.S. Wabale , Research Guide,

Vice Principle & Head Department of Botany and Research center PVP college , Loni [Ref.No. /PVPC/Bot/2024-25/359(1)]

C. *Preparation of Extract of Crude Drugs*

Ethanolic extracts of Vitex *negundo* and *Azadirachta Indica* were prepared through maceration. Specifically, 10 grams of dried plant materials were coarsely powdered and then subjected to ethanol extracted using the maceration technique. These resulting extracts were subsequently used in the preparation of a polyherbal gel, employing Carbopol 934 as the gelling agent. [12][13]

Aloe vera component, leaves were obtained from a local nursery, washed and had their rinds removed. The inner gel was then scraped out, cut into pieces, solar-dried at 30-40°C for two-three hours, and the resulting semisolid gel was collected. [14]

Fig. 9. Extraction of crude drug vitex nigunda and Neem

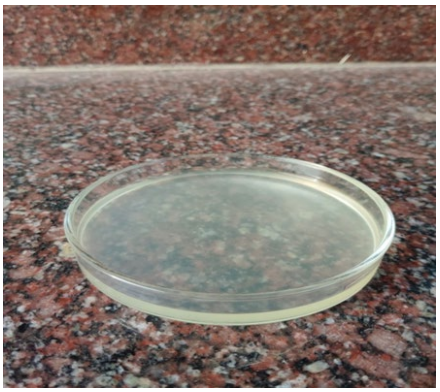

Fig. 10. Extraction of crude drug aloe vera

D. *Formula*

Table 2
Formulation table

Sr.no	Ingredient	Quantity
1.	Extract of Vitex negundo	1 ml
2.	Extract of Azadirachata Indica	1ml
3.	Extract of Aloe barbadensis Miller	1ml
4.	Carbopol 934	0.50 gm
5.	Alcohol	1ml
6.	Methyl paraben	0.1gm
7.	Propyl paraben	0.01gm
8.	Propylene glycol	2ml
9.	Papermint Oil	1ml
10.	Triethanolamine	Qs
11.	Distilled Water	50ml

E. *Method of Formulation of Polyherbal Gel*

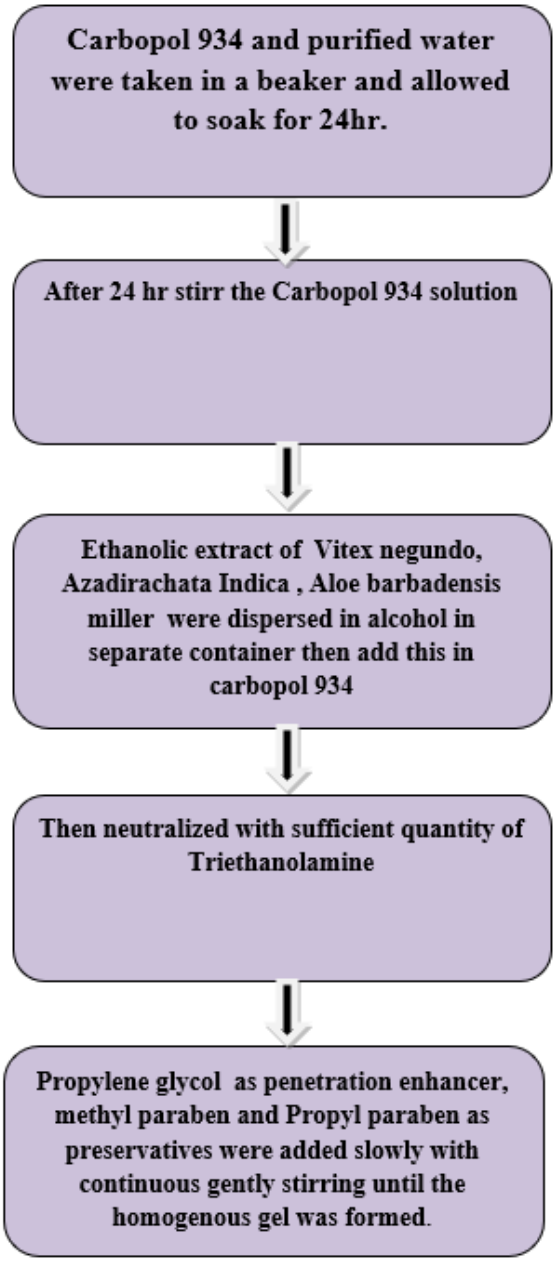

Fig. 11. E. Method of Formulation of Polyherbal Gel

4. Evaluation of Polyherbal Gel

A. *Physical Examination*

1) *Homogeneity and Appearance*

All formulated gels were packed in containers and then tested for homogeneity by visual inspection. They were tested for their appearance and presence of any aggregates.[15][16]

2) Color, Odour, Appearance and Feel

The formulated gels were inspected visually for color, presence of any clog and to evaluate the feel the formulated gel were applied on skin and feel was experienced psychorheologically.[17]

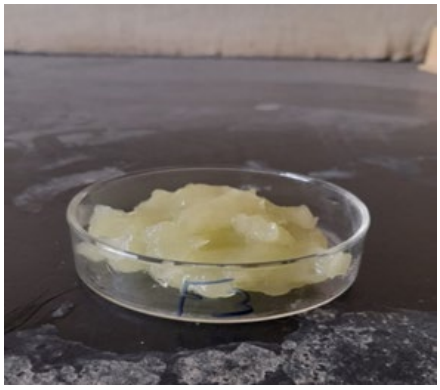

Fig. 12. formulated gel

Table 13

Colour	Yellowish green
Odour	Characteristics
Appearance	Smooth
Homogeneity	Homogeneous

B. Determination of pH (Normal range 5-7)

The pH was determined by using pH strip. The strip was deep into the gel and the obtained colour was compared with the chart provided with strip. [18]

Fig. 13. pH Measure

Table 14

pH range	5-6

C. Viscosity Measurement (Normal Rang 2000-4000 cps)

The viscosity of individual and polyherbal gels was measured by Brookfield viscometer (Model RVTDV II) at 100 rpm using spindle no 6 [19]

Table 15

Viscosity	3800 cps

*D. Spreadability (Normal Range 18.14-33.91 g*cm/sec)*

When gel applied or rubbed on the skin surface, it should have a sufficient spreading coefficient. Spread ability was evaluated by placing 1 gm of gel on a glass slide. Another glass slide of the same length was placed above that and mass of 50 gm was put on the glass slide so that the gel gets sandwiched between the two glass slides and spread certain distance. The time taken for separating two slides from each other was noted. It was determined by following formula: [20]

$S = M \times L \div T$

where,

S = Spreadability , M = Weight put on the upper slide

L = Length of glass slide

T = Time taken for separation of two slide

Calculation **:-**

M (Weight put on the upper slide)= 50 gm

L (Length of glass slide) = 15 cm

T (Time taken for separation of two slide)= 31 sec

$S = M \times L \div T$

$: 50 \times 15 \div 31$

$S = 24.19$

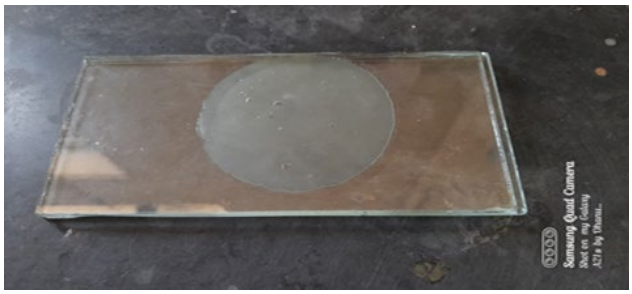

Fig. 14. Skin surface

Table 16

Spreadability	24.19 g×cm/sec

E. Washability

The product was applied on hand and observed under running water.[4]

Fig. 15. After application of the gel

Fig. 16. After washing the gel

Table 17

Washability	Excellent

The given polyherbal gel formulation was found to be having excellent washability.

F. Skin Irritancy

Test gel was applied on left hand dorsal side surface of 1sq.cm and observed in equal intervals up to 24 hours for irritancy, redness and oedema. [4]

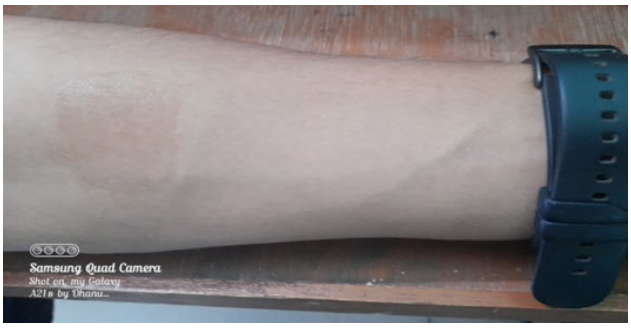

Fig. 17. The gel showed no signs of irritation when applied on the skin

G. Swelling and Syneresis

All the formulations were tested for swelling and syneresis. 5 gm of sample was from each of formulation was taken in cylinder and volume was made up to 100 ml using water, the samples were observed up to the one month. Neither swelling no syneresis was observed in any of the formulation. [17]

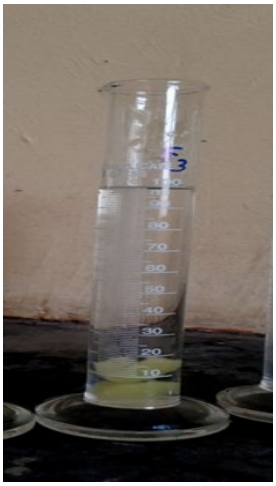

Fig. 18. Formulation Gel

5. Result and Discussion

Gels, recognized for their semi-solid nature in drug delivery, are highly regarded pharmaceutical dosage forms. The demand for herbal gels is increasing due to their perceived safety and efficacy. Research indicates that Vitex negundo leaves have analgesic properties, Azadirachta indica leaves possess anti-inflammatory effects, and Aloe vera gel exhibits both analgesic and anti-inflammatory capabilities. Consequently, this study aimed to create an herbal analgesic gel incorporating an ethanolic extract of Vitex negundo leaves, an ethanolic extract of Azadirachta indica leaves, and Aloe vera gel. Carbopol was employed as the gelling agent, with peppermint oil added for its cooling effect and fragrance. A 50g gel formulation was developed, containing 1ml of each drug extract, 1ml of peppermint oil, and 1g of Carbopol 934, prepared using an appropriate method.

The resulting herbal gel was evaluated for various parameters and found to be yellowish-green in color, homogeneous, smooth, easily spreadable with a pH close to that of normal skin. A 24-hour skin irritation study showed no adverse reactions. Microscopic examination revealed no particulate matter within the gel. In conclusion, the prepared gel meets all the necessary criteria for a topical formulation.

Table 18
Result for evaluation parameter

Sr no	Evaluation Parameter	Results
1.	Colour	Yellowish green
2.	Odour	Characteristics
3.	Appearance	Smooth
4.	Homogeneity	Homogeneous
5.	Determination of pH	5-6
6.	Viscosity Measurement	3800 cps
7.	Spreadability	24.19g×cm/sec
8.	Washability	Excellent
9.	Skin Irritancy	No Irritation
10.	Swelling and Syneresis	Neither swelling no syneresis

6. Conclusion

To develop an analgesic treatment, a gel was formulated using *Vitex negundo, Azadirachta indica* and *Aloe vera*. Carbopol 934 was used to prepare the gel formulation, which exhibited no skin irritation. The resulting herbal gel was then assessed for various characteristics, including pH, viscosity, spreadability, washability, and skin irritation. A Brookfield viscometer was employed to analyse the rheological properties of the gel formulations, revealing a consistent viscosity that was neither excessively thick nor thin. Formulation F3 demonstrated the most favourable properties across all evaluations. Therefore, based on these parameters, formulation F3 was identified as the most promising. This study concludes that the herbal analgesic gel presents a valuable composition, displaying all the necessary attributes for a topical formulation, including ease of use and absence of skin irritation. Furthermore, being an herbal gel, it potentially reduces the likelihood of adverse effects. Future research should focus on in-depth phytochemical analysis and analgesic activity evaluation to prepare the product for potential human use.

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