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FORMULATION AND EVALUATION OF DENTAL PAIN RELIEF GEL USING CLOVE OIL

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ABSTRACT :

The main aim of this study is the formulation and evaluation of pain relief dental gel for the pain occurring in the tooth cavity. Pain in the tooth cavity is one of the major public health problems globally and occurs in all population groups, genders and socio-economic levels. The active pharmaceutical ingredient of this dental gel is clove oil. Clove oil has the pain relief property and is extracted from the clove bud, and it is evaluated by physical parameters like specific gravity, acid value, ester value, saponification value. Many of the ingredients are used to prepare dental gel such as carbopol 940, polyethylene glycol, propylparaben, glycerin, honey, etc. The prepared gel was evaluated for various properties such as pH, antimicrobial activity, spreadability, etc.

Keywords : Clove oil, Dental gel, Antimicrobial activity, Carbopol 940.

INTRODUCTION :

The investigation of natural therapies, including clove oil, has resulted from the search for affordable and efficient dental pain relief alternatives. Long prized for its analgesic and antibacterial qualities, clove oil is extracted from the clove plant (Syzygium aromaticum)[1]. Clove oil has been a popular addition in dental pain treatment gel formulations as a result of this. Potential benefits of such formulations over synthetic counterparts include perceived safety, availability, and price. However, aspects including formulation stability, efficacy, safety, and patient acceptance must be carefully considered throughout the creation and assessment of these gels. In this work, we examine the development and assessment of clove oil-infused dental pain relief gels, considering their potential as a practical dental treatment alternative[2]. Dental gels are essential to oral wellness

because they provide focused treatment for a variety of dental issues, such as sensitivity, discomfort, and inflammation. These gels are topical preparations intended to deliver targeted therapy directly to oral cavity affected areas[3]. Their adaptability makes it possible to include different active components, successfully addressing particular dental issues. Dental gel formulation calls for a careful balancing act between chemicals to guarantee the best possible stability, effectiveness, and patient comfort[4]. In order to obtain the correct viscosity, texture, and flavor, key considerations include the selection of appropriate gelling agents and additions as well as the choice of active substances, such as analgesics, antimicrobials, or desensitizing agents[5]. A thorough examination of the physical, chemical, and biological characteristics of dental gels is included in the evaluation process. Studies on the stability of the formulation, rheological behavior, active component release kinetics, antibacterial activity, and possible side effects on oral tissues are all included in this. In this regard, the creation and assessment of dental gels constitute an active area of study and research with the goal of offering practical, patient-friendly answers to a range of oral health issues[6].

MERITS :

- Targeted Relief: Dental gels provide targeted relief for certain dental diseases like pain, inflammation, and sensitivity by delivering active ingredients directly to the affected areas within the mouth cavity[7].
- Convenience: Dental gels need no effort to administer and are simple to apply. They are portable and ideal for usage when traveling because they come in handy packaging like tubes or syringes[8].
- Versatility: To address a range of dental issues, dental gels can be prepared with different active components. There are formulations available to suit different oral health demands, such as pain treatment, desensitization, antibacterial action, and gum care[9].
- Quick Action: Upon application, many dental gels provide patients with fast-acting treatment by promptly reducing symptoms like toothache or gum irritation and bringing them comfort[10].
- Diminished Systemic Side Effects: Dental gels have a lower chance of systemic side effects than systemic drugs like oral analgesics since they mostly work locally in the oral cavity, lowering the possibility of negative reactions in other body parts[11].
- Increased Patient Compliance: Patients are more likely to follow instructions when a product is convenient and works well, which is why dental gels' targeted action and convenience of use frequently lead to increased patient compliance with treatment regimens[12].
- Enhanced Comfort: Dental gels may include calming substances that give patients who are uncomfortable in their mouths even more comfort, encouraging a feeling of relief and wellness[13].
- Adjunct to Professional Treatment: Dental gels can improve overall treatment outcomes and patient satisfaction by acting as a symptomatic relief while patients wait for or undergo more extensive procedures[14].

Together, these benefits provide dental gels their widespread acceptance and efficacy as an essential part of oral hygiene treatments.

DEMERITS :

- Limited Duration of Action: Dental gels usually only last a short while and may need to be applied again and again, particularly for gum irritation and toothaches. This can reduce their convenience and effectiveness over time[15].
- Possible Taste and Texture Problems: Patients may find certain dental gels unpleasant to the taste or have a grainy texture, which may make them less likely to follow usage guidelines[16].
- Danger of Ingestion: Because they are applied directly in the oral cavity, there is a chance that they could be accidentally swallowed. This is especially true for small children or people who have trouble swallowing. This could result in poisoning or unwanted adverse effects[17].
- Allergy Reactions: Preservatives, flavorings, and active agents are some of the chemicals in dental gels that may cause allergic reactions or sensitivities in people who are vulnerable, leading to discomfort in the mouth or other negative effects[18].
- Limited Effectiveness for Some disorders: Dental gels can relieve the symptoms of a number of common dental problems, but they might not work for more serious or persistent disorders that call for medical intervention or systemic treatment[19].
- Possibility of Oral Tissue Irritation: If dental gels are used excessively or if a patient is allergic to any of the chemicals, they may irritate or sensitize the oral tissues, which could cause discomfort or exacerbate symptoms[20].
- Dependency and Masking of Underlying Issues: If dental gels are used indefinitely to relieve pain without treating the underlying dental problem, this could hide symptoms, postpone appropriate diagnosis and treatment, and eventually make tooth problems worse[21].
- Cost: Dental gels can be more expensive than other over-the-counter oral care products, depending on the composition and brand. This can be a financial hardship for some patients, particularly if frequent or long-term use is necessary[22].

It is imperative that patients and healthcare practitioners weigh the pros and cons of dental gels when making decisions about their use in the management of oral healthcare.

AIM AND OBJECTIVES :

To prepare a dental pain relief gel using clove oil as a cheap constituent for the pain occurs in the tooth cavity.

- To perform clove oil characterization
- To formulate dental gel of clove oil using gelling agent and other ingredients

LITERATURE REVIEW :

To perform a thorough analysis of the body of research on dental pain treatment gels, especially those that contain clove oil.

To comprehend clove oil's pharmacological qualities that are pertinent to treating tooth pain.

PLAN OF WORK :

- Exhaustive literature survey
- Selection of suitable drug and excipients
- Procurement of materials

PLANT PROFILE :

Fig no. 1: Clove Plant

Synonym : Caryophyllum; clove flower, clove bud; launge[23].

Biological source : Cloves consist of dried flower buds of Eugenia caryophyllus (Myrtaceae). It should contain not less than 15% (v/v) of clove oil[24].

Chemical constituents : 15-20% of volatile oil; 10-13% of tannin(gallotannic acid), chromone and eugenin. The volatile oil contains eugenol (about 70 to90%), eugenol acetate, methyl amyl ketone.caryophyllene and small quantities of ester and alcohols. Some Important components are; Flavonoids, Hydroxybenzoic acid,Hydroxycinnamic acid, Hydroxyphenyl propane, Eugenol, Phenolic acids, Gallic acid, Kaempferol, Quercetin, Caffeic acid, Ferulic acid, Elagicacid, Salicylic acids. B-cariofileno.Eugenol is the main bioactive compound of clove, which is found in concentrations ranging from 9 381.70 to 14 650.00 mg per 100 g of fresh plant material[25].

HISTORY :

As early as 200 BCE, envoys from Java to the Han-dynasty court of China brought cloves that were customarily held in the mouth to perfume the breath during audiences with the emperor. During the late Middle Ages, cloves were used in Europe to preserve, flavor, and garnish food[26]. Clove cultivation was almost entirely confined to Indonesia, and in the early 17th century the Dutch eradicated cloves on all islands except Amboina and Ternate in order to create scarcity and sustain high prices. In the latter half of the 18th century the French smuggled cloves from the East Indies to Indian Ocean islands and the New World, breaking the Dutch monopoly. In the early 21st century, Indonesia was the world's largest producer of cloves, followed by Madagascar, Tanzania, and Sri Lanka. The clove tree is an evergreen that grows to about 8 to 12 meters (25 to 40 feet) in height. Its gland-dotted leaves are small, simple, and opposite. The trees are usually propagated from seeds that are planted in shaded areas[27]. Flowering begins about the fifth year; a tree may annually yield up to 34 kg (75 pounds) of dried buds. The buds are hand-picked in late summer and again in winter and are then sun-dried. Cloves vary in length from about 13 to 19 mm (0.5 to 0.75 inch)[28].

The buds contain 14 to 20 percent essential oil, the principal component of which is the aromatic oil eugenol. Cloves are strongly pungent owing to eugenol, which is extracted by distillation to yield oil of cloves. This oil is used to prepare microscopic slides for viewing and is also a local anesthetic for toothaches. Eugenol is used in germicides, perfumes, and mouthwashes, in the synthesis of vanillin, and as a sweetener or intensifier[29].

USES OF CLOVE :

Clove (Syzygium aromaticum) has a wide range of uses across various domains, including culinary, medicinal, and cosmetic applications. Here are some of its key uses:

Culinary Uses:

1. Flavoring Agent: For both savory and sweet recipes, cloves are frequently employed to improve flavor. They are an essential component of spice mixtures like pumpkin spice and garam masala[30].
2. Preservative: Cloves are utilized in pickling and food preservation because of their antibacterial qualities[31].
3. Beverages: Mulled wine, teas, and other drinks are flavored with cloves[32].

Medicinal Uses:

1. Dental Care: Because of its analgesic and antibacterial qualities, clove oil is frequently used in dentistry to treat gum disease and toothaches[33].
2. Digestive Health: Bloating, indigestion, and nausea are among the digestive problems that cloves can aid with.
3. Anti-inflammatory: Due to their anti-inflammatory qualities, cloves can help lessen pain and inflammation in ailments including arthritis[34].

4. Antimicrobial: Clove oil is helpful in the treatment of infections since it demonstrates potent antimicrobial activity against a variety of bacteria, fungi, and viruses.
5. Respiratory Health: Because of their expectorant qualities, cloves are employed in cough, cold, and bronchitis medicines[35].

Cosmetic Uses:

1. Skincare: Because of its antiseptic and antibacterial qualities, clove oil is used in skincare products to treat acne and other skin ailments.
2. Aromatherapy: The potent, spicy scent of clove oil is used to ease headaches, elevate mood, and lower stress[36].

SCIENTIFIC CLASSIFICATION :

Fig no. 2: Clove Bud

Kingdom : Plantae

Clade : Tracheophytes

Order : Myrtales

Family : Myrtaceae

Genus : Syzygium

Species : S. aromaticum[37]

BIOLOGICAL ACTIVITY :

Because of its many pharmacological benefits, which have been documented in literature and cemented from centuries of traditional use, clove is a significant medicinal plant[38].

ANTIMICROBIAL ACTIVITY :

Clove has been shown to have antibacterial properties against a variety of bacterial and fungal species. The antibacterial properties of several Indian spice plants, including clove, ginger, garlic, mustard, cinnamon, and mint, were investigated by Sofia et al. The aqueous extract of clove at 3% was the only sample that showed full bactericidal action against all food-borne pathogens tested, including Escherichia coli (E. coli), Staphylococcus aureus, and Bacillus cereus. Clove extract also showed strong inhibitory activity at 1% concentration[39].

MORPHOLOGICAL STUDY :

A morphological study of clove (Syzygium aromaticum) involves examining its physical structure and form, both at the macroscopic and microscopic levels. Here is an overview of the morphological characteristics of clove[40]:

Macroscopic Characteristics:

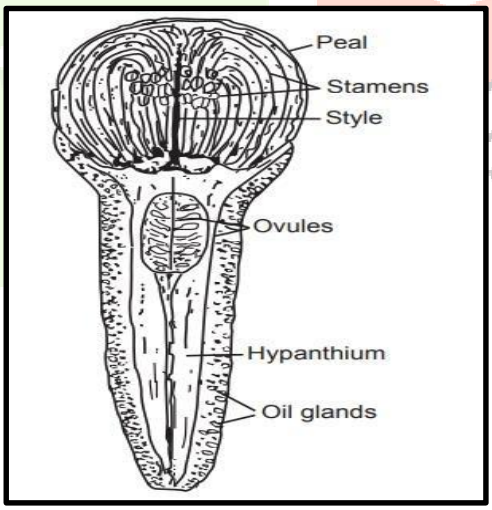

Fig no. 3: L. S. Of Clove Bud

1. **Tree:**
    - Height: Clove trees can grow up to 10-20 meters tall.
    - Trunk: The trunk is straight, with a grayish-brown bark that is rough and furrowed.
    - Branches: The tree has a dense canopy with branches spreading horizontally[41].

2. **Leaves:**
    - Shape: Clove leaves are simple, opposite, and ovate to lanceolate in shape.
    - Size: They are 8-12 cm long and 2.5-6 cm wide.
    - Color: Leaves are glossy and dark green on the upper surface and lighter on the underside.
    - Texture: The leaves are smooth and have a leathery texture.
    - Aroma: When crushed, the leaves emit a strong aromatic smell due to the presence of essential oils[42].
3. **Flowers:**
    - Inflorescence: Clove flowers are arranged in terminal clusters known as cymes.
    - Bud: The flower bud, before blooming, is reddish to purple and resembles a nail or clove.
    - Bloom: Each flower consists of four small sepals, four unopened petals forming a small ball in the center, and numerous stamens.
    - Size: The flower buds are about 1.5-2 cm long[43].
4. **Fruit:**
    - Type: The fruit is a berry-like drupe.
    - Shape: It is oblong and slightly fleshy.
    - Size: Each fruit is about 2-2.5 cm long.
    - Color: The fruit turns from green to purple when ripe[44].

Microscopic Characteristics:

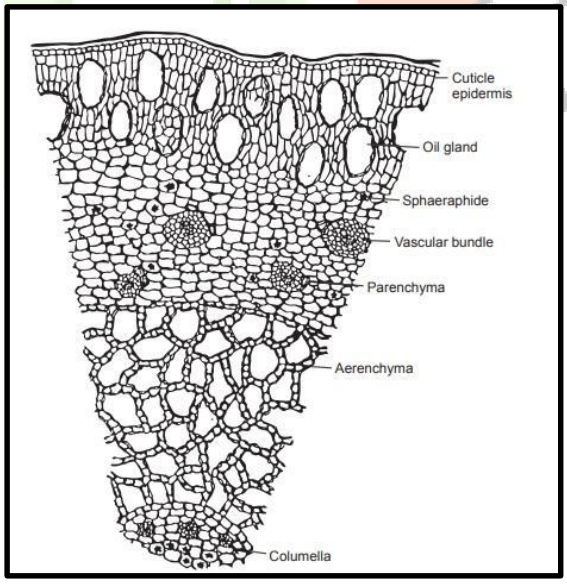

Fig no. 4: T. S. Of Clove Bud

1. **Leaves:**
    - Epidermis: The epidermal cells are rectangular, and the surface is covered with a thin cuticle.
    - Stomata: Stomata are present on both surfaces (amphistomatic) and are surrounded by subsidiary cells.
    - Mesophyll: The mesophyll consists of palisade parenchyma (one to two layers) and spongy parenchyma[45].
2. **Flower Buds:**
    - Glandular Cells: The buds contain numerous glandular cells that produce essential oils, primarily eugenol.
    - Pollen: Pollen grains are spherical, with a smooth exine[46].
3. **Wood:**
    - Vessels: The wood has a diffuse-porous structure with vessels distributed evenly throughout.
    - Fibers: Fibers are present and contribute to the strength of the wood.
    - Parenchyma: The parenchyma cells are present in both axial and radial forms.

By examining these morphological characteristics, both macroscopically and microscopically, one can gain a comprehensive understanding of the clove plant's structure and form. This knowledge is essential for various applications, including botany, agriculture, and pharmacognosy[47].

HERBAL INGREDIENTS :

1. **Turmeric :**

Fig no. 5: Turmeric

Synonyms : Curcuma, Genus curcuma, Curcuma longa, Haldi, Rhizoma curcumae

Biological Source :

Turmeric is the dried rhizome of Curcuma longa Linn. belonging to the family zingiberaceae.

Chemical Constituents : Curcumin, Curcuminoid, Desmethoxycurcumin, Bisdemethoxycurcumin, Vanillideneacetone, Curcumol, Germacrone, Curcumenol, Zingiberene, Bisacurone[48].

Kingdom : Plantae

Clade : Tracheophytes

Order : Zingiberales

Family : Zingiberaceae

Genus : Curcuma

Species : C. longa

Anti Inflammatory Activity :

Because curcumin, the active ingredient in turmeric (Curcuma longa), is present, turmeric is well known for having strong anti-inflammatory effects[49].

2. **Neem :**

Fig no. 6: Neem

Synonyms : Neem, Margosa, Nimtlilac, Indian lilac

Biological Source :

Neem consists of the fresh or dried leaves and seed oil of Azadirachta indica Juss (Melia Indica or M. azadirachta Linn.).

Chemical Constituents : Azadirachtin, Nimbin, Gedunin, Epoxyazadiradione, Gedunin, Azadiradione, azadirone, salannin.

Kingdom : Plantae

Clade : Tracheophytes

Order : Sapindales

Family : Meliaceae

Genus : Azadirachta

Species : A. indica

Antimicrobial Activity :

Azadirachta indica, or neem, is widely recognized for having a wide range of antibacterial qualities. Its efficacy against a range of infections has been scientifically investigated, and it has been utilized in traditional medicine for millennia[50].

3. Honey :

Fig no. 7: Honey

Synonyms : Madhu

Biological Source :

Honey is a sugary substance/secretion deposited in the honey comb by the hive bee Apis Mellifera and other species of Apis belonging to the family Apidae.

Chemical Constituents : Maltose, Table sugar, Gallic acid, Pinobanksin, Pinocembrin, Luteolin, Galangin, Isorhamnetin, Caffeic acid, Kaempferol, p-Coumaric acid, Chrysin, Isoferulic acid, Methylglyoxal, Fructose, Glucose, Water, Vanillic acid, Protocatechuic acid, Chlorogenic acid, 4-Hydroxybenzoic acid, Syringic acid, Apigenin, Myricetin, Phenolic acid, o-Coumaric acid, Phenolic content in wine, Taxifolin, Naringin, Glucose oxidase, Hydroxymethylfurfural, Maltulose, erlose, Melezitose, Inverted sugar syrup[51].

OTHER EXCIPIENTS :

1) **Carbopol -**

Structure :

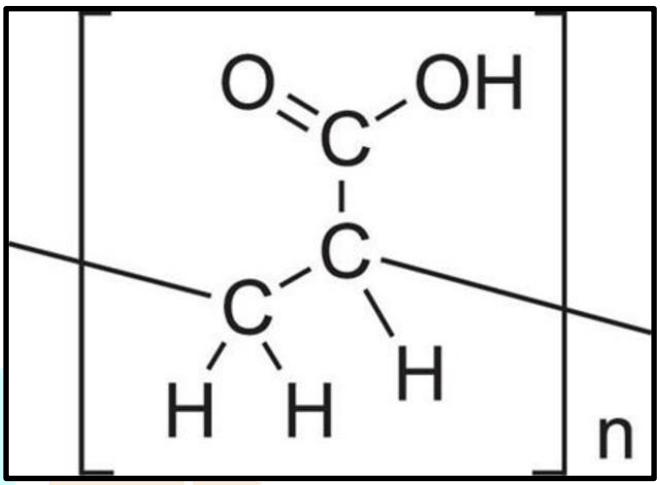

Fig no. 8: Carbopol

IUPAC Name : prop-2-enoic acid

Chemical Formula : (C3H4O2)n

Uses :

It is an extremely efficient rheology modifier capable of providing high viscosity and forms sparkling clear gels or hydro-alcoholic gels and creams.

2) **Polyethylene Glycol -**

Structure :

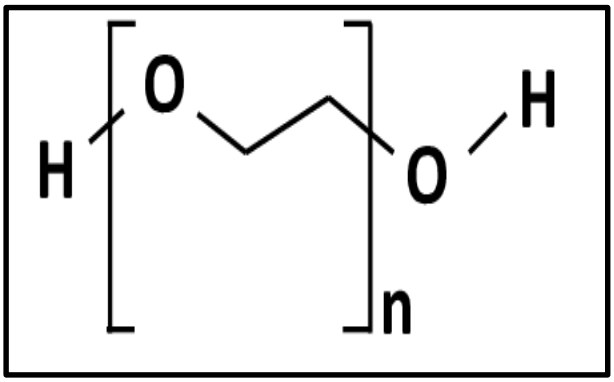

Fig no. 9: Polyethylene Glycol

Chemical Formula : C2nH4n+2On+1

IUPAC Name : poly(ethylene)oxide

Uses :

Periodic constipation can be treated with polyethylene glycol 3350. Polyethylene glycol 3350 is a member of the osmotic laxative drug class. The way it functions is by making the feces retain water. As a result, there are more bowel motions and the stool becomes softer and simpler to pass.

3) Propylparaben -

Structure :

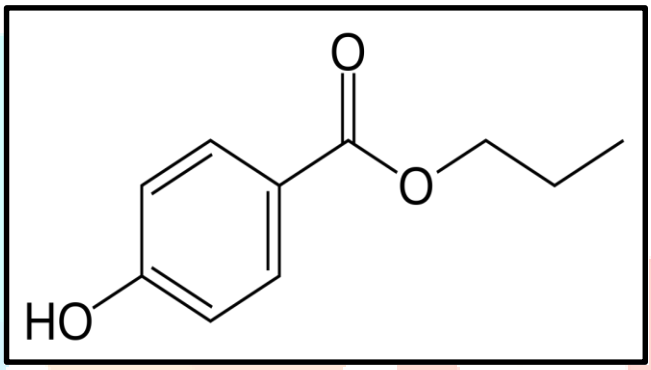

Fig no. 10: PropylParaben

IUPAC Name : 4-hydroxybenzoic acid

Chemical Formula : C10H12O3

Uses :

It is extensively employed as a preservative by the cosmetics and pharmaceutical industries.They work well.The primary uses of these substances and their salts are related to their antifungal and antibacterial qualities.

4) **Glycerine -**

Structure :

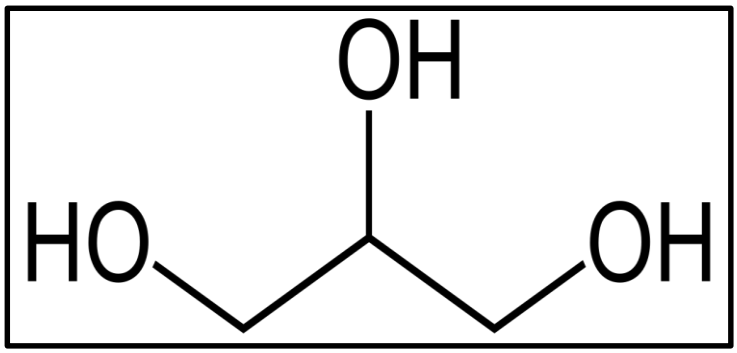

Fig no. 11: Glycerine

IUPAC Name : propane-1,2,3-triol

Chemical Formula : C3H8O3

Uses :

Glycerin is mostly used in the food and beverage sector, where it serves as a solvent, sweetener, and humectant. Food items are also preserved with glycerin when they are stored.

5) **TriethanolAmine -**

Structure :

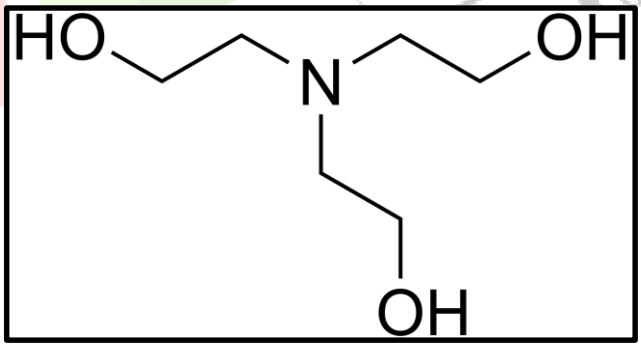

Fig no. 12: TriethanolAmine

IUPAC Name : 2-[bis(2-hydroxyethyl)amino]ethanol

Chemical Formula : C6H15NO3

Uses :

The most widely used neutralizer with carbomer and other acid polymer gels is triethanolamine[52].

FORMULATION OF DENTAL GEL :

Composition :

Table no. 1

Sl. No.	Ingredients	Function	Quantity
1	Clove Oil	API	0.5 ml
2	Carbopol 940	Used to form the gel base	0.5 g
3	Polyethylene Glycol	Helps in dissolving the ingredients and providing a smooth consistency	2.5 ml
4	Propylparaben	Used as preservative	0.05 g
5	Glycerin	Keeps the gel hydrated and improve texture	2.5 ml
6	Distilled Water	Makes up	39.2 ml
7	Honey	Used as sweetening agent	1.5 ml
8	Turmeric Powder	Provides antiinflammatory benefits	1 g
9	Triethanolamine	Adjust the pH and helps in forming the gel	0.25 ml
10	Neem Oil	Provides antimicrobial property	2 ml

Preparation Method :

1. **Disperse the carbopol :**
   Sprinkle 0.5 g of Carbopol 940 into 39.2 g of distilled water while stirring continuously to avoid lumps. Let it hydrate for about 30 minutes.
2. **Dissolve the active ingredients :**
   Mix 0.5 g of clove oil, 2 g of neem extract or oil, and 1 g of turmeric powder in 2.5 g of PEG 400. Stir until the ingredients are uniformly dispersed.
3. **Add humectants and honey :**
   Add 2.5 g of glycerin and 1.5 g of honey to the Carbopol mixture and stir well.
4. **Combine the solutions :**
   Slowly add the dissolved active ingredients mixture into the hydrated Carbopol solution, stirring continuously.
5. **Preservative addition :**
   Dissolve 0.05 g of propyl paraben in a small amount of warm distilled water before adding it to the main mixture to ensure even distribution.
6. **Adjust pH and form gel :**
   Slowly add 0.25 g of triethanolamine dropwise to the mixture while stirring until the gel forms and reaches the desired consistency. The pH should be around 6-7.
7. **Final mixing :**
   Ensure all ingredients are thoroughly mixed to obtain a homogeneous gel.
8. **Packaging :**
   Transfer the prepared gel into a suitable container for storage[53].

EVALUATION TESTS :

- **Physicochemical Evaluation :**
  1. **pH Measurement :** Check the gel's pH to make sure it is between the appropriate ranges for oral application (usually pH 6-7).
  2. **Viscosity :** To make sure the gel has the right consistency for application, use a viscometer to measure its viscosity.
  3. **Spreadability :** Evaluate the gel's spreading properties at the application site. A spreadability test that measures the spread diameter of a set quantity of gel between two glass slides can be used to do this.
  4. **Homogeneity :** Verify the gel's homogeneity visually to make sure there are no lumps or phase separation.
  5. **Appearance :** Analyze the gel's color, clarity, and general aesthetic appeal.

❖ **Stability Studies :**

1. **Physical Stability :** Evaluate the gel's stability over time under various storage settings (such as room temperature or refrigeration). Keep an eye out for any variations in phase separation, color, or consistency.
2. **Chemical Stability :** Utilizing methods such as high-performance liquid chromatography (HPLC), examine the stability of active substances over time, especially clove oil.

❖ **Microbiological Evaluation :**

1. **Sterility Testing :** Use sterility testing to make sure the gel is free of microbiological contamination.
2. **Antimicrobial Efficacy :** To verify the gel's antimicrobial efficacy, test it against common oral infections such Lactobacillus acidophilus, Streptococcus mutans, and Candida albicans[54].

RESULT AND DISCUSSION :

Fig no. 13: Dental Pain Relief Gel

- **Formulation Development :**

➢ Successful Creation of Gel : the creation of a uniform, stable dental painkiller gel with a consistent texture and look utilizing clove oil.

➢ Optimization of Ingredients : Finding the best combinations of clove oil, polyethylene glycol, propylparaben, glycerin, honey, distilled water, triethanolamine, clove powder, and neem to produce the required gel qualities.

- **Physicochemical Properties :**

➢ pH : To be used orally, the gel's pH should be near to neutral—roughly 6-7.

➢ Viscosity : In order for the gel to be easily applied and adhere to oral tissues, its viscosity needs to be within a reasonable range.

➢ Spreadability : In order to ensure that the afflicted region is covered evenly, the gel should have strong spreadability.

- **Safety and Biocompatibility :**

➢ Cytotoxicity Tests : As demonstrated by in vitro cytotoxicity tests, the gel ought to be non-toxic to oral mucosal cells.

➢ Biocompatibility : The gel must be gentle on oral tissues and not irritate or react negatively when applied.

- **Clinical Evaluation** :

➢ Pain Relief : Clinical testing on the gel should show that it is an effective analgesic by significantly reducing tooth pain.

CONCLUSION :

In conclusion, the development and testing of a gel for dental pain alleviation with clove oil shows promise for a safe, all-natural treatment for tooth pain. The gel's active ingredient is clove oil, which has antibacterial and analgesic qualities. Consistency, stability, and effectiveness of the gel can be maximized during the formulation process. The gel's capacity to significantly reduce pain, inflammation, and possibly infection is usually confirmed by evaluation studies. In keeping with the increasing inclinations of consumers toward natural and holistic health treatments, this natural formulation provides an alternative to traditional synthetic analgesics.

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