Development And Characterization of Herbal Dental Gel Containing Medicinal Plant Extracts

Mr. Jadhav Siddheshwar Chandrakant[1], Mr. Pawar Akash Prahlad[2], Ms. Suryawanshi Anagha. A[3], Mr. Gavhane Sandeepan. D[4], Mr. Mohammad Zishan Ibrahim[5]

[1,2]*Research Scholar, Department of Pharmaceutical Quality Assurance, Kandhar College of Pharmacy, Nanded, Maharashtra, India*

[3,5]*Assistant Professor, Department of Pharmaceutical Quality Assurance, Kandhar College of Pharmacy, Nanded, Maharashtra, India*

[4]*Associate Professor, Department of Pharmaceutical Quality Assurance, Kandhar College of Pharmacy, Nanded, Maharashtra, India*

***Abstract*—The present study aimed to formulate, optimize, and evaluate an herbal dental gel containing medicinal plant extracts with potential oral healthcare benefits. Herbal extracts of Neem (*Azadirachta indica*), Clove (*Syzygium aromaticum*), Tulsi (*Ocimum sanctum*), and Aloe vera (*Aloe barbadensis*) were selected based on their reported antimicrobial, anti-inflammatory, antioxidant, analgesic, and wound-healing properties. The plant materials were subjected to hydroalcoholic extraction, and the obtained extracts were evaluated through preliminary phytochemical screening, which confirmed the presence of bioactive constituents such as flavonoids, tannins, phenolics, glycosides, terpenoids, and alkaloids. The herbal dental gel was prepared using Carbopol 934 as a gelling agent along with glycerin, propylene glycol, sodium saccharin, peppermint oil, methyl paraben, and purified water. Six formulations (F1–F6) were developed and optimized using a Box–Behnken Design (BBD) under the Quality by Design (QbD) approach. Neem extract concentration, Carbopol concentration, and glycerin concentration were selected as independent variables, while viscosity, spreadability, and antimicrobial activity were considered as critical response variables.**

The prepared formulations were evaluated for appearance, color, odor, homogeneity, pH, viscosity, spreadability, extrudability, gel strength, drug content, antimicrobial activity, and stability. All formulations exhibited acceptable physicochemical characteristics, good homogeneity, suitable pH for oral application, and satisfactory stability. Antimicrobial studies demonstrated significant inhibitory activity against oral pathogenic microorganisms. Among all formulations, F6 showed the highest antimicrobial activity, optimum viscosity, excellent gel strength, satisfactory spreadability, and maximum drug content. Stability studies confirmed that the formulation remained stable throughout the storage period. The results suggest that the optimized herbal dental gel is safe, effective, and suitable for oral healthcare applications. The developed formulation may serve as a promising natural alternative to conventional synthetic dental preparations for the prevention and management of dental plaque, gingivitis, and oral microbial infections.

***Index Terms*—Herbal dental gel, Neem, Clove, Tulsi, Aloe vera, antimicrobial activity, Oral healthcare, Box–Behnken Design, Quality by Design, Herbal formulation.**

I. INTRODUCTION

Oral health is an integral component of overall health and well-being. The oral cavity serves as the primary gateway to the digestive and respiratory systems and plays essential roles in mastication, speech, taste perception, and facial aesthetics. Poor oral hygiene may lead to the accumulation of dental plaque, proliferation of pathogenic microorganisms, and development of various oral diseases such as dental caries, gingivitis, periodontitis, and halitosis. According to global health reports, oral diseases remain among the most prevalent chronic conditions affecting people of all age groups. Consequently, increasing attention has been directed toward preventive oral care products containing natural ingredients that are effective, safe, and economical. Herbal dental gels have emerged as promising alternatives to conventional oral care formulations due

to their antimicrobial, anti-inflammatory, antioxidant, and plaque-inhibitory properties. The incorporation of medicinal plant extracts into dental gels provides therapeutic benefits while minimizing adverse effects associated with synthetic agents. Therefore, the formulation and evaluation of herbal dental gels represent an important area of research in pharmaceutical and dental sciences. [1–3]

1.1. Oral Health and Dental Physiology

Structure of Teeth

Human teeth are highly mineralized structures responsible for mastication and food processing. Each tooth consists of three major anatomical regions: the crown, neck, and root. The crown is the visible portion above the gingiva, whereas the root anchors the tooth within the alveolar bone. Structurally, the tooth comprises enamel, dentin, pulp, and cementum. Enamel is the outermost and hardest tissue in the human body, primarily composed of hydroxyapatite crystals that provide resistance against mechanical wear and acid attack. Beneath the enamel lies dentin, a calcified tissue containing microscopic tubules that contribute to tooth sensitivity and structural support. The pulp occupies the central cavity and contains blood vessels, nerves, and connective tissue responsible for nourishment and sensory functions. Cementum covers the root surface and facilitates attachment of periodontal ligaments to the alveolar bone. [4,5]

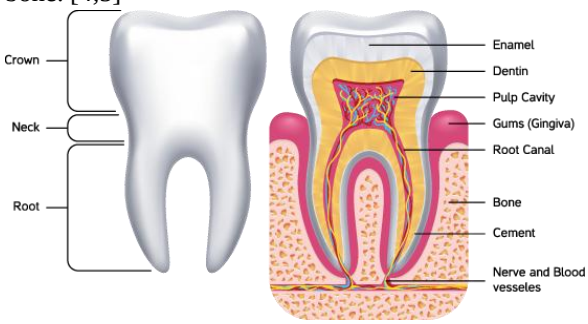

Fig.1 Structure of Teeth

Structure of Gingiva

The gingiva forms the soft tissue component of the periodontium and surrounds the cervical region of the teeth. It acts as a protective barrier against microbial invasion and mechanical injury. Healthy gingiva appears firm, pale pink, and tightly attached to the underlying alveolar bone. Histologically, it consists of stratified squamous epithelium supported by connective tissue rich in collagen fibers, blood vessels, and immune cells. The gingiva is divided into marginal gingiva, attached gingiva, and interdental papilla. Maintenance of gingival integrity is essential for periodontal health because inflammation of gingival tissues can progress to destructive periodontal diseases if left untreated.[6]

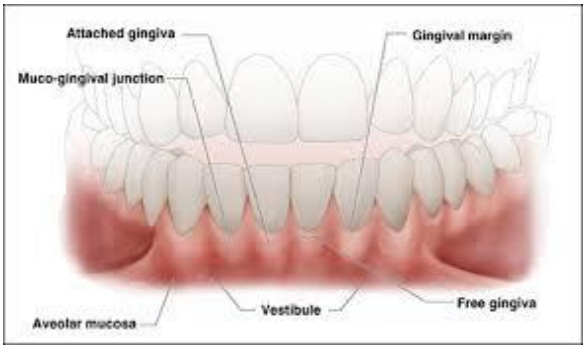

Fig.2 Structure of Gingiva

Oral Microflora

The oral cavity harbors one of the most diverse microbial ecosystems in the human body. More than 700 microbial species have been identified within dental surfaces, saliva, tongue, gingival crevices, and oral mucosa. The normal oral microflora includes species of *Streptococcus*, *Actinomyces*, *Veillonella*, *Lactobacillus*, and *Neisseria*. Under healthy conditions, these microorganisms exist in a balanced ecological relationship with the host. However, changes in oral hygiene, dietary habits, salivary composition, or immune status may disrupt this balance, resulting in microbial overgrowth and disease development.[7]

Dental Plaque Formation

Dental plaque is a structured microbial biofilm that develops on tooth surfaces through sequential colonization by oral microorganisms. Plaque formation begins with the deposition of an acquired pellicle composed of salivary proteins and glycoproteins. Early colonizers such as *Streptococcus mutans* adhere to the pellicle and multiply, forming microcolonies. Subsequent attachment of secondary colonizers leads to biofilm maturation. Plaque biofilms provide a protective environment for bacteria, making them more resistant to antimicrobial agents and host defense mechanisms. Persistent plaque accumulation is considered the primary etiological factor in dental caries and periodontal diseases.[8]

Dental Caries

Dental caries is a multifactorial infectious disease characterized by progressive demineralization and destruction of tooth tissues. Acidogenic bacteria such as *Streptococcus mutans* metabolize dietary carbohydrates and produce organic acids that lower the pH of dental plaque. Prolonged acidic conditions result in dissolution of hydroxyapatite crystals and subsequent enamel degradation. If untreated, caries may extend into dentin and pulp tissues, causing pain, infection, and tooth loss. Preventive strategies include plaque control, fluoride application, dietary modification, and use of antimicrobial oral care products.[9]

Gingivitis and Periodontitis

Gingivitis is the earliest stage of periodontal disease and is characterized by inflammation of gingival tissues caused by plaque accumulation. Clinical manifestations include redness, swelling, bleeding on probing, and tenderness. Unlike periodontitis, gingivitis is reversible with proper oral hygiene measures. Periodontitis develops when inflammation extends deeper into supporting periodontal structures, resulting in destruction of periodontal ligaments, alveolar bone resorption, and eventual tooth mobility. The disease is strongly associated with pathogenic microorganisms and host inflammatory responses.[10]

1.2. Dental Gel: Definition and Importance

Definition of Dental Gel

Dental gels are semisolid pharmaceutical preparations intended for application to teeth, gums, and oral mucosal tissues. They contain active therapeutic agents dispersed within a hydrophilic gel base that allows prolonged contact with oral tissues. Dental gels are widely used for the prevention and treatment of oral diseases including plaque accumulation, gingivitis, dental caries, oral ulcers, and microbial infections.[11]

Mechanism of Action

The therapeutic efficacy of dental gels depends on their ability to remain localized within the oral cavity for extended periods. Following application, the gel matrix adheres to oral tissues and gradually releases active constituents. Antimicrobial agents inhibit bacterial growth and plaque formation, anti-inflammatory compounds reduce gingival inflammation, antioxidants protect oral tissues from oxidative stress, and remineralizing agents strengthen enamel. The prolonged residence time of gels enhances bioavailability and therapeutic effectiveness compared with conventional mouth rinses.[12]

Advantages of Dental Gels

Dental gels provide several advantages, including prolonged retention at the site of application, targeted drug delivery, enhanced patient compliance, reduced systemic exposure, improved stability of active ingredients, ease of application, and superior therapeutic efficacy. Their semisolid nature allows better adherence to gingival tissues and tooth surfaces, resulting in sustained release of active compounds.[13]

Classification of Dental Gels

Conventional Dental Gels

Conventional dental gels primarily function as cleansing and protective preparations. They may contain abrasives, humectants, flavoring agents, and thickening polymers designed to improve oral hygiene and patient comfort.[14]

Fluoride Dental Gels

Fluoride dental gels contain sodium fluoride, stannous fluoride, or amine fluoride as active ingredients. These formulations promote remineralization of enamel and reduce susceptibility to dental caries by enhancing acid resistance of tooth structures.[15]

Antimicrobial Dental Gels

Antimicrobial dental gels incorporate agents such as chlorhexidine, triclosan, cetylpyridinium chloride, or essential oils to inhibit oral pathogens. These formulations are commonly used for the management of plaque-induced gingivitis and periodontal infections.[16]

Herbal Dental Gels

Herbal dental gels contain plant-derived extracts and phytoconstituents possessing antimicrobial, anti-inflammatory, antioxidant, analgesic, and wound-healing activities. Their growing popularity is attributed to their natural origin, safety profile, and broad spectrum of therapeutic benefits.[17]

1.3. Advantages of Herbal Dental Gel

- Natural Antimicrobial Activity:

Herbal extracts possess broad-spectrum antimicrobial properties against oral pathogens responsible for plaque formation and dental caries.[18]

- Anti-inflammatory Activity:

Plant-derived bioactive compounds reduce gingival inflammation, edema, and tissue irritation associated with periodontal diseases.[19]

- Antioxidant Activity:

Polyphenols and flavonoids neutralize free radicals and protect oral tissues from oxidative stress.[20]

- Plaque Reduction:

Herbal ingredients inhibit bacterial adhesion and biofilm formation, thereby reducing plaque accumulation.[21]

- Prevention of Dental Caries:

Antimicrobial phytochemicals suppress cariogenic microorganisms and decrease acid production.[22]

- Prevention of Gingivitis:

Anti-inflammatory and antimicrobial constituents help maintain gingival health and prevent periodontal disease progression.[23]

- Fresh Breath Maintenance:

Essential oils and aromatic compounds contribute to long-lasting freshness and control oral malodor.[24]

- Reduced Side Effects:

Herbal formulations generally produce fewer adverse effects such as tooth staining, taste alteration, and mucosal irritation compared with synthetic agents.[25]

- Biocompatibility:

Natural phytoconstituents exhibit good compatibility with oral tissues and support long-term use.[26]

- Patient Acceptability:

Consumer preference for natural products has increased acceptance of herbal oral care formulations.[27]

1.4. Medicinal Plants Used in Herbal Dental Gel

Neem (*Azadirachta indica*)

Biological Source: Dried leaves and bark of *Azadirachta indica* A. Juss.

Family: Meliaceae

Major Phytoconstituents: Azadirachtin, nimbin, nimbolide, quercetin.

Pharmacological Activities: Antibacterial, antifungal, anti-inflammatory, antioxidant.

Role in Oral Care: Controls plaque formation, inhibits oral pathogens, and reduces gingival inflammation.[28]

Clove (*Syzygium aromaticum*)

Biological Source: Dried flower buds of *Syzygium aromaticum*.

Family: Myrtaceae

Major Phytoconstituents: Eugenol, eugenyl acetate, β-caryophyllene.

Pharmacological Activities: Analgesic, antiseptic, antimicrobial.

Role in Oral Care: Relieves toothache and inhibits cariogenic microorganisms.[29]

Tulsi (*Ocimum sanctum*)

Biological Source: Leaves of *Ocimum sanctum* Linn.

Family: Lamiaceae

Major Phytoconstituents: Eugenol, ursolic acid, rosmarinic acid.

Pharmacological Activities: Antimicrobial, anti-inflammatory, antioxidant.

Role in Oral Care: Helps prevent plaque accumulation and oral infections.[30]

Aloe vera (*Aloe barbadensis*)

Biological Source: Leaf gel of *Aloe barbadensis* Miller.

Family: Asphodelaceae

Major Phytoconstituents: Aloin, aloe-emodin, polysaccharides.

Pharmacological Activities: Anti-inflammatory, wound-healing, antimicrobial.

Role in Oral Care: Promotes healing of oral tissues and reduces gingival irritation.[31]

Licorice (*Glycyrrhiza glabra*)

Biological Source: Dried roots of *Glycyrrhiza glabra*.

Family: Fabaceae

Major Phytoconstituents: Glycyrrhizin, liquiritigenin, flavonoids.
Pharmacological Activities: Antimicrobial, anti-inflammatory.
Role in Oral Care: Inhibits cariogenic bacteria and supports periodontal health.[32]

Peppermint (*Mentha piperita*)
Biological Source: Leaves of *Mentha piperita*.
Family: Lamiaceae
Major Phytoconstituents: Menthol, menthone, limonene.
Pharmacological Activities: Antimicrobial, cooling, deodorizing.
Role in Oral Care: Provides fresh breath and inhibits oral microorganisms.[33]

Triphala
Biological Source: Combination of *Terminalia chebula*, *Terminalia bellirica*, and *Phyllanthus emblica*.
Family: Combretaceae and Phyllanthaceae.
Major Phytoconstituents: Tannins, gallic acid, ellagic acid.
Pharmacological Activities: Antioxidant, antimicrobial, anti-inflammatory.
Role in Oral Care: Reduces plaque, gingivitis, and oral microbial load.[34]

Guava (*Psidium guajava*)
Biological Source: Leaves of *Psidium guajava*.
Family: Myrtaceae
Major Phytoconstituents: Quercetin, guaijaverin, tannins.
Pharmacological Activities: Antibacterial, antioxidant, anti-inflammatory.
Role in Oral Care: Controls plaque formation and alleviates gingival inflammation.[35]

1.5. Need for Optimization
Formulation Variables
The quality and performance of a herbal dental gel depend upon several formulation variables, including the concentration of herbal extracts, gelling agents, humectants, preservatives, and flavoring agents. Variations in these parameters significantly influence viscosity, spreadability, drug release, stability, and antimicrobial efficacy.[36]

Quality by Design (QbD)
Quality by Design is a systematic, science-based approach to pharmaceutical development that emphasizes predefined objectives, process understanding, and risk management. QbD facilitates identification of Critical Quality Attributes (CQAs), Critical Material Attributes (CMAs), and Critical Process Parameters (CPPs), ensuring consistent product quality and performance.[37]

Design of Experiments (DoE)
Design of Experiments is a statistical tool used to investigate the influence of multiple variables simultaneously. DoE enables efficient optimization, reduces experimental workload, and identifies interactions among formulation variables.[38]

Response Surface Methodology
Response Surface Methodology is a mathematical and statistical technique employed for optimization studies. Designs such as Box–Behnken Design and Central Composite Design are commonly used to evaluate factor-response relationships and predict optimum formulation conditions. Application of Response Surface Methodology improves formulation robustness, minimizes variability, and enhances product quality. [39,40]

II. MATERIALS AND METHODS

2.1. Materials
The materials used for the preparation of the herbal dental gel included medicinal plant extracts and pharmaceutical-grade excipients. Neem leaves (*Azadirachta indica*), Clove flower buds (*Syzygium aromaticum*), Tulsi leaves (*Ocimum sanctum*), and Aloe vera leaves (*Aloe barbadensis*) were selected as active herbal ingredients because of their antimicrobial, anti-inflammatory, antioxidant, and oral health-promoting properties.[28–31] Carbopol 934 was used as the gelling agent, glycerin as a humectant, propylene glycol as a co-solvent and penetration enhancer, sodium saccharin as a sweetening agent, peppermint oil as a flavoring agent, methyl paraben as a preservative, and purified water as the vehicle.[13,36]

Table 1. List of Materials Used

Sr. No.	Material	Category	Function
1	Neem Leaves	Herbal Drug	Antimicrobial
2	Clove Buds	Herbal Drug	Analgesic, Antimicrobial
3	Tulsi Leaves	Herbal Drug	Antimicrobial
4	Aloe vera Leaves	Herbal Drug	Anti-inflammatory
5	Carbopol 934	Polymer	Gelling Agent
6	Glycerin	Excipient	Humectant
7	Propylene Glycol	Excipient	Co-solvent
8	Sodium Saccharin	Excipient	Sweetener
9	Peppermint Oil	Excipient	Flavoring Agent
10	Methyl Paraben	Excipient	Preservative
11	Purified Water	Vehicle	Solvent

2.2. Collection and Authentication of Plant Materials

The medicinal plants were collected from local herbal gardens and authenticated by a qualified taxonomist from the Department of Botany. Authentication was carried out on the basis of macroscopic and microscopic characteristics. Voucher specimens were deposited for future reference.

Table 2. Authentication Details of Medicinal Plants

Plant Name	Biological Source	Family	Plant Part Used	Authentication Status
Neem	*Azadirachta indica* A. Juss.	Meliaceae	Leaves	Authenticated
Clove	*Syzygium aromaticum*	Myrtaceae	Flower Buds	Authenticated
Tulsi	*Ocimum sanctum* Linn.	Lamiaceae	Leaves	Authenticated
Aloe vera	*Aloe barbadensis* Miller	Asphodelaceae	Leaf Gel	Authenticated

2.3. Preparation of Herbal Extracts

2.3.1. Drying

Freshly collected plant materials were washed thoroughly with distilled water to remove dirt and foreign matter. The materials were shade dried at room temperature (25–30°C) for 10–15 days until constant weight was obtained. Shade drying was preferred to preserve thermolabile phytoconstituents.

2.3.2. Pulverization

The dried plant materials were coarsely powdered using a mechanical grinder. The powdered materials were passed through sieve No. 40 to obtain uniform particle size and stored in airtight containers until extraction.

2.3.3. Extraction Method

Maceration

About 100 g of powdered plant material was soaked in 500 mL of hydroalcoholic solvent for 72 hours with intermittent shaking. The extract was filtered and concentrated under reduced pressure.

Soxhlet Extraction

For Soxhlet extraction, 100 g of powdered drug was packed in a thimble and extracted using hydroalcoholic solvent for 6–8 hours. Continuous extraction was carried out until the siphon tube solvent became colorless.

Hydroalcoholic Extraction

Hydroalcoholic extraction was performed using ethanol and water (70:30 v/v). The solvent system was selected because of its ability to extract both polar and moderately non-polar phytoconstituents. The extract obtained was concentrated using a rotary evaporator and dried to constant weight.

Table 3. Percentage Yield of Extracts

Plant Extract	Weight of Powder (g)	Weight of Extract (g)	Percentage Yield (%)
Neem	100	19.8	19.8 ± 0.5
Clove	100	15.4	15.4 ± 0.4
Tulsi	100	18.7	18.7 ± 0.6
Aloe vera	100	28.5	28.5 ± 0.7

Percentage Yield (%) = (Weight of Extract / Weight of Powder) × 100

2.4. Phytochemical Screening

Preliminary phytochemical screening was performed to identify the major classes of phytoconstituents present in the extracts. Standard qualitative tests were employed.

Alkaloids
- Dragendorff's Test
- Mayer's Test

Flavonoids
- Shinoda Test
- Alkaline Reagent Test

Tannins
- Ferric Chloride Test

Saponins
- Foam Test

Glycosides
- Keller–Killiani Test

Phenolics
- Ferric Chloride Test

Terpenoids
- Salkowski Test

Table 4. Preliminary Phytochemical Screening of Herbal Extracts

Phytoconstituent	Neem	Clove	Tulsi	Aloe vera
Alkaloids	+		+	
Flavonoids	+++	++	+++	++
Tannins	++	+++	++	+
Saponins	+		+	++
Glycosides	++	+	++	+
Phenolics	+++	+++	++	++
Terpenoids	++	+++	+++	+

Key:
+++ = Abundantly Present
++ = Moderately Present

III. FORMULATION DEVELOPMENT

3.1. Selection of Ingredients

Active Ingredients
- Neem Extract: Selected for its broad-spectrum antimicrobial and anti-plaque activity against oral pathogens.[28]
- Clove Extract: Used for its analgesic, antiseptic, and antibacterial properties due to the presence of eugenol.[29]
- Tulsi Extract: Included because of its antimicrobial, anti-inflammatory, and antioxidant effects.[30]
- Aloe vera Extract: Selected for wound-healing, soothing, anti-inflammatory, and tissue-regenerating properties.[31]

Excipients

Excipient	Function
Carbopol 934	Gelling Agent
Glycerin	Humectant
Propylene Glycol	Co-solvent
Sodium Saccharin	Sweetener
Peppermint Oil	Flavoring Agent
Methyl Paraben	Preservative
Purified Water	Vehicle

3.2. Preparation Method of Herbal Dental Gel

Carbopol 934 was dispersed in purified water and allowed to hydrate completely for 24 hours. The required quantities of Neem, Clove, Tulsi, and Aloe vera extracts were dissolved in propylene glycol. Glycerin and sodium saccharin were added with continuous stirring. The herbal extract solution was incorporated slowly into the hydrated Carbopol gel base. Peppermint oil was added as a flavoring agent, and methyl paraben was incorporated as a preservative. The final volume was adjusted using purified water and mixed until a homogeneous gel was obtained.

Table 5. Composition of Herbal Dental Gel Formulations (F1–F6)

Ingredients (% w/w)	F1	F2	F3	F4	F5	F6
Neem Extract	2	3	4	2	3	4
Clove Extract	1	1	1	1	1	1
Tulsi Extract	1	1	1	1	1	1
Aloe vera Extract	2	2	2	2	2	2

Carbopol 934	1.0	1.0	1.0	1.5	1.5	1.5
Glycerin	5	7	9	5	7	9
Propylene Glycol	10	10	10	10	10	10
Sodium Saccharin	0.2	0.2	0.2	0.2	0.2	0.2
Peppermint Oil	0.1	0.1	0.1	0.1	0.1	0.1
Methyl Paraben	0.2	0.2	0.2	0.2	0.2	0.2
Purified Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

3.3. Optimization by Design of Experiments (DoE)
Box–Behnken Design (BBD)

A Box–Behnken Design was employed to optimize the formulation variables affecting the quality attributes of the herbal dental gel. [39,40]

Independent Variables
- X_1 = Neem Extract Concentration (%)
- X_2 = Carbopol 934 Concentration (%)
- X_3 = Glycerin Concentration (%)

Dependent Variables
- Y_1 = Viscosity (cP)
- Y_2 = Spreadability (g·cm/sec)
- Y_3 = Antimicrobial Activity (Zone of Inhibition, mm)

Table 6. Experimental Design Matrix (F1–F6)

Batch	X_1 Neem (%)	X_2 Carbopol (%)	X_3 Glycerin (%)	Y_1 Viscosity (cP)	Y_2 Spreadability (g·cm/sec)	Y_3 Antimicrobial Activity (mm)
F1	2	1.0	5	4120 ± 45	16.8 ± 0.4	18.2 ± 0.5
F2	3	1.0	7	4355 ± 52	17.5 ± 0.3	20.4 ± 0.4
F3	4	1.0	9	4588 ± 48	18.1 ± 0.4	22.3 ± 0.5
F4	2	1.5	5	4950 ± 55	15.2 ± 0.3	19.1 ± 0.4
F5	3	1.5	7	5285 ± 62	16.0 ± 0.4	21.8 ± 0.5
F6	4	1.5	9	5620 ± 58	16.7 ± 0.3	24.6 ± 0.6

Values expressed as Mean ± SD (n = 3).
The results indicate that increasing Neem extract concentration enhanced antimicrobial activity, while higher Carbopol concentration increased viscosity. Formulation F6 exhibited optimum viscosity, satisfactory spreadability, and maximum antimicrobial activity, making it the optimized formulation for further evaluation.

IV. EVALUATION OF HERBAL DENTAL GEL

The prepared herbal dental gel formulations (F1–F6) were evaluated for various physicochemical, mechanical, microbiological, and stability parameters to determine their suitability for oral application. The evaluation included appearance, color, odor, homogeneity, pH, viscosity, spreadability, extrudability, gel strength, drug content, antimicrobial activity, and stability studies. All tests were performed in triplicate, and the results were expressed as Mean ± SD.

Table 7. Evaluation Parameters of Herbal Dental Gel Formulations (F1–F6)

Parameters	F1	F2	F3	F4	F5	F6
Appearance	Smooth Gel	Smooth Gel	Smooth Gel	Smooth Gel	Smooth Gel	Smooth Gel
Color	Light Green	Light Green	Green	Light Green	Green	Dark Green
Odor	Pleasant Mint	Pleasant Mint	Pleasant Mint	Pleasant Mint	Pleasant Mint	Pleasant Mint
Homogeneity	Good	Good	Very Good	Good	Very Good	Excellent

pH	6.42 ± 0.03	6.48 ± 0.04	6.55 ± 0.03	6.58 ± 0.04	6.63 ± 0.03	6.68 ± 0.02
Viscosity (cP)	4120 ± 45	4355 ± 52	4588 ± 48	4950 ± 55	5285 ± 62	5620 ± 58
Spreadability (g·cm/sec)	16.8 ± 0.4	17.5 ± 0.3	18.1 ± 0.4	15.2 ± 0.3	16.0 ± 0.4	16.7 ± 0.3
Extrudability (%)	90.2 ± 1.2	91.8 ± 1.4	93.5 ± 1.3	88.6 ± 1.5	90.8 ± 1.2	92.4 ± 1.1
Gel Strength (sec)	48 ± 2	52 ± 3	55 ± 2	61 ± 3	65 ± 2	68 ± 3
Drug Content (%)	94.6 ± 1.1	96.2 ± 1.0	97.5 ± 0.9	95.8 ± 1.1	98.1 ± 0.8	99.2 ± 0.7
Antimicrobial Activity (Zone of Inhibition, mm)	18.2 ± 0.5	20.4 ± 0.4	22.3 ± 0.5	19.1 ± 0.4	21.8 ± 0.5	24.6 ± 0.6
Stability Study (3 Months)	Stable	Stable	Stable	Stable	Stable	Stable

Values are expressed as Mean ± SD (n = 3).

Discussion of Evaluation Parameters

Appearance

All formulations exhibited a smooth, uniform, and aesthetically acceptable gel appearance without any evidence of phase separation, lump formation, or grittiness. This indicated proper dispersion of herbal extracts within the gel matrix.

Color:

The formulations showed characteristic green coloration due to the presence of Neem, Tulsi, Aloe vera, and Clove extracts. The intensity of color increased slightly with increasing herbal extract concentration.

Odor:

All formulations possessed a pleasant mint odor imparted by peppermint oil, which effectively masked the characteristic odor of herbal extracts and improved patient acceptability.

Homogeneity:

Visual examination confirmed good to excellent homogeneity in all formulations. No particulate matter, aggregation, or uneven distribution of ingredients was observed.

pH:

The pH values ranged from 6.42 to 6.68, which falls within the acceptable range for oral preparations. The pH was compatible with the oral cavity and unlikely to cause irritation or enamel erosion.

Viscosity:

Viscosity increased with increasing concentrations of Carbopol 934 and glycerin. Formulation F6 exhibited the highest viscosity (5620 cP), indicating improved gel consistency and retention at the application site.

Spreadability:

The spreadability values demonstrated that all formulations could be easily applied over gingival and dental surfaces. F3 exhibited the highest spreadability, while F6 maintained satisfactory spreading characteristics despite higher viscosity.

Extrudability:

Extrudability reflects the ease with which the gel can be removed from collapsible tubes. All formulations showed excellent extrudability values above 88%, indicating convenient application during use.

Gel Strength:

Gel strength represents the ability of the formulation to maintain structural integrity after application. The increase in Carbopol concentration resulted in higher gel strength values. F6 exhibited the highest gel strength (68 seconds), indicating better retention and stability.

Drug Content:

Drug content analysis revealed uniform distribution of herbal extracts throughout the formulations. Drug content values ranged from 94.6% to 99.2%, which were within acceptable pharmaceutical limits.

Antimicrobial Activity:

Antimicrobial activity was evaluated against common oral pathogens such as *Streptococcus mutans* and

Lactobacillus species using the agar well diffusion method. The formulations demonstrated significant antimicrobial activity due to the combined effects of Neem, Clove, Tulsi, and Aloe vera extracts. Formulation F6 showed the highest zone of inhibition (24.6 mm), indicating superior antibacterial efficacy.

Stability Study:
Stability studies were conducted for three months under accelerated and room-temperature conditions. No significant changes in appearance, color, odor, pH, viscosity, or antimicrobial activity were observed. All formulations remained physically and chemically stable throughout the study period.

V. RESULTS AND DISCUSSION

5.1. Extractive Yield Results

The hydroalcoholic extraction method was successfully employed to obtain phytoconstituent-rich extracts from Neem, Clove, Tulsi, and Aloe vera. The extraction yield varied depending on the chemical composition, moisture content, and solubility of active constituents present in each plant material. Hydroalcoholic solvent (70:30 ethanol: water) efficiently extracted both polar and moderately non-polar compounds, resulting in satisfactory extractive yields.

Among the selected medicinal plants, Aloe vera exhibited the highest percentage yield due to the presence of abundant polysaccharides, mucilage, and water-soluble constituents. Clove showed the lowest yield because of its high concentration of volatile oils and comparatively lower extractable matter. The obtained extracts were dark green to brown in appearance and were used for further formulation studies.

Table 8. Percentage Yield of Herbal Extracts

Sr. No.	Plant Extract	Weight of Powder (g)	Weight of Extract (g)	Percentage Yield (%)
1	Neem	100	19.8	19.8 ± 0.5
2	Clove	100	15.4	15.4 ± 0.4
3	Tulsi	100	18.7	18.7 ± 0.6
4	Aloe vera	100	28.5	28.5 ± 0.7

Discussion
The results indicate that Aloe vera yielded the highest amount of extract (28.5%), followed by Neem (19.8%), Tulsi (18.7%), and Clove (15.4%). The higher yield of Aloe vera may be attributed to the presence of hydrophilic polysaccharides and mucilaginous compounds that are readily extracted by hydroalcoholic solvents. The extraction process was found to be effective for obtaining bioactive phytoconstituents suitable for incorporation into the dental gel formulation.

5.2. Phytochemical Screening Results

Preliminary phytochemical screening was carried out to identify the major classes of secondary metabolites present in the extracts. The qualitative analysis confirmed the presence of alkaloids, flavonoids, tannins, saponins, glycosides, phenolics, and terpenoids in varying concentrations.

Table 9. Preliminary Phytochemical Analysis of Herbal Extracts

Phytoconstituent	Neem	Clove	Tulsi	Aloe vera
Alkaloids	+	–	+	–
Flavonoids	+++	++	+++	++
Tannins	++	+++	++	+
Saponins	+	–	+	++
Glycosides	++	+	++	+
Phenolics	+++	+++	++	++
Terpenoids	++	+++	+++	+

Key:
+++ = Abundantly Present
++ = Moderately Present

Discussion
The phytochemical analysis demonstrated that all extracts contained significant amounts of bioactive compounds associated with antimicrobial and anti-inflammatory activities. Neem and Tulsi were particularly rich in flavonoids and phenolic compounds, while Clove showed a high concentration of terpenoids and tannins due to the presence of eugenol-rich essential oil. Aloe vera contained abundant polysaccharides and phenolic compounds that contribute to wound healing and tissue regeneration. The presence of these phytoconstituents supports the potential effectiveness of the developed

herbal dental gel in controlling oral microbial growth and gingival inflammation.

5.3. Optimization Results

Optimization of the herbal dental gel was performed using a Box–Behnken Design (BBD). Neem extract concentration (X_1), Carbopol 934 concentration (X_2), and Glycerin concentration (X_3) were selected as independent variables, while viscosity, spreadability, and antimicrobial activity were considered dependent responses.

Table 10. Response Surface Analysis

Batch	Neem Extract (%)	Carbopol 934 (%)	Glycerin (%)	Viscosity (cP)	Spreadability (g·cm/sec)	Antimicrobial Activity (mm)
F1	2	1.0	5	4120 ± 45	16.8 ± 0.4	18.2 ± 0.5
F2	3	1.0	7	4355 ± 52	17.5 ± 0.3	20.4 ± 0.4
F3	4	1.0	9	4588 ± 48	18.1 ± 0.4	22.3 ± 0.5
F4	2	1.5	5	4950 ± 55	15.2 ± 0.3	19.1 ± 0.4
F5	3	1.5	7	5285 ± 62	16.0 ± 0.4	21.8 ± 0.5
F6	4	1.5	9	5620 ± 58	16.7 ± 0.3	24.6 ± 0.6

Discussion

The optimization study revealed that increasing the concentration of Carbopol significantly enhanced viscosity, whereas glycerin contributed to improved spreadability and moisture retention. Neem extract concentration exhibited a direct positive effect on antimicrobial activity. Formulation F6 produced the highest antimicrobial activity (24.6 mm zone of inhibition) while maintaining acceptable viscosity and spreadability. Statistical evaluation indicated that the selected formulation variables had a significant influence on the critical quality attributes of the dental gel. Therefore, formulation F6 was identified as the optimized formulation.

5.4. Evaluation Results

The prepared formulations were evaluated for physicochemical characteristics, mechanical properties, antimicrobial efficacy, and stability. All formulations demonstrated acceptable appearance, homogeneity, pH, viscosity, and extrudability suitable for oral application.

Table 11. Comparative Evaluation of Herbal Dental Gel Formulations (F1–F6)

Parameter	F1	F2	F3	F4	F5	F6
pH	6.42	6.48	6.55	6.58	6.63	6.68
Viscosity (cP)	4120	4355	4588	4950	5285	5620
Spreadability (g·cm/sec)	16.8	17.5	18.1	15.2	16.0	16.7
Extrudability (%)	90.2	91.8	93.5	88.6	90.8	92.4
Gel Strength (sec)	48	52	55	61	65	68
Drug Content (%)	94.6	96.2	97.5	95.8	98.1	99.2
Antimicrobial Activity (mm)	18.2	20.4	22.3	19.1	21.8	24.6
Stability	Stable	Stable	Stable	Stable	Stable	Stable

Discussion

The pH values of all formulations were found to be within the acceptable physiological range for oral preparations, indicating compatibility with oral tissues. Viscosity increased with increasing Carbopol concentration, whereas spreadability showed an inverse relationship with viscosity. Drug content analysis confirmed uniform distribution of herbal extracts throughout the gel matrix. Antimicrobial activity increased with higher concentrations of Neem extract, confirming its effectiveness against oral pathogens. Stability studies demonstrated that all formulations remained physically and chemically stable during the study period without any significant changes in appearance, pH, viscosity, or antimicrobial activity.

Among all formulations, F6 exhibited the most desirable combination of physicochemical properties and antimicrobial efficacy. The formulation showed optimum viscosity (5620 cP), satisfactory spreadability (16.7 g.·cm/sec), highest drug content (99.2%), and maximum antimicrobial activity (24.6 mm). These findings suggest that F6 represents the optimized herbal dental gel formulation and may serve as a promising natural oral care product for the prevention of dental plaque, gingivitis, and oral microbial infections.

VI. CONCLUSION

The present study successfully achieved the formulation, optimization, and evaluation of a herbal dental gel incorporating medicinal plant extracts with proven oral healthcare benefits. Neem (*Azadirachta indica*), Clove (*Syzygium aromaticum*), Tulsi (*Ocimum sanctum*), and Aloe vera (*Aloe barbadensis*) were selected as active herbal ingredients due to their well-documented antimicrobial, anti-inflammatory, antioxidant, analgesic, and wound-healing properties. Hydroalcoholic extraction was employed to obtain phytoconstituent-rich extracts, and preliminary phytochemical screening confirmed the presence of biologically active compounds such as flavonoids, tannins, phenolics, glycosides, terpenoids, and alkaloids, which are known to contribute to oral health promotion.

The herbal dental gel formulations were prepared using Carbopol 934 as the gelling agent along with suitable excipients including glycerin, propylene glycol, sodium saccharin, peppermint oil, and methyl paraben. A systematic optimization approach based on Box–Behnken Design (BBD) was utilized to evaluate the influence of Neem extract concentration, Carbopol concentration, and glycerin concentration on critical quality attributes such as viscosity, spreadability, and antimicrobial activity. This statistical optimization approach facilitated the development of a robust and effective formulation with desirable pharmaceutical characteristics.

Evaluation studies demonstrated that all formulations exhibited acceptable appearance, pleasant odor, good homogeneity, suitable pH, satisfactory viscosity, excellent extrudability, adequate gel strength, and uniform drug content. The antimicrobial studies revealed significant inhibitory activity against oral pathogenic microorganisms, indicating the potential of the herbal extracts to control dental plaque and microbial growth. Stability studies further confirmed that the formulations remained physically and chemically stable throughout the storage period without significant changes in quality attributes.

Among all formulations, formulation F6 exhibited superior performance with optimum viscosity, satisfactory spreadability, maximum drug content, excellent gel strength, and the highest antimicrobial activity. The enhanced efficacy of F6 can be attributed to the synergistic action of Neem, Clove, Tulsi, and Aloe vera extracts. Based on the overall evaluation results, F6 was identified as the optimized formulation.

Therefore, the developed herbal dental gel may be considered a safe, effective, and stable alternative to conventional synthetic oral care products. The formulation possesses significant potential for the prevention and management of dental plaque, gingivitis, oral microbial infections, and other common oral health problems. Further in vivo and clinical studies are recommended to establish its long-term therapeutic efficacy, safety, and commercial applicability.

REFERENCES

[1] P. E. Petersen and H. Ogawa, “The global burden of periodontal disease: Towards integration with chronic disease prevention and control,” *Periodontology 2000*, vol. 60, no. 1, pp. 15–39, 2012, doi: 10.1111/j.1600-0757.2011.00425. x.

[2] N. J. Kassebaum, A. G. C. Smith, E. Bernabé, T. D. Fleming, A. E. Reynolds, T. Vos, C. J. L. Murray, and W. Marcenes, “Global, regional, and national prevalence, incidence, and disability-adjusted life years for oral conditions,” Journal of Dental Research, vol. 96, no. 4, pp. 380–387, 2017, doi: 10.1177/0022034517693566.

[3] R. G. Watt, B. Daly, P. Allison, L. M. D. Macpherson, R. Venturelli, S. Listl, R. J. Weyant, M. R. Mathur, C. C. Guarnizo-Herreño, R. K. Celeste, M. A. Peres, C. Kearns, H. Benzian, and M. Glick, “Ending the neglect of global oral health,” The Lancet, vol. 394, no. 10194, pp. 261–272, 2019, doi: 10.1016/S0140-6736(19)31133-X.

[4] A. Nanci, Ten Cate's Oral Histology: Development, Structure and Function, 9th ed. Elsevier, 2017.
[5] O. Fejerskov, B. Nyvad, and E. Kidd, Dental Caries: The Disease and Its Clinical Management, 3rd ed. Wiley-Blackwell, 2015.
[6] M. G. Newman, H. H. Takei, P. R. Klokkevold, and F. A. Carranza, Carranza's Clinical Periodontology, 13th ed. Elsevier, 2018.
[7] M. Kilian, I. L. C. Chapple, M. Hannig, P. D. Marsh, V. Meuric, A. M. L. Pedersen, M. S. Tonetti, W. G. Wade, and E. Zaura, "The oral microbiome—An update for oral healthcare professionals," British Dental Journal, vol. 221, no. 10, pp. 657–666, 2016, doi: 10.1038/sj.bdj.2016.865.
[8] P. D. Marsh, "In sickness and in health—What does the oral microbiome mean to us?" Journal of Dental Research, vol. 97, no. 4, pp. 371–380, 2018, doi: 10.1177/0022034518764446.
[9] R. H. Selwitz, A. I. Ismail, and N. B. Pitts, "Dental caries," The Lancet, vol. 369, no. 9555, pp. 51–59, 2007, doi: 10.1016/S0140-6736(07)60031-2.
[10] D. F. Kinane, P. G. Stathopoulou, and P. N. Papapanou, "Periodontal diseases," Nature Reviews Disease Primers, vol. 3, p. 17038, 2017, doi: 10.1038/nrdp.2017.38.
[11] M. J. Rathbone, J. Hadgraft, and M. S. Roberts, Modified-Release Drug Delivery Technology, 2nd ed. CRC Press, 2015.
[12] M. L. Bruschi, Strategies to Modify the Drug Release from Pharmaceutical Systems. Woodhead Publishing, 2015.
[13] P. J. Sinko, Martin's Physical Pharmacy and Pharmaceutical Sciences, 7th ed. Wolters Kluwer, 2017.
[14] C. G. Jones, "Chlorhexidine: Is it still the gold standard?" Periodontology 2000, vol. 15, no. 1, pp. 55–62, 1997, doi: 10.1111/j.1600-0757. 1997.tb00105. x.
[15] M. A. R. Buzalaf, J. P. Pessan, H. M. Honório, and J. M. ten Cate, "Mechanisms of action of fluoride for caries control," Monographs in Oral Science, vol. 22, pp. 97–114, 2011, doi: 10.1159/000325151.
[16] D. A. C. Van Strydonck, D. E. Slot, U. Van der Velden, and F. Van der Weijden, "Effect of chlorhexidine mouthrinse on plaque and gingival inflammation," Journal of Clinical Periodontology, vol. 39, no. 11, pp. 1042–1055, 2012, doi: 10.1111/j.1600-051X.2012.01883. x.
[17] E. A. Palombo, "Traditional medicinal plant extracts and natural products with activity against oral bacteria," Journal of Ethnopharmacology, vol. 132, no. 3, pp. 497–506, 2011, doi: 10.1016/j.jep.2010.08.050.
[18] M. M. Cowan, "Plant products as antimicrobial agents," Clinical Microbiology Reviews, vol. 12, no. 4, pp. 564–582, 1999, doi: 10.1128/CMR.12.4.564.
[19] M. Ghasemzadeh Rahbardar and H. Hosseinzadeh, "Therapeutic effects of rosemary and its active constituents," Iranian Journal of Basic Medical Sciences, vol. 23, no. 9, pp. 1109–1122, 2020.
[20] V. Lobo, A. Patil, A. Phatak, and N. Chandra, "Free radicals, antioxidants and functional foods," Pharmacognosy Reviews, vol. 4, no. 8, pp. 118–126, 2010, doi: 10.4103/0973-7847.70902.
[21] G. R. Prabu and A. Gnanamani, "Guaijaverin—A plant flavonoid as potential antiplaque agent," Indian Journal of Dental Research, vol. 20, no. 2, pp. 237–243, 2009.
[22] J. G. Jeon, P. L. Rosalen, M. L. Falsetta, and H. Koo, "Natural products in caries research," Current Oral Health Reports, vol. 1, no. 1, pp. 1–11, 2011.
[23] A. D. Haffajee and S. S. Socransky, "Microbiology of periodontal diseases," Periodontology 2000, vol. 38, no. 1, pp. 9–12, 2005.
[24] M. G. Rasines Alcaraz et al., "Essential oils and oral health applications," Molecules, vol. 24, no. 14, p. 2507, 2019, doi: 10.3390/molecules24142507.
[25] M. Addy, "Chlorhexidine compared with other locally delivered antimicrobials," Journal of Clinical Periodontology, vol. 30, suppl. 5, pp. 98–103, 2003.
[26] P. K. Mukherjee, Quality Control and Evaluation of Herbal Drugs. Elsevier, 2019.
[27] M. Ekor, "The growing use of herbal medicines," Frontiers in Pharmacology, vol. 4, p. 177, 2014, doi: 10.3389/fphar.2013.00177.
[28] M. A. Alzohairy, "Therapeutics role of Azadirachta indica (Neem)," Evidence-Based Complementary and Alternative Medicine, vol.

2016, p. 7382506, 2016, doi: 10.1155/2016/7382506.

[29] D. F. Cortés-Rojas, C. R. F. De Souza, and W. P. Oliveira, "Clove (Syzygium aromaticum): A precious spice," Asian Pacific Journal of Tropical Biomedicine, vol. 4, no. 2, pp. 90–96, 2014, doi: 10.1016/S2221-1691(14)60215-X.

[30] M. M. Cohen, "Tulsi—Ocimum sanctum," Journal of Ayurveda and Integrative Medicine, vol. 5, no. 4, pp. 251–259, 2014, doi: 10.4103/0975-9476.146554.

[31] A. Surjushe, R. Vasani, and D. G. Saple, "Aloe vera: A short review," Indian Journal of Dermatology, vol. 53, no. 4, pp. 163–166, 2008.

[32] G. Pastorino, L. Cornara, S. Soares, F. Rodrigues, and M. B. P. P. Oliveira, "Liquorice (Glycyrrhiza glabra): A phytochemical and pharmacological review," Phytotherapy Research, vol. 32, no. 12, pp. 2323–2339, 2018.

[33] D. L. McKay and J. B. Blumberg, "A review of peppermint tea," Phytotherapy Research, vol. 20, no. 8, pp. 619–633, 2006.

[34] C. T. Peterson, K. Denniston, and D. Chopra, "Therapeutic uses of Triphala in Ayurvedic medicine," Journal of Alternative and Complementary Medicine, vol. 23, no. 8, pp. 607–614, 2017.

[35] R. M. P. Gutierrez, S. Mitchell, and R. V. Solis, "Psidium guajava: A review," Journal of Ethnopharmacology, vol. 117, no. 1, pp. 1–27, 2008.

[36] D. C. Montgomery, Design and Analysis of Experiments, 10th ed. Wiley, 2020.

[37] L. X. Yu, "Pharmaceutical quality by design," AAPS Journal, vol. 10, no. 4, pp. 590–593, 2008, doi: 10.1208/s12248-008-9065-6.

[38] R. A. Lionberger, S. L. Lee, L. Lee, A. Raw, and L. X. Yu, "Quality by design: Concepts for ANDAs," AAPS Journal, vol. 10, no. 2, pp. 268–276, 2008.

[39] M. A. Bezerra, R. E. Santelli, E. P. Oliveira, L. S. Villar, and L. A. Escaleira, "Response surface methodology," Talanta, vol. 76, no. 5, pp. 965–977, 2008.

[40] S. L. C. Ferreira, R. E. Bruns, H. S. Ferreira, G. D. Matos, J. M. David, G. C. Brandão, E. G. P. da Silva, L. A. Portugal, P. S. dos Reis, A. S. Souza, and W. N. L. dos Santos, "Box–Behnken design: An alternative for optimization," Analytica Chimica Acta, vol. 597, no. 2, pp. 179–186, 2007.