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Research Article

Formulation and Evaluation of Clove and Eucalyptus Extracts Loaded Dental Film for Treatment of Periodontal Disease

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ABSTRACT

The study focuses on the formulation and evaluation of a novel dental film incorporating clove (*Syzygium aromaticum*) and eucalyptus (*Eucalyptus globulus*) extracts, aimed at providing an effective localized therapy for periodontal disease. Periodontal disease, characterized by inflammation and degeneration of the supporting structures of the teeth, remains a significant public health concern, necessitating the development of innovative, targeted treatment modalities. In this research, herbal extracts known for their potent antimicrobial, anti-inflammatory, and analgesic properties were incorporated into a biodegradable film matrix, designed to adhere to periodontal pockets and deliver sustained therapeutic effects. The dental films were prepared using a solvent casting method, with optimal concentrations of clove and eucalyptus extracts and different concentrations and ratios of polymers. The physicochemical properties, including thickness, weight variation, surface pH, percentage moisture loss, percentage moisture absorption and folding endurance, were systematically evaluated. *In vitro* studies assessed the release profile of active compounds, while antimicrobial efficacy was determined against common periodontal pathogens using disk diffusion method. The results demonstrated that the formulated dental films exhibited desirable mechanical properties, controlled drug release, and significant antimicrobial activity against *Staphylococcus aureus*. These findings suggest that clove and eucalyptus extract-loaded dental films could serve as an effective, patient-friendly adjunct in the management of periodontal disease, offering localized, sustained therapeutic benefits with minimal side effects.

INTRODUCTION

Gingivitis and periodontitis are the two phases of periodontal disease. The first, curable stage of the disease process, known as gingivitis, occurs when the gingiva is the only area that is inflamed [1, 2]. Plaque bacteria cause this irritation, which may be stopped with regular at-home care and comprehensive dental prophylaxis [2, 3]. The later stage of the disease process is called periodontitis, which is characterized as an inflammatory condition brought on by microbes that affect the tooth's deeper supporting components, such as the alveolar bone and periodontal ligament [4]. When oral bacteria cling to teeth in the form of plaque, periodontal disease begins.

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Plaque is a biofilm formed of salivary glycoproteins and extracellular polysaccharides, and it is virtually exclusively constituted of oral bacteria [1, 5]. In essence, calculus, also known as tartar, is plaque that has been hardened by salivary minerals [6].

Folk medicine uses eucalyptus, a member of the *Myrtaceae* family, to treat a variety of illnesses and health issues [7]. According to the chemical makeup of eight essential oils from Eucalyptus species from Tunisia, 1,8-cineole was the main component. Cryptone, α-pinene, p-cymene, α-terpineol, phellandral, cuminal, globulol, limonene, aromadendrene, sapthulenol, and terpinene-4-ol were the next most common ingredients [8]. EOs from seven Eucalyptus species have been shown to contain significant amounts of 1,8-cineole and α-pinene [9]. EO's aromatic ingredients are utilized as antipyretic, anti-inflammatory, and analgesic treatments [7]. EO from E. globulus was found to have moderate

antimicrobial activity towards Gram-positive (*Staphylococcus aureus*, Enterococcus fecium, Listeria monocytogenes 4b, and Listeria monocytogenes EGD-e) and Gram-negative (Salmonella enteritidis, Escherichia coli, and Pseudomonas aeruginosa) bacteria, as well as bacteriostatic activity towards all the strains tested (except for Pseudomonas aeruginosa) [10]. Porphyromonas gingivalis and Prevotella intermedia were among the periodontopathic bacteria that were shown to be susceptible to antibacterial activity by 60% ethanol extracts from the E. globulus leaf [11].

Clove, or *Syzygium* (S.) *aromaticum*, is a dried flower bud that is native to Indonesia's Maluku islands and is a member of the *Myrtaceae* family. It has lately been cultivated in many locations around the world [12, 13]. According to pharmacological research, clove is the primary source of gallic acid derivatives like hidrolizable tannins and phenolic molecules like hidroxibenzoic acids, flavonoids, hidroxiphenyl propens, hidroxicinamic acids, and eugenol ($C_{10}H_{12}O_2$), the main bioactive molecule, which is present in high concentrations in the fresh plant. [12, 14, 15]. Up to 18% of clove flower buds contain essential oil, which is made up of cariafileno, eugenol, and eugenol acetate [16]. Certain fragrant herbs, such as cinnamon, oregano, clove, thyme, and mint, have been shown in several studies to possess antibacterial, antiviral, anticarcinogenic, and antifungal properties. But among other spices, clove has drawn a lot of interest because of its strong antioxidant and antibacterial properties [14]. Clove essential oil (CEO) has long been used to heal burns and wounds, as well as to ease dental discomfort and cure toothaches and infections [17].

The present study aims to formulate and evaluate the extract of eucalyptus and clove loaded dental film for the treatment of periodontal disease.

MATERIALS AND METHODS

Extracts of clove and eucalyptus were obtained from college laboratory. Hydroxypropyl methylcellulose C15s was procured from Research-lab Fine Chem Industries, Mumbai, India. Ethyl cellulose, polyethylene glycol (PEG), ethanol and dichloromethane were purchased from Loba Chemie Pvt. Ltd., Mumbai, India. All other chemicals utilized for the investigation were of analytical grade.

Extraction of Eucalyptus Leaves

The extracts were prepared by the maceration method, which involved adding 50 grams of powdered eucalyptus leaves to 250 milliliters of 96% ethanol or distilled water, stirring the extract of ethanol mixture every few hours with a glass rod, boiling the aqueous mixture for 20 minutes over a low flame until a cream-colored substance came out, and centrifuging to collect the excess fluid for an additional ten minutes at 3000 rpm up to the concentration of the resulting extract (supernatant) reached its starting point with ethanol or distilled water. The results were then kept in a dark-colored vehicle at the fridge after being filtered through 0.45 µ Whatman filter paper [18].

Extraction of Clove Buds

Clove buds can be extracted using the maceration method, involving grinding, steeping in a solvent (1:10 ratio), and filtration. The mixture is steeped for 2-3 weeks, followed by expression and combination of the liquids. The solvent is then evaporated to obtain the extract, which is stored in a cool, dark place [19-21].

Formulation of Periodontal Films

To obtain varying amounts of polymer solution, ethyl cellulose, and HPMC c 15s mixtures were mixed separately and together in 10mL of ethanol and dichloromethane using a magnetic stirrer. With constant stirring, the polymer solution was supplemented with the clove extract, eucalyptus extract and plasticizer (Table 1). Following thorough mixing, the mixture was transferred into a sanitized Petri dish that was positioned horizontally. A cotton-plugged glass funnel was inverted to allow the solvent to gently evaporate. For 24 hours, the stem was left at room temperature. Cast films were produced once the solvent had completely evaporated; they were subsequently wrapped in aluminum foil and kept in a desiccator [22].

Table 1: Composition of Dental Film

Ingredients	F1	F2	F3
Clove extract (gm)	3.18	3.18	3.18
Eucalyptus extract (gm)	3.18	3.18	3.18
Ethyl cellulose (mg)	150	100	200
Hydroxypropyl methyl cellulose (HPMC) c15s (mg)	150	200	100
PEG (mL)	0.90	0.90	0.90
Ethanol (mL)	5	5	5
Dichloro methane (mL)	5	5	5

Evaluation of Dental Films

Thickness of the Film

Using a screw gauge, the thickness of each 1 cm^2 film was measured at several locations, and an average thicknesses was computed [23, 24].

Weight Variation

Ten patches were cut into various sections after being weighed. The weighing device was used to measure the individuals weight, and the average weight was then computed [25].

Surface pH

In order to examine the likely effects of pH changes *in vivo*, the surface pH of the films was determined sequentially. This is because an acidic or alkaline pH may cause irritation to the periodontal mucosa. The film under investigation was put in a Petri dish, immersed in 0.5 milliliters of phosphate buffer with a pH of 6.6, and left for an hour. After placing the pH meter's electrode on the formulation's surface and letting it equilibrate for one minute, the pH was highlighted [26-30].

Percentage Moisture Loss

The periodontal films were kept in desiccants for the purpose to calculate the % moisture loss [31]. The following formula was used to determine the percent moisture value:

$$\% \text{ moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100 \quad (1)$$

Percentage Moisture Absorption

Weighing and placing a known-size sample in a desiccator with 100 mL of an aluminum chloride saturated solution while maintaining 79.5% relative humidity allowed us to perform the percentage moisture absorption test. The implants were removed and weighed again after three days [32]. The following formula was used to determine the percent of moisture absorption.

$$\% \text{ moisture absorbtion} = \frac{\text{final weight} - \text{initial weight}}{\text{Initial weight}} \times 100 \quad (2)$$

Folding Endurance

One film was folded repeatedly at the same spot until it broke or folded 350 times, which is deemed sufficient to demonstrate good film qualities. This was done to test the films' folding durability. The value of folding endurance was determined by folding the film a certain number of times at the same location without breaking [33-35]. All of the films underwent this test six times.

Drug Content Uniformity

In volumetric flasks, 1 cm^2 films were dissolved in 10 mL of ethanol. Until the film had fully dissolved, the volumetric flask was set aside. Using ultraviolet (UV)-visible spectroscopy, 1 mL of this solution was pipetted out, suitably diluted, and its absorbance was measured [36].

Fourier Transforms Infrared Spectroscopy (FTIR)

FTIR spectrum analyses were performed utilizing a FTIR Spectrophotometer [37-41].

In Vitro Drug Release

Separate films with known weights and measurements were placed in tiny test tubes with 10 milliliters of phosphate buffer at pH 7.4. The aluminum foil was used to seal the test tubes, which were then stored at ambient temperature. Fresh 1 mL of pH 7.4 was added every hour for a total of six hours after the sample was removed. A UV spectrophotometer was used to quantify the medication concentration in the buffer [25, 42-44].

In Vitro Antibacterial Activity

For the tests, the 1 cm^2 films were collected, and 60 mL of nutritious agar medium was prepared and autoclaved for 20 minutes at 15 lb. pressure. While everything was aseptic, twenty milliliters of nutritious agar medium were placed in sterile Petri dishes. After solidification, the medium was treated with 0.1 mL of a microbial solution with a specified concentration, and it was incubated for 168 hours at 37°C. Next, the zone of inhibition was measured using the "Hi Antibiotic Zone Scale [45-52]."

RESULTS AND DISCUSSION

Tables 2 and 3 illustrate the physical and chemical properties of polyherb periodontal films.

Thickness Uniformity of the Films

Each film's thickness was measured four times, and the average thickness with S.D. was determined. The film thickness statistics show that there was little variation in the formulations' thicknesses. The findings are shown in Table 2. The thickness of the film was determined to be between 22.59±0.51 and 22.94±0.30 mm (n = 3).

Table 2: Thickness, Weight Uniformity, Percent Moisture Loss and Percent Moisture Absorption of Dental Film Containing Polyherb

Periodontal Film Code	Thickness (mm)	Weight Uniformity (mm)	Percent Moisture Loss (%)	Percent Moisture Absorption (%)
F:1 (1:1)	22.59±0.51	16.33±1.66	5.34±0.08	1.87±0.2
F:2 (1:2)	22.91±0.31	15.66±0.3333	6.39±0.15	4.31±0.23
F:3 (2:1)	22.94±0.0.30	16.00±1	7.10±0.17	2.37±0.04

Mean±SD (n=3)

Table 3: Folding Endurance, Surface pH and Drug Content of Dental Film Containing Polyherb

Periodontal Film Code	Folding Endurance	Surface pH	Drug Content (%)
F:1 (1:1)	145	6.26	92.43
F:2 (1:2)	137	6.32	94.46
F:3 (2:1)	160	6.29	95.21

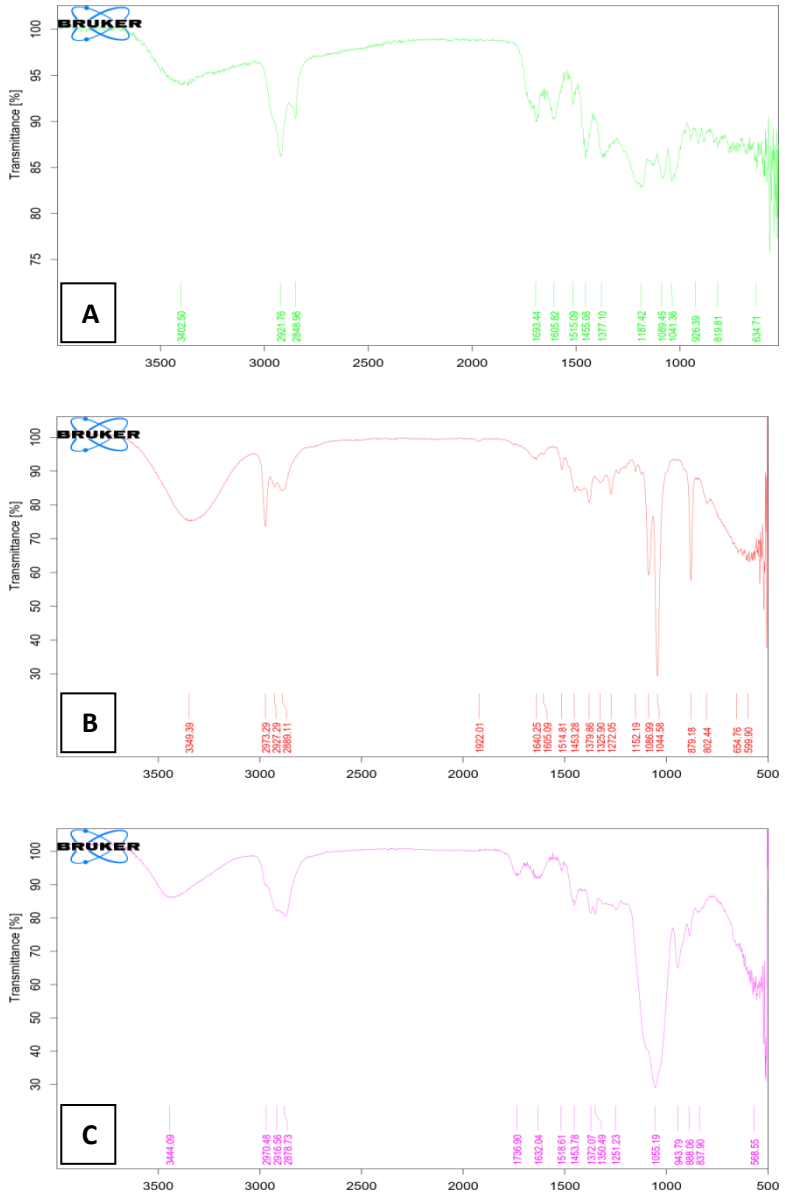

Figure 1: FTIR of Clove Extract (A), Eucalyptus Extract (B) and Formulation (C)

Weight Variation of Films

The results of testing drug-loaded films (1cm × 1cm) for weight homogeneity are shown in Table 2. Every patch's film had a consistent weight, ranging from 16.33±1.6666 to 16.00±1 mg. Proper medication and polymeric mixture is responsible for this.

Surface pH

According to the technique chapter, the surface pH of each formulation was measured. It was discovered that the pH of each formulation ranged from 6.26 to 6.29. This indicates that the produced films might not irritate the gingival fluid in the periodontal pocket since they wouldn't change its pH.

Percentage Moisture Loss

All of the formulations underwent moisture loss investigations, which are detailed in Table 2. The % moisture loss for each formulation ranged from 5.34±0.08 to 7.10±0.17. Formulation F1 had the lowest percentage of moisture loss because of hydrophobic ethyl cellulose, whereas formulation F3 displayed the greatest amount of moisture loss because of a higher concentration of HPMC c15s experiencing moisture loss in dry conditions.

Percentage Moisture Absorption

The % moisture loss for each formulation ranged from 1.87±0.2 to 4.31±0.23, with Table 2 providing the results. The formula with the highest moisture absorption percentage was F2.

Folding Endurance

All formulas exhibited optimal film qualities, as evidenced by the folding endurance value of > 200 for all films.

Drug Content Uniformity

The medicine was evenly distributed, according to the content uniformity results. Table 3 shows that the percentage drug content in the different formulations varied from 92.43 to 95.21%.

Fourier Transforms Infrared Spectroscopy (FTIR)

At 3402.50, 2971.76, 1605.82, 1187.42, and 1693.44, clove extract exhibits peaks that correlate to -OH, =CH-, -C-O, O-CH, AND C=O (Fig. 1A). Eugenol (4-Ally-2-methoxy-phenol) is shown by the first four peaks, while additional secondary polyphenols are indicated by the carbonyl groups that follow.

At 3349.39, 2973.29, 1605.09, 1514.81, 1453.28, and 1272.05, respectively, eucalyptus extract exhibits peaks that correspond to O-H, -C-H, N-H, N=O, -C-H, and C-X (Fig. 1B).

Plant extracts-loaded dental film FTIR spectrum showed characteristic bands which are in line with FTIR spectra of clove and eucalyptus extracts (Fig. 1C). Small shifts in the peaks may be due to transition during film formation.

***In Vitro* Drug Release**

Separate films with known weights and measurements were placed in tiny test tubes with 10 milliliters of phosphate buffer at pH 7.4. The aluminum foil was used to seal the test tubes, which were then stored at ambient temperature. Fresh 1 mL of pH 7.4 was added every hour for ten hours after the sample was removed. A UV spectrophotometer was used to quantify the drug concentration in the buffer, as shown in Fig. 2.

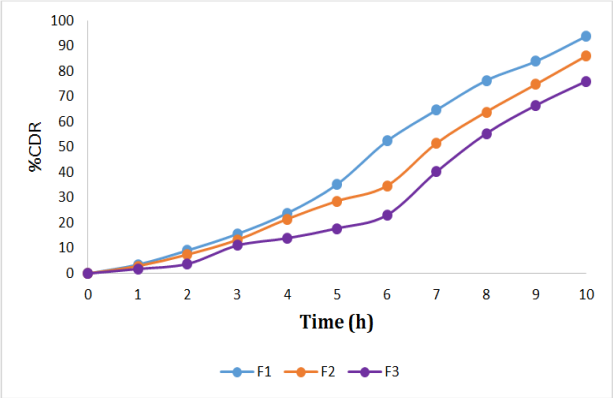

Figure 2: *In Vitro* Drug Release

***In Vitro* Antibacterial Activity**

Fig. 3 and Table 4 show *in vitro* antibacterial activity against *Staphylococcus aureus*. After 168 hrs the zone of inhibition of clove extract and eucalyptus extract was found to be 15 mm & 13 mm. respectively whereas, poly herbal dental film containing mixture of clove and eucalyptus extract shows significant increase in the Zone of inhibition that is 20 mm as compared to individual plant extracts. The combination of clove and eucalyptus extracts in a dental film formulation enhances antibacterial activity might be due to synergistic effects, sustained release, improved retention, and better penetration into bacterial biofilms.

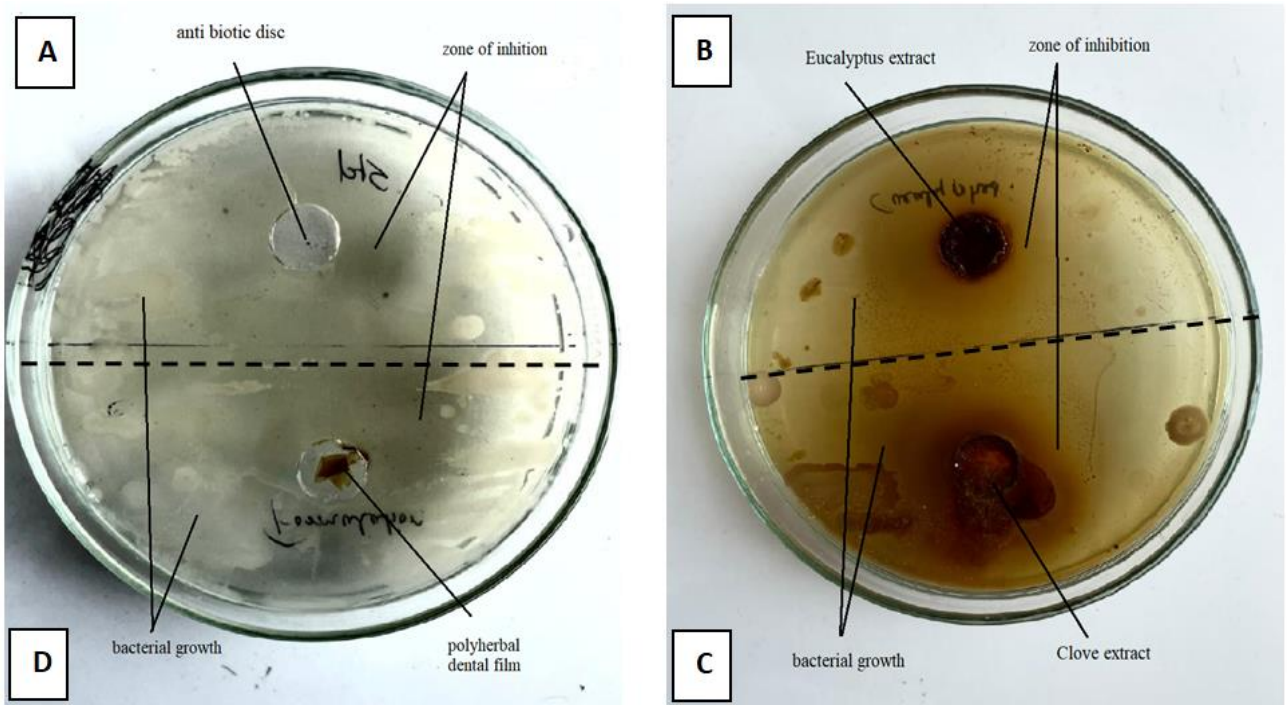

Figure 3: Zone of Inhibition Study

A: Standard Drug (Amikacin), **B**: Eucalyptus Extract, **C**: Clove Extract, **D**: Polyherbal Dental Film

Table 4: Zone of inhibition (ZOI) of various test samples

Sample	Zone of inhibition (mm)
Amikacin (standard) (30µg)	25 mm
Clove extract (50mg)	15 mm
Eucalyptus extract (50mg)	13 mm
Polyherbal dental film (50mg)	20 mm

CONCLUSION

The formulation and evaluation of dental films containing clove extract and eucalyptus extract demonstrated promising results in terms of antibacterial activity. The films exhibited significant antimicrobial effects against common oral pathogens, including *Streptococcus aureus*, suggesting their potential as effective agents for oral care. Both extracts contributed to the films' ability to combat bacterial growth, with clove extract providing strong antibacterial properties due to its eugenol content, while eucalyptus extract enhanced the overall antimicrobial spectrum. The films also showed favorable physical properties, such as tensile strength, surface pH, folding endurance and controlled drug release, indicating their suitability for practical use in dental care. Based on these findings, the formulated dental films could be considered as innovative therapeutic alternatives for preventing oral infections such as periodontal disease and improving oral hygiene.

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