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Formulation Development and Evaluation of Eugenol Base Dental Gel for Periodontitis

Dr. Amuthavalli Velayutham* and Dr. Balaji Subramanian

Department of Dentistry
Sri Lakshmi Narayana Institute of Dental Sciences, Puducherry
***Corresponding Author**
Dr. Amuthavalli Velayutham,
Associate Professor,
Department of Dentistry,
Sri Lakshmi Narayana Institute of Dental Sciences,
Puducherry, India.
dramutha.arun@gmail.com

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Abstract: The purpose of the study was to develop and evaluate a dental gel using eugenol as its primary component for the treatment of periodontitis. It is chosen for the treatment of periodontitis because it has a broad spectrum of antibacterial activity against a variety of periodontal infections. In order to formulate eugenol gel, PBC Carbomer 940 is used as a gelling agent, eugenol is used as a medicinal agent, Propanediol is used as a co-solvent, methyl paraben is used as preservative, and the necessary amount of distilled water is used as the vehicle. The eugenol was evaluated for acid value, ester value, specific gravity and refractive index and it shown satisfactory results. The prepared gel was evaluated for antimicrobial activity, pH, spreadability, extrudability, drug content etc. The eugenol dental gel formulations was tested against, *Lactobacillus acidophilus*, *Pseudomonas aeruginosa* and *Eschericha coli* and compared with other formulations. Antimicrobial activity demonstrated that the formulation EDG3 is a suitable dosage form for the treatment of periodontitis.

Introduction

Periodontal diseases are mainly the result of infections and inflammation of the gums and bone that surround and support the teeth. In its early stage, called gingivitis, the gums can become swollen and red, and they may bleed. In its more serious form, called periodontitis, the gums can pull away from the tooth, bone can be lost, and the teeth may loosen or even fall out. Periodontal disease is mostly seen in adults. Periodontal disease and tooth decay are the two biggest threats to dental health [1]. It is caused by bacteria in the mouth infect tissue surrounding the tooth, causing inflammation around the tooth leading to periodontal disease. When bacteria stay on the teeth long enough, they form a film called plaque, which eventually hardens to tartar, also called calculus. Tartar build-up can spread below the gum line, which makes the teeth harder to clean. Gingivitis, the moderate stage of disease caused by an accumulation of supragingival plaque and characterized by swelling, light bleeding and redness of the marginal gingival. Gingivitis is associated with a change in the microflora, shifting from a Gram-positive anaerobic flora to a more Gram negative one. Periodontitis is an inflammatory response to the overgrowth of anaerobic organisms such as Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Campylobacter rectus, Prevotella melaninogenica, and Actinobacillus actinomycetem comitans are examples of anaerobic organisms that can overgrow and cause periodontitis. The traditional methods of treating periodontal disease,

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including oral, topical, and systemic dosage forms, have significant drawbacks, including superinfection, low compliance, low antibiotic levels in gingival crevicular fluid, systemic side effects, a short duration of action, and a high relative cost. The goals of periodontal therapy are to treat inflammatory tissue, lessen the amount of pathogenic germs, and remove diseased pockets[1]. Recent developments in dentistry have encouraged the use of herbal and natural remedies to treat a variety of oral illnesses. There are several reports of conventional plants and natural products being used to cure oral problems. One such substance with numerous advantages is eugenol, which has become quite important in clinical research [2]. Eugenol is extremely helpful in dentistry because it exhibits low intrinsic toxicity and a wide range of biological actions, including analgesic, antiseptic, antispasmodic, anti-neurogenic, carminative, anti-infectious, disinfectant, insecticide, stimulant, stomachic, and other beneficial properties [3]. Our present study was to formulate dental gel containing eugenol and evaluated for their physicochemical properties including drug content, spreadability, extrude ability, in-vitro antibacterial activity.

Materials and Methods

Carbomer 940 purchased from charco-chemicals, India. Eugenol, Propanediol**,** Methyl paraben were procured from S.D. Fine chemicals Pvt. Ltd, Mumbai, India. All other chemicals and reagents used in the study were analytical grade.

Preparation of Gel

Dental gels were prepared by soaking carbomer 940 in water and bringing the pH up to 6.4 using triethanolamine to form gel. Weighed amount of methyl paraben was added to the water prior to the addition of carbomer 934. In another beaker, the required quantity of propanediol was taken and to which accurately measured the amount of eugenol corresponding to its MIC was incorporated and finally this mixture was added to the beaker containing carbomer with stirring [4]. The sweetener was also added to the polymer dispersion and continually mixed until a homogeneous result was produced [5]. Distilled water was used to make up the volume, and it was forcefully stirred. All the prepared dental gels were then subjected to evaluation in order to select the best formulation. The composition of different gel formulations is shown in Table 1.

Table 1 Composition of Dental Gel

Ingredients	EDG1	EDG2	EDG3	EDG4	EDG5
Eugenol (ml)	0.5	0.5	0.5	0.5	0.5
Carbomer (mg)	200	400	600	800	1000
Propanediol (ml)	10	10	10	10	10
Methyl paraben (g)	0.18	0.18	0.18	0.18	0.18
Aspartame (g)	0.4	0.4	0.4	0.4	0.4
Distilled water	q.s	q.s	q.s	q.s	q.s

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Determination of Physicochemical Characteristics of Eugenol

The eugenol was analyzed for physicochemical characteristics like acid value, ester value, density, refraction index and solubility

Acid value [6]

A mass of 300 mg of the oil sample was taken in a conical flash and dissolved in 30 mL of distilled alcohol by gentle warming. It was then titrated against 0.1N potassium hydroxide (KOH) using phenolphthalein as indicator until a slight pink color appeared. For this titer value, the acid value was calculated by using following equation.

$$AV = TD \times N \times 56.1/M$$

Where, TD = Titer difference in mL, N = Normality of KOH, M = Molecular weight of KOH in grams. The factor 56.1 is the equivalent mass of KOH.

Ester Value [6]

The ester value is defined as the mass in milligrams (mg) of KOH required to react with glycerin (glycerol or glycerin) after saponifying one gram of fat. It is calculated from the saponification value and the acid value

$$\text{Ester Value} = \text{Saponification Value} - \text{Acid Value}$$

Estimation of Density, Refraction index and Solubility [7,8]

The determination of the density using the gravimetric method used piknometer at 20 °C the refractive index used the refractometry method at 20 °C; and the solubility in 70% ethanol used volumetric method with turbidity comparison solution, namely silver nitrate 0.1 N.

Determination of pH [9]

The pH of gel was determined using digital pH meter by dipping the electrode entirely into the gel system.

Determination of Viscosity [10]

Viscosity of the formulated gels was estimated using Brooke field viscometer, spindle no. 7 and spindle speed 60rpm at 25◦C was used for gels, the corresponding dial reading on the viscometer was noted.

Determination of Extrudability

It was determined by using a tube filled with the gel, having a tip of 5mm opening and by measuring the amount of gel that extruded through the tip when a pressure was applied on the tube was noted down.

Determination of Homogeneity [11]

All the developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.

Determination of Spreadability [12]

Spreadability was determined by modified wooden block and glass slide apparatus. The apparatus consisted of a wooden block with fixed glass slide and a pulley. A pan was attached to another glass slide (movable) with the help of a string. For the determination of spread ability measure amount of gel was placed in the fixed glass slide, the movable glass slide with a pan attached to it, was placed on the fixed glass slide such that the gel was sandwiched between the two slides for 5 minutes. Now about 50 grams of weight was added to the pan. Time taken for the slides to separate was noted. Spread ability was determined using following formula:

$$S = M.L/T$$

Where S is the spread ability in grams.cm/sec, M is the mass in grams, T is the time in seconds

Determination of Drug Content

An accurately weighed quantity of 1 g dental gel was dissolving in 100 ml of solvent (Mixture of methanol and phosphate buffer pH 6.8). The solutions were kept for shaking for 2 hr and then kept for 5 hr for complete dissolution of the eugenol from the gel [13]. The solutions were filtered through a 0.45-µm nylon filter. The drug content was estimated using UV spectrometer at 280nm and calculated from the calibration data [14].

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Determination of Antimicrobial Activity: The antibacterial activity of eugenol gel was screened by using the agar cup plate method. All the formulations containing around 2% eugenol were placed aseptically in agar plates that had already been inoculated with culture [15]. Before the plates were incubated at 37°C for 24 hours, they were left at room temperature for 30 minutes. Tetracycline, a broad spectrum antibiotic, was utilized as a positive control to provide comparative results. After 24-48 hours of incubation, plates were checked to see if the zone of inhibition had materialized. By measuring the diameter of the zones that inhibited microbial growth (in millimetres), antimicrobial activity was assessed.

Results

Physicochemical Characteristics

Table 2. Physicochemical Characteristics of Procured and Standard Eugenol

Parameters	Eugenol Procured	Eugenol Standard
Color	Pale yellow	Pale yellow
Odor	Warm, spicy, floral	Warm, spicy, floral
Acid value (mg KOH g-1)	18.66	16.0 - 20.0
Ester value	119.24	90- 180
Solubility in ethanol	Freely soluble	Freely soluble
Density (kg m^3) at 25ºC	1.000	0.8 - 1.00
Refractive index	1.5405 at 20 °C	1.540-1.542

The physiochemical characteristics of procured and standard eugenol was shown in table 2. The purchased eugenol was characterized, it was found to have the following characteristics that were in accordance with standard values for standard eugenol. Acid value was 18.66 mg KOH g-1, ester value was 119.24, Free soluble in ethanol, density was 1.00 kg m^3 and refractive index was 1.5405 at 20 °C.

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Characterization of various Dental Gel Formulations

Figure1. Formulations of Eugenol Dental Gel

Table 3. Characterization of prepared Dental Gel formulations

Dental Gel Formulations	EDG1	EDG2	EDG3	EDG4	EDG5
Appearance	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow
Homogeneity	Good	Good	Very good	Good	Very good
pH	6.4	6.4	6.5	6.7	6.4
Spreadability (gm/sec)	17.21	18.0	18.4	19.6	18.4
Extrudability %	92.14	92.51	95.32	90.34	91.13
Drug Content %	95.2	94.2	96.0	94.5	93.2

The characterization of various dental gel preparations were given in Table 3. (Picture of various formulation in figure 1) Various dental gel formulations containing eugenol were EDG1 to EDG5. The formulations were prepared by using carbomer 940 at various concentrations and eugenol at the same concentration. Physical attributes of each of the five batches of formulations were evaluated. All of the formulations had the distinctive spicy aroma odor and were light yellow in color. The pH of all formulations varied from 6.4 to 6.7, which was well within the buccal cavity's typical pH range of 6 to 7 and provides evidence that the created gels won't irritate the skin. The spreadability was more in EDG4 with 19.6 gm/sec and EDG1 showed least

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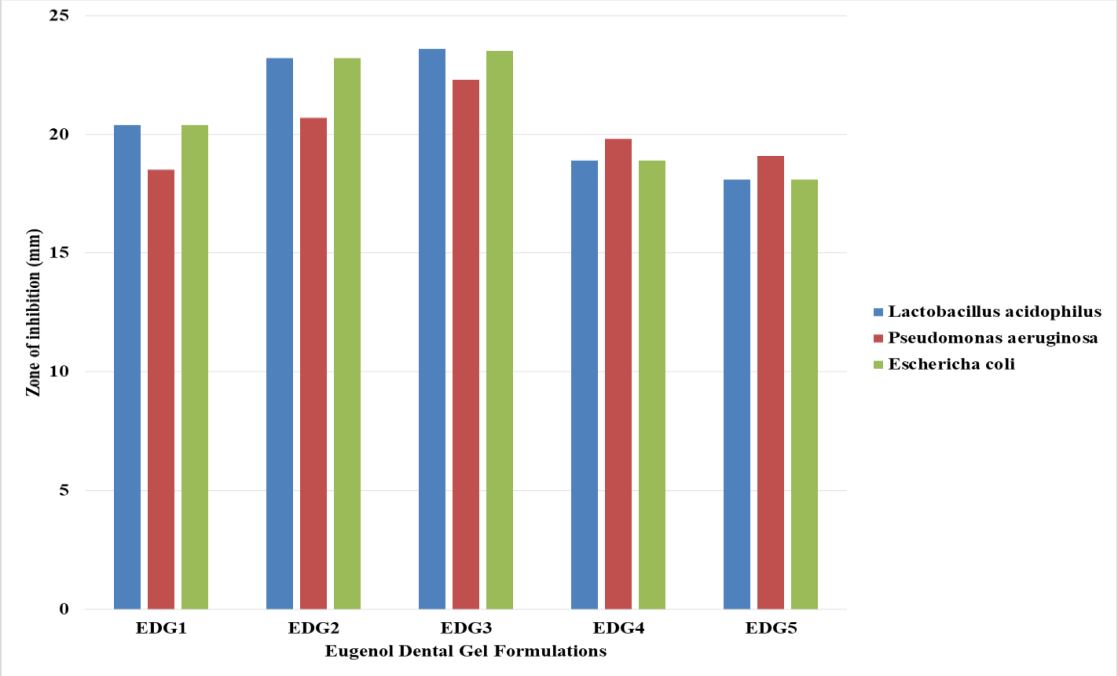
with 17.21gm/sec. The percentage of extrudability was more in the formulation EDG3 with 95.32 and 90.34 with the formulation WDG4. Percentage of drug content was more in the formulation EDG3 and least in formulation EDG5. From the above it indicating that they can spread consistently and smoothly. The compositions had a shiny, transparent appearance. In all formulations, the homogeneity and tube extrudability were satisfactory. The formulations' drug content ranged from 93.2% to 96.0%. It was found that there was no drug degradation during production from the values obtained from the drug content. It was discovered that the formulation EDG3 had the most drug content. When compared to other formulations, the dental gel formulations of eugenol EDG3 displayed good physicochemical characteristics as well as good drug content. These formulations were consequently chosen for additional antibacterial research.

Chart 1. Antimicrobial activity of Eugenol Dental Gel Formulations against various microorganisms



Antimicrobial activity of various eugenol dental gel formulations against microorganism were shown in chart 1. Among the formulations EDG1 to EDG5, EDG2 and EDG3, showed significant antimicrobial activity against various tested organism like *Lactobacillus acidophilus, Pseudomonas aeruginosa* and *Eschericha coli* compared to other formulations

Conclusion

Eugenol is an allyl chain substituted guaiacol, a member of the allylbenzene class of chemical compound extracted from certain essential oils especially from clove. It was discovered to exhibit antibacterial activity against *Lactobacillus acidophilus, Pseudomonas aeruginosa*, and *Eschericha coli*. The formulations developed were found to have considerable results and can be utilized commercially to create dental gels. However, further research is still required to discover whether they can effectively replace others as gel for periodontitis as alone or incombinations**.**

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