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Formulation and development of dental gel containing clove oil for the treatment of human periodontal diseases

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ABSTRACT:

Aim: The study was aimed to develop and evaluate dental gel containing clove oil as the chief constituent for the treatment of periodontitis.

Methods: It has a wide spectrum of antibacterial activity against a number of periodontal pathogens, hence it is selected for the treatment of periodontitis. Clove oil gel is formulated by using carbopol 934 as gelling agent, clove oil as medicinal agent, polyethylene glycol co-solvent, methyl paraben and propyl paraben as preservative and required quantity of distilled water as vehicle.

Results: The clove oil was evaluated for physical parameters like acid value, ester value, specific gravity and refractive index and it shown satisfactory results. The prepared gel was evaluated for various properties such as antimicrobial activity, pH, spreadability, extrudability, drug content etc. In-Vitro experiments demonstrated that the formulation F3 is a suitable dosage form for the treatment of periodontitis. Clove oil showed the zone of inhibition of about 22.05 ± 0.04 mm.

Conclusion: On the basis of the result obtained in this present study we conclude that the gel formulations of clove oil F3 showed good physicochemical properties as well as good drug content compared to other formulations.

Key words: Clove oil, Carbopol 934, Periodontitis, Anti microbial activity.

INTRODUCTION

Periodontal disease is recognized as a major public health problem throughout the world and occurs in all groups, ethnicities, races, genders and socioeconomic levels. It is characterized by inflammation and degeneration of the gums, supporting bone, periodontal ligament and cementum and accumulation of bacterial pathogens, mainly within the periodontal pockets [1]. The periodontal disease commonly refers to inflammatory diseases that are plaque induced i.e. gingivitis and periodontitis. 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, a

more severe stage of periodontal disease, results in the resorption of the alveolar bone and detachment of the periodontal ligament supporting tooth [2]. 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. The conventional method of treatment the periodontal disease like oral, topical and systemic dosage forms have major disadvantages like superinfection, low or non-compliance, low gingival crevicular fluid levels of antibiotics, systemic side effects, short duration and high relative cost [3]. Periodontal treatment aims to cure inflamed tissue, reduce the number of pathogenic bacteria and eliminate the diseased pockets. Recent advances in the field of dentistry have promoted the use of herbal and natural

products for the treatment of various oral diseases. There have been numerous reports of the use of traditional plants and natural products for the treatment of oral diseases. Clove oil is one such product exhibiting multiple benefits and has gained considerable importance in clinical research [4]. Since clove oil shows low intrinsic toxicity along with a wide spectrum of biological actions like analgesic, antiseptic, antispasmodic, anti-neuralgic, carminative, anti-infectious, disinfectant, insecticide, stimulant, stomachic and other useful properties, it is very useful in dentistry also [5]. The present study was aimed to formulate dental gel containing clove oil for the treatment of periodontal diseases and then evaluated for their physicochemical properties including drug content, spreadability, extrude ability, in-vitro antibacterial activity.

MATERIALS AND METHODS

Clove oil is purchased from local market in Nellore. Methyl paraben and propyl paraben were procured from S.D. Fine chemicals Pvt. Ltd, Mumbai, India.

Preparation of gel:

Carbopol 934 gels were prepared by soaking carbopol 934 in water and by neutralizing with triethanolamine to pH 6.4. Weighed amount of methyl and propyl paraben were added to the water prior to the addition of carbopol 934 [6]. In another beaker, the required quantity of propylene glycol was taken in another test tube to which accurately measured the amount of clove oil corresponding to its MIC was incorporated and finally this mixture was added to the beaker containing carbopol with stirring [7]. The sweetening agent was also added to the polymer dispersion and stirred continuously till it forms a homogenous product [8]. The volume was made up with distilled water and stirring was done vigorously. All the prepared gels were then subjected to evaluation tests in order to select the best formulation. The composition of different gel formulations is listed in Table 1.

Physicochemical characteristics of clove oil:

The clove oil was analyzed for physicochemical characteristics like acid value, ester value, solubility, density, refractive index and results were tabulated in the Table 2.

Evaluation of gel formulation

Physical appearance:

- **Color**
The color of the formulation was checked out against a white background.
- **Consistency**
The consistency was checked by applying on skin.

- **Greasiness**
The greasiness was assisted by the application on to the skin.
- **Odor**
The odor of the gels was checked by mixing the gel in water and taking the smell.

Determination of pH:

The pH of gel was determined using digital pH meter by dipping the glass electrode completely into the gel system [9].

Determination of viscosity:

Viscosities of the formulated gels was determined 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 [10] Table 5

Determination of spreadability:

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 [11]. A pan was attached to another glass slide (movable) with the help of a string [12-15]. 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 [16-18]. 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 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:

All the developed gels were tested for homogeneity by visual inspection after the gels have been set in the container [19-20]. They were tested for their appearance and presence of any aggregates.

Determination of drug content:

The drug content of the gel formulations was determined by dissolving an accurately weighed quantity 1 g of gel in 100 ml of solvent (a mixture of ethanol and phosphate buffer pH 6.8 for the formulation of clove oil). The solutions were kept for

shaking for 4 hr and then kept for 6 hr for complete dissolution of the formulations [21]. Then the solutions were filtered through 0.45 mm membrane filters and proper dilutions were made and solutions were subjected to the spectro photometric analysis [22]. The drug content was calculated from the linear regression equation obtained from the calibration data.

Determination of antimicrobial activity:

Agar cup plate method was used for screening of antimicrobial activity of clove oil gel. All formulations of clove oil gel of about 2% were placed aseptically in cups of agar plate which was previously inoculated with culture [23]. The plates were left at ambient temperature for 30 mins prior to incubation at 37°C for 24 hrs. The broad spectrum antibiotic i.e., tetracycline was used as positive control for obtaining comparative results. Plates were observed after 24-48 hrs incubation for the appearance of the zone of inhibition [24]. Antimicrobial activity was evaluated by measuring the diameter of zones of inhibition (millimeters) of microbial growth [25].

RESULT

DISCUSSION

The procured clove oil was characterized for the following parameters:

- ✓ Acid value : 3.66
- ✓ Ester value: 37.21
- ✓ Solubility : freely soluble in ethanol
- ✓ Density : 1.02gm/ml
- ✓ Refractive index : 1.492

The formulations were developed by using clove oil of same concentration and carbopol 934 at different concentrations. Formulation composition is given in Table-1. All the five batches of formulations were evaluated for physical properties. All the formulations were pale yellow in color and had characteristic odor of clove oil. The pH of all formulations ranged from 6.4-6.7, which was well within the normal pH range of buccal cavity 6-7, which substantiates that the prepared gels will be irritation free.

Table: 1 Anti microbial activity of clove oil gel formulations Composition of gel formulation

Ingredients	F1	F2	F3	F4	F5
Clove oil (ml)	0.75	0.75	0.75	0.75	0.75
Carbopol (g)	0.3	0.4	0.5	0.6	1
Poly ethylene glycol (ml)	15	15	15	15	15
Glycerin (ml)	5	5	5	5	5
Methyl paraben (g)	0.18	0.18	0.18	0.18	0.18
Propyl paraben (g)	0.02	0.02	0.02	0.02	0.02
Aspartame (g)	0.4	0.4	0.4	0.4	0.4
Distilled water	q.s	q.s	q.s	q.s	q.s

Table: 2 physicochemical characteristics of clove oil

S.no.	Parameters	Clove oil procured	Clove oil standard
1.	Color	Pale yellow	Pale yellow
2.	Odor	Aromatic	Aromatic
3.	Acid value	3.66	3.84
4.	Ester value	37.21	38.22
5.	Solubility in ethanol	Freely soluble	Freely soluble
6.	Density	1.02g/ml	1.05g/ml
7.	Refractive index	1.492	1.532

Table: 3 Antimicrobial activity of formulation of clove oil and tetracycline (standard)

Microorganisms	Zone of inhibition in mm(F3)	Clove oil	Tetracycline (standard)
<i>S.salivarius</i>	22.05±0.04 n=3	23±0.2 n=3	25±1.1 n=3
<i>S.sanguis</i>	21.56±0.02 n=3	22±0.04 n=3	23±2.2 n=3
<i>L.acidophilus</i>	20.32±0.4 n=3	20±0.06 n=3	21±1.4 n=3
n=3, Mean ± S.D

Fig. 1: Formulations of clove oil gel

Fig. 2 Zone of inhibition of Streptococcus salivarius

Fig. 3 Zone of inhibition of Streptococcus sanguis

Fig. 4 Zone of inhibition of Lactobacillus acidophilus

Table: 4 Anti microbial activity of clove oil gel formulations

Formulation	Zone of inhibition (S. salivarius)	Zone of inhibition (S. sanguis)	Zone of inhibition (L. acidophilus)
F1	19.53±0.3	18.24±0.2	17.52±0.5
F2	21.5±0.2	20.3±0.1	19.29±0.2
F3	22.05±0.04	21.56±0.02	20.32±0.4
F4	18.6±0.1	18.1±0.03	17.59±0.1
F5	17.06±0.02	16.13±0.4	15.43±0.6
n=3, Mean ±S.D

Fig5Antimicrobial activity on *S.salivarius*
1 – F3 (Gel Formulation)
2 – Clove oil
3 – Tetracycline

Fig: Anti microbial activity of clove oil gel formulations on *S.salivarius*

Fig: 6 Antimicrobial activity on *S. salivarius*

Table: 5 characteristics of gel formulations

Formulations	Appearance	pH	Spreadability(g-cm/sec)	Extrudability%	Homogeneity	Drug % content
F1	Pale yellow	6.6	18.20	92.14	Good	95.00
F2	Pale yellow	6.7	18.14	93.15	Good	95.20
F3	Pale yellow	6.7	17.49	94.10	Very good	95.40
F4	Pale yellow	6.6	16.72	90.23	Good	93.62
F5	Pale yellow	6.4	15.59	89.10	Very good	89.80

The spreadability of the gels was found to be in the range of 15.59-18.20gm-cm/sec, confirming that thus gels may spread smoothly and uniformly. The formulations were glossy and translucent. The homogeneity and tube extrudability of all formulations was good.

The drug content of the formulations was ranged from 89.8% to 95.40% (Table 5). From the values obtained from the drug content, it was concluded that there was no degradation of the drug during the preparation process. The formulation F3 was found to have maximum drug content.

The gel formulations of clove oil F3 showed good physicochemical properties as well as good drug content compared to other formulation (Table 5). Hence, these formulations were further selected for antimicrobial studies. The results of antimicrobial studies showed that gel formulation of clove oil F3 showed a maximum zone of inhibition on *Streptococcus salivarius*.

Table: 7 Antimicrobial activity on *Streptococcus salivarius*

Microorganisms	F3	Clove oil	Tetracycline
<i>S.salivarius</i>	22.05±0.04	23±0.2	25±1.1

CONCLUSION

The clove oil was found to have antimicrobial activity against *Streptococcus salivarius*, *Streptococcus sanguis*, *Lactobacilli acidophilus*. The formulations developed from clove showed significant results so it can be further used commercially to develop dental gels after conducting clinical trials on human beings. Nevertheless further research is still needed in order to determine if they efficiently could substitute the synthetic antibiotics or uses in combinations.

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