Formulation & Evaluation of Mucoadhesive Gel of Coriandrum sativum Fruit Extract

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ABSTRACT

Intra-periodontal pocket, mucoadhesive drug delivery systems have been shown to be clinically effective in the treatment of periodontitis. The aim of this study was to formulate a mucoadhesive gel from the fruits of *Coriander sativum* for the treatment of periodontitis. Coriander (Coriandrum sativum) fruit from umbeliferae family is an annual herb originates in India, used as medicine in disorder of digestive, respiratory and urinary system, as it has diuretic, carminative and stimulant activity. Pharmacological studies have demonstrated the hypoglycaemic, hypolipidemic, antimutagenic, antihypertensive, antioxidant, antimicrobial and postcoital antifertility activity of Coriander sativum. The semisolid concentrated extracts were incorporated in gel base. Mucoadhesive gel was prepared by using Carbopol 940, sodium CMC and HPMC as bio adhesive polymer. Physiochemical tests, mucoadhesive strength measurement and in-vitro drug release study were carried out on all formulations (F1-F5) containing Carbopol 940 sodium CMC polymers. Mucoadhesion and viscosity of F5 were good.

Keywords: coriander, mucoadhesive gel, periodontitis, HPMC, Carbopol

INTRODUCTION

Periodontal disease, also known as gum disease, is a set of inflammatory conditions affecting the tissues surrounding the teeth. In its early stage, called gingivitis, the gums become swollen, red, and 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 fallout. Bad breath may also occur.

Periodontal disease is generally due to bacteria in the mouth infecting the tissue around the teeth. Risk factors include smoking, diabetes, HIV/AIDS, family history, and certain medications. Diagnosis is by inspecting the gum tissue around the teeth both visually and with a probe and X-rays looking for bone loss around the teeth.

Treatment involves good oral hygiene and regular professional teeth cleaning. Recommended oral hygiene includes daily brushing and flossing. In certain cases antibiotics or dental surgery may be recommended. Globally 538 million people were estimated to be affected in 2015. In the United States nearly half of those over the age of 30 are affected to some degree, and about 70% of those over 65 have the condition. Males are affected more often than females.

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.

This condition is more common in men than women (56.4% Vs 38.4%), those living below the federal poverty level (65.4%), those with less than a high school education (66.9%), and current smokers (64.2%).

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. Then, only a dental health professional can remove the tartar and stop the periodontal disease process.

Teeth

The teeth are the hardest substances in the human body. Besides being essential for chewing, the teeth play an important role in speech. Parts of the teeth include:

• **Enamel:** The hardest, white outer part of the tooth. Enamel is mostly made of calcium phosphate, a rock-hard mineral.

• **Dentin**: A layer underlying the enamel. It is a hard tissue that contains microscopic tubes. When the enamel is damaged, heat or cold can enter the tooth through these paths and cause sensitivity or pain.

• **Pulp:** The softer, living inner structure of teeth. Blood vessels and nerves run through the pulp of the teeth.

• **Cementum:** A layer of connective tissue that binds the roots of the teeth firmly to the gums and jawbone.

• **Periodontal ligament**: Tissue that helps hold the teeth tightly against the jaw.

A normal adult mouth has 32 teeth, which (except for wisdom teeth) have erupted by about age 13:

•**Incisors (8 total):** The middlemost four teeth on the upper and lower jaws.

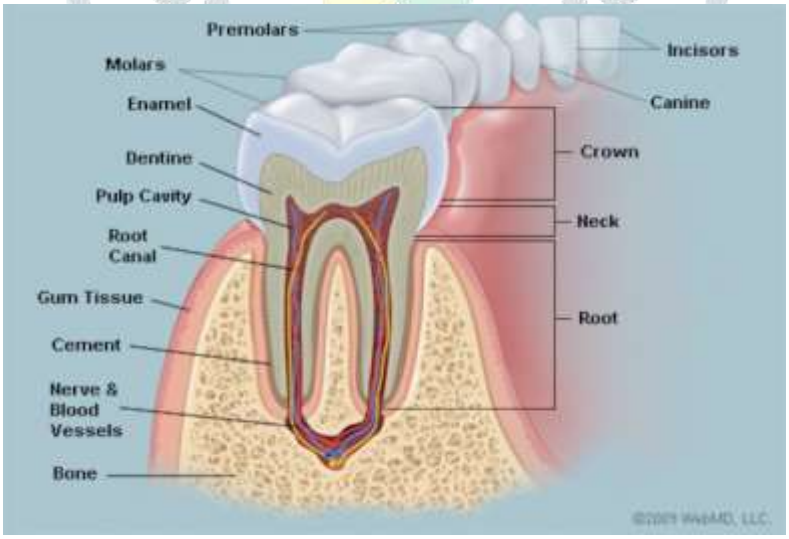
•**Canines (4 total):** The pointed teeth just outside the incisors.

•**Premolars (8 total):** Teeth between the canines and molars.

•**Molars (8 total):** Flat teeth in the rear of the mouth, best at grinding food.

•**Wisdom teeth or third molars (4 totals):** These teeth erupt at around age 18, but are often surgically removed to prevent displacement of other teeth.

The crown of each tooth projects into the mouth. The root of each tooth descends below the gum line, into the jaw.



Anatomy of Teeth

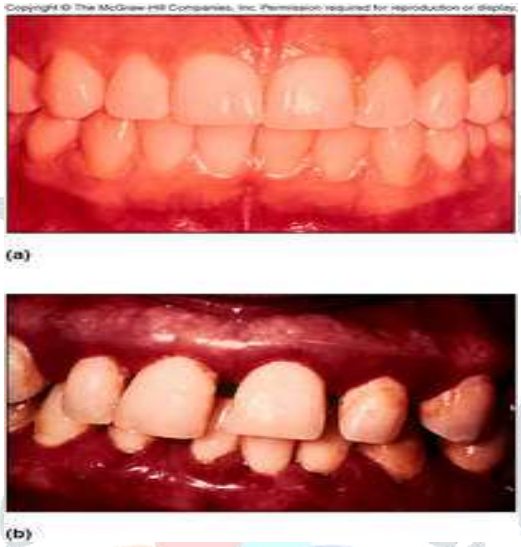
ANATOMY OF TEETH:

Tooth, plural teeth, any of the hard, resistant structures occurring on the jaws and in or around the mouth and pharynx areas of vertebrates. Teeth are used for catching and masticating food, for defence, and for other specialized purposes. The teeth of vertebrates represent the modified descendants of bony dermal (skin) plates that armoured ancestral fishes. A tooth consists of a crown and one or more roots. The crown is the functional

part that is visible above the gum. The root is the unseen portion that supports and fastens the tooth in the jawbone. The root is attached to the tooth-bearing bone the alveolar processes—of the jaws by a fibrous ligament called the periodontal ligament or membrane. The "neck" of the root is embraced by the fleshy gum tissue (a specialized area of connective tissue covered with mucous membrane that lines the mouth cavity). The shape of the crown and root vary among different teeth and among different species of animals.

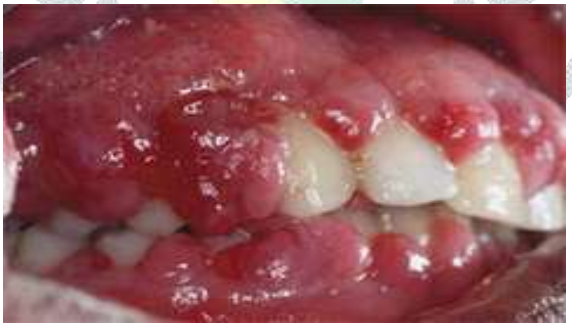
Classification of periodontal diseases:

• **Gingivitis**



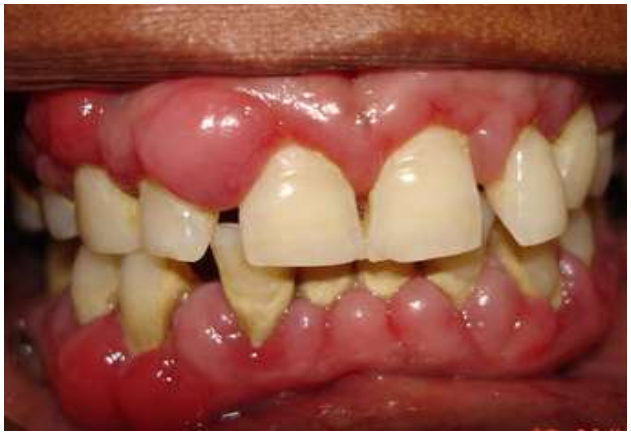
Gingivitis

• **Gingival enlargement:**



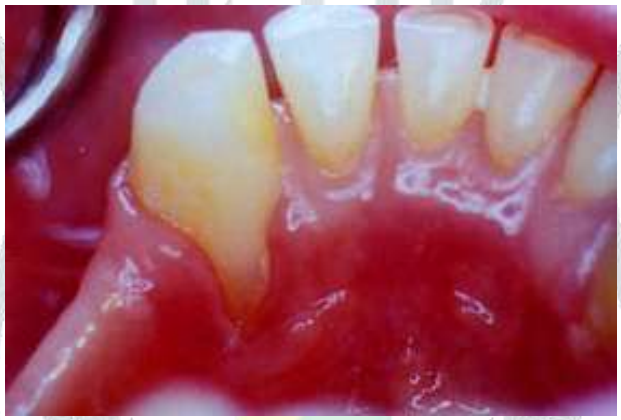
Gingival enlargement

Periodontitis:



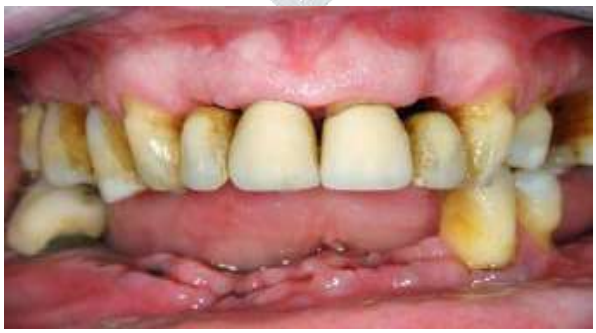
Periodontal

• Periodontal occlusal trauma:



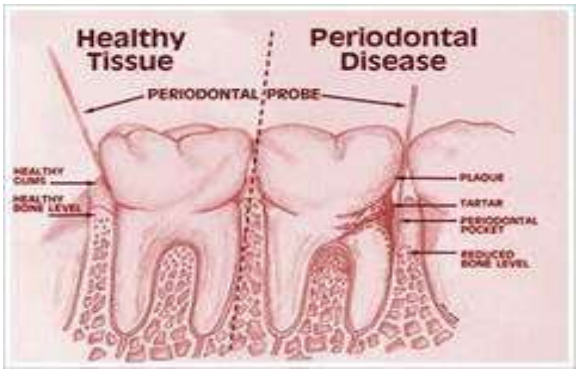
Periodontal occlusal trauma

• Gingival recession:



Gingival recession

- **Periodontitis:**



Periodontitis

Warning signs

The following are warning signs of periodontal disease:

- Bad breath or bad taste that won't go away
- Red or swollen gums
- Tender or bleeding gums
- Painful chewing
- Loose teeth
- Sensitive teeth
- Gums that have pulled away from your teeth
- Any change in the way your teeth fit together when you bite
- Any change in the fit of partial dentures

Risk factors

Certain factors increase the risk for periodontal disease:

- Smoking
- Diabetes
- Poor oral hygiene
- Stress
- Heredity
- Crooked teeth
- Underlying immune-deficiencies—e.g., AIDS
- Fillings that have become defective
- Taking medications that cause dry mouth
- Bridges that no longer fit properly

Prevention and treatment:

Gingivitis can be controlled and treated with good oral hygiene and regular professional cleaning. More severe forms of periodontal disease can also be treated successfully but may require more extensive treatment. Such treatment might include deep cleaning of the tooth root surfaces below the gums, medications prescribed to take by mouth or placed directly under the gums, and sometimes corrective surgery.

To help prevent or control periodontal diseases, it is important to:

- Brush and floss every day to remove the bacteria that cause gum disease.
- See a dentist at least once a year for checkups, or more frequently if you have and of the warning signs or risk factors mentioned above.

Treatment: Advanced gum disease, called periodontitis, affects almost half of Americans over the age of 30, according to a recent study by the Centres for Disease Control and Prevention (CDC). As common as the condition is, tooth loss is often the unfortunate outcome when left untreated. But today, with so many successful treatment options available for advanced periodontal disease, losing teeth doesn't have to be your next step with an unhealthy gum line.

Pocket Reduction Procedure: After scaling and root planning, if the gum tissue is not fitting snugly around the tooth and you can't keep the deep pocket area clean, you may be a candidate for periodontal pocket reduction or flap surgery. By folding back the gum tissue, your dentist or periodontist can remove infectious bacteria and smooth areas of damaged bone, allowing the gum tissue to reattach to healthy bone.

Gum Grafts: Exposed roots due to gum recession can be covered with gum grafts, wherein gum tissue is taken from your palate or from another source and used to cover the roots of one or more teeth. Covering exposed roots helps reduce sensitivity and protects your roots from decay, while stopping further gum recession and bone loss.

Regenerative Procedures: Bone grafting is a surgical procedure that promotes the growth of bone in an area where bone has been destroyed by periodontal disease. During this type of treatment, your dentist or periodontist will eliminate bacteria and then place either natural or synthetic bone in the area of bone loss, along with tissue-stimulating proteins to help your body effectively regrow bone and tissue.

MATERIAL AND METHODS

Crude Coriander was purchased from local market of Roorkee, Uttarakhand. Carbopol 940, sodium CMC, HPMC, PEG 400, Methyl Paraben, Propyl Paraben, Triethanolamine were issued from Institute laboratory.

Extraction of coriander seeds

i) **Percolation Method:** 100 gm plant materials (Coriandrum Sativum) were powered and soaked in 300 ml ethanol 70%. After 2 hrs, extracts were concentrated with ethanol 70% (700 ml) by percolation method. After 48 hrs, extracts were concentrated by rotary vaccum evaporator (Heidolph VV 2000). Further concentration was done over the boiling water bath.

ii) **Soxhlet Method:**

- 100 gm of coriander plant material dissolve in petroleum ether**.**
- heat 8 hrs, of the Soxhlet apparatus
- Extract filter
- Water bath
- Extract (honey type)

Preliminary phyco-chemical evaluation of crude extract:

The crude extract was evaluated for the presence of various phyto constituents such as carbohydrates, proteins, Alkaloids, glycosides, terpenes, steroids, flavanoids, tannins and Saponins using commonly employed precipitation and coloration reactions reported in standard reference books.

Carbohydrates:

The extract was dissolved in 10 ml of distilled water and filtered through Whatman No.1 filter paper and the filtrate is subjected to tests for carbohydrates.

a) **Molish test:** 2 ml solution was placed in a test tube. 1 drop of Molish Reagent wasadded. 2 ml of conc. HCL was added from the sides of the test tube. The test tube was observed for formation of a violet ring. A violet ring at the junction of the two liquids indicates presence of carbohydrates.

Alkaloid:

About 50 mg of Solvent free extract was stirred with 3 ml of dilute hydrochloric acid and then filtered thoroughly. The filtrate was tested carefully with various alkaloid reagents as follows:

a) **Mayer's test:** To a 1 ml of filtrate, few drops of Mayer's reagent are added by the side of the test tube. The white or creamy precipitate indicated test as positive.
b) **Wagner's test:** To a 1 ml of filtrate, few drops of Wagner's reagent are added by the side of the test tube. The color change was observed. A reddish-brown precipitates confirms the test as positive.
c) **Dragendorff's test:** To 1 ml of filtrate, 2 ml of Dragendorff's reagent are added and the result was observed carefully. A prominent yellow precipitate confirms the test as positive.

Glycosides:

a) **Borntrager's Test:** Extract was boiled with dilute sulphuric acid, filtered and to the filtrate chloroform was added and shaken well. The organic layer was separated to which ammonia is added slowly. Presence of glycoside is denoted by pink to red color in the ammonical layer.
b) **Legal Test:** The test is employed for digitoxose containing glycosides. The extract was dissolved in pyridine; sodium nitroprusside solution was added to it and made alkaline. Pink or red color indicates presence of gylcosides.

Terpenoid and steroid:

4 milligrams of extract was treated with 0.5 ml of acetic anhydride and 0.5 ml of chloroform. Then concentrated solution of sulphuric acid was added slowly and red violet color was observed for Terpenoid and green bluish color for steroids.

Flavonoids:

4 millilitres of extract solution was treated with 1.5 ml of 50% methanol solution. The solution was warmed and metal magnesium was added. To this solution, 5-6 drops of concentrated hydrochloric acid was added and red color was observed for Flavonoids and orange color for flavones.

Tannins:

To 0.5 ml of extract solution 1 ml of water and 1-2 drops of ferric chloride solution was added. Blue color was observed for Gallic tannins and green black for catecholic tannins.

Saponins:

About 0.2 g of the extract was shaken with 5 ml of distilled water and then heated to boil. Frothing (appearance of creamy miss of small bubbles) shows the presence of Saponins.

Thin Layer Chromatography (TLC):

Preparation of the plate:

The adsorbent used for thin layer chromatography was silica gel G. about 25g of silica gel G was taken in a glass mortar and about 35 ml of distilled water was added to it.

The mixture was stirred with glass rod until it became homogenous. This mixture was then allowed to swell for about 15 minutes. Then additional 15 ml of distilled water was added to it with string. The suspension was then transferred to a 150 ml flask fitted with a plastic stopper, and was shaken vigorously for about 2 minutes. This suspension was then spread immediately on thin layer chromatographic plates with the help of thin layer chromatography (TLC) applicator.

Drying and Storage of the plates:

The freshly coated plates were then air dried until the transparence of the layer had disappeared. The plates were then stacked in a drying rack and were heated in an oven for 30 minutes at 110^{o}C. The activated plates were kept in a desicator, till required for further use.

Application of the samples:

For applying test samples on TLC plate, glass capillaries were used. The spot were applied with the help of a transparent template, keeping a minimum distance of 1 cm between the two adjacent spots. The spots of the samples were marked on the top of the plate to know their identity.

Chromatographic Chamber, Condition of Saturation and the Development of TLC Plates:

The TLC chamber is rectangular glass chamber was used in the experiments. To avoid insufficient saturation and the undesirable edge effect, a smooth sheet of filter paper was placed in the TLC chamber in a U shaped and was allowed to be soaked in the developing solvents. The chamber was allowed to saturate for 24 hours before use. The experiments were carried out at room temperature in diffused daylight.

Developing solvent system

A chamber of developing solvent system was tried, for each residue, and the satisfactory resolution system were noted down.

Detector/Spraying Equipment

Compressed air sprayer with a fine nozzle was used to detect the different constituents present on TLC plates. Air compressor was attached to a glass sprayer. The sprayer was filled with 50 ml of the detecting reagent and then used. After each spray, the sprayer was washed separately with water, chromic acid, and distilled water and then with acetone. UV chamber can use for the substances exhibiting fluorescence.

TLC Profiling:

The various extract was subjected to thin layer chromatography to access the presence of constituents in each extract. Percolated silica gel plates were used for experiments.

TLC for flavonoids:

Presence of Flavonoids in various extract was investigated by using the following mobile phase.

Solvent system	Ratio
Ethyl acetate: Formic acid: GAA: Water	100: 11: 11: 26
Formic acid: Water: Ethyl acetate	7: 3

Mobile phase ratio of flavonoids

The development was done by using vanillin sulphuric acid regent (1% vanillin in H_2SO_4) development agent and observation of spots either in normal or UV light.

TLC for Alkaloids:

Presence of alkaloids in various extract was investigated by using the following mobile phase:

Solvent system	Ratio
Methanol: Benzene	39.1:60.9
Methanol: Chloroform	8:2

Mobile phase Ratio for Alkaloids

The development was done by using Dragendroff's reagent as the development agent and observation of spot either in normal or UV light.

TLC for Xanthones:

Presence of xanthones in Methanolic extract was investigated by using the following mobile phase.

Mobile phase	Ratio
Dichloromethane : Acetone	8:2
Chloroform : Acetic Acid	4:1

Mobile phase Ratio for Xanthones

The development was done by using Ammonia vapour chamber as the development agent and observation of spots either in normal or UV light.

TLC for ethyl acetate:

Mobile Phase	Ratio
Toulene : ethyl acetate	7:3
Chloroform : benzene	7:3

Mobile phase Ratio of ethyl acetate

The development was done by using Vanillin agent and observation of spot ethyl acetate in normal or UV light.

Preparation of gel formulation:

For preparation of gel formulation semisolid concentrated extract fruit of Coriandrum Sativum were used. Carbapol 940, Sodium CMC and HPMC polymers were used as gelling agent.

Composition of gel formulation with different polymers:

Ingredient (gm)	Formulation				
	F1	F2	F3	F4	F5
C. Sativum Extract	1	1	1	1	1
Carbopol 940	0.5	-	-	0.5	1
HPMC	-	2	-	3	5
PEG 400	13	13	13	13	13
Methyl Paraben	0.18	0.18	0.18	0.18	0.18
Propyl Paraben	0.02	0.02	0.02	0.02	0.02
Triethanolamine	q s	q s	-	-	-
Water qs upto	100	100	100	100	100
Sodium CMC	-	-	3	3	3

i) Evaluation of gel formulations

Physical appearance of gel formulations

Gel formulations were usually inspected for clarity, colour, homogeneity, consistency and presence of particles. Homogeneity was examined by microscope. In order to investigate the consistency of the formulations, a small quantity of gel was pressed between the thumb and the index fingers and the consistency of the gel was noticed.

Determination of pH in gel, formulations

pH was measured in each gel using a ph meter, which was celebrated before each use with standard buffer solution at ph 4 and 7. One gram each of the gel formulations was accurately weighed and dispersed in 10 ml of purified water. The electrode was inserted into the sample 10 min priors to taking the reading at the room temperature. The measurement of ph of each formulation was done in triplicate and average values are calculated. The measurement of ph was performed at 48 h, 1 week2 week1 month, 3 month and 6 months after preparation o detect any ph fluctuation with time.

RESULT & DISUSSION:

Morphology: Coriander fruits

FRUITS OF CORIANDER	
Condition	Fresh
Colour	Yellowish colour
Odour	Characteristics
Taste	Bitter
Size	1.5-3.0 mm (0.06-0.12)

Chemical test:

S.NO.	TEST	OBSERVATION
1	**Alkaloids**	
	Mayer test	(-ve)
	Dragendorff test	(+ve)
2	Carbohydrate	(+ve)
3	Glycosides	(+ve)
4	Flavonoids	(-ve)
5	Terponide (Salkowski test)	(+ve)
6	Saponin	(+ve)
7	Tannin	(+ve)

Evaluation of parameter:

Parameters	F1	F2	F3	F4	F5
pH meter	Good	Good	Good	Good	Good
Color	Good	Good	Good	Good	Good
Homogeneity	Good	Good	Not good	Not good	Good
Mucoadhesion	Average	Not Good	Satisfactory	Satisfactory	Good
Consistency	Average	Medium	Medium	Not good	Good
Release profile	Optimum	Optimum	Optimum	Optimum	Good

pH in gel formulation:

Physiochemical parameter	F_1	F_2	F_3	F_4	F_5
pH	5	5.8	5.5	6.7	7

CONCLUSION

The seed coriander fruits contain considerably polyphenols. Polyphenols can be used in periodontal pocket therapy due to antioxidant and antibacterial activity. Based on above result profile, F5 was selected as the best formulation. F5 containing 0.5% Carbopol 940 and shows satisfactory mucoadhesion property and optimum release profile. F5 produced significant growth inhibition zone against P. gingivalis. It is concluded that F5 could be used as antiseptic in the treatment of periodontitis.

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