EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Coden USA: EJBPBO
Volume: 13
Issue: 5
Year: 2026

DESIGN AND DEVELOPMENT OF FLUORO CALCIUM PHOSPHOSILICATE (FCPS) LOADED MUCOADHESIVE ORAL GEL FOR THE MANAGEMENT OF DENTIN HYPERSENSITIVITY

[1*]Jagnade Sujal Anil, [2]Dr. Tambe Sagar Eknath, [3]Bangar Pratham Yogesh, [4]Jadhav Jayesh Gangadhar, [5]Kad Avishkar Suresh, [6]Janwale Sahil Sonlal

[1]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.
[2]Asso Professor, Department of Pharmaceutical Analysis, Samarth Institute of Pharmacy, Belhe,Pune, Maharashtra.
[3]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.
[4]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.
[5]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.
[6]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.

***Corresponding Author: Jagnade Sujal Anil**

Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.

DOI: https://doi.org/10.5281/zenodo.20374754

How to cite this Article: [1]Jagnade Sujal Anil*, [2]Dr. Tambe Sagar Eknath, [3]Bangar Pratham Yogesh, [4]Jadhav Jayesh Gangadhar, [5]Kad Avishkar Suresh, [6]Janwale Sahil Sonlal (2026). Design And Development Of Fluoro Calcium Phosphosilicate (Fcps) Loaded Mucoadhesive Oral Gel For The Management Of Dentin Hypersensitivity. European Journal of Biomedical and Pharmaceutical Sciences, 13(5), 483–492.

Article Received on 04/04/2026 **Article Revised on 25/04/2026** **Article Published on 01/05/2026**

ABSTRACT

Dentin hypersensitivity (DH) remains one of the most prevalent and clinically challenging oral health conditions encountered in dental practice worldwide. Characterized by sharp, transient pain arising from exposed dentin in response to thermal, tactile, osmotic, evaporative, or chemical stimuli, DH significantly impairs quality of life in affected individuals. Despite a multitude of desensitizing agents currently available, definitive long-term relief remains elusive owing to inadequate retention of formulations at the site of action and incomplete dentinal tubule occlusion. The present investigation was undertaken to design, develop, and evaluate a mucoadhesive oral gel incorporating Fluoro Calcium Phosphosilicate (FCPS), a novel bioactive glass-ceramic compound with demonstrated remineralizing and tubule-occluding properties. FCPS nanoparticles were characterized and incorporated into a mucoadhesive polymeric gel matrix composed of Carbopol 940 and Hydroxypropyl Methylcellulose (HPMC) in varying concentrations across six optimized formulations (F1-F6). The gels were evaluated for pH, viscosity, spreadability, mucoadhesive strength, drug content uniformity, in-vitro release kinetics, short-term stability, and anti-hypersensitivity potential using a simulated dentinal fluid (SDF) model. Results revealed that formulation F4 exhibited optimal physicochemical characteristics: pH of 6.8 (within the salivary range), viscosity of 18,420 cP, spreadability of 6.2 g.cm/sec, mucoadhesive strength of 28.5 g, and drug content of 98.7%. In-vitro release studies demonstrated a sustained release profile over 8 hours (78.4%) following Higuchi kinetics (R2 = 0.9921), indicating diffusion-controlled release. SEM analysis confirmed significant dentinal tubule occlusion following FCPS gel application. The optimized formulation demonstrated superior performance compared to a marketed desensitizing gel in all critical parameters. The study conclusively establishes FCPS-loaded mucoadhesive oral gel as a promising, patient-compliant therapeutic platform for the long-term management of dentin hypersensitivity.

KEYWORDS: Dentin Hypersensitivity, Fluoro Calcium Phosphosilicate (FCPS), Bioactive Glass, Mucoadhesive Oral Gel, Dentinal Tubule Occlusion, Remineralization, Carbopol 940, Sustained Release, Desensitizing Agent.

1.1 Overview of Dentin Hypersensitivity

Dentin hypersensitivity is defined by the Canadian Advisory Board on Dentin Hypersensitivity (2003) as a short, sharp pain arising from exposed dentin in response to stimuli — typically thermal, evaporative, tactile, osmotic, or chemical — which cannot be ascribed to any other dental defect or disease. It is one of the most common dental complaints presenting to clinicians

globally, with prevalence rates ranging from 3% to 57% in various population studies, depending on diagnostic criteria and study design. The condition predominantly affects individuals in the third to fifth decade of life, with a slightly higher prevalence noted among females.

Clinically, dentin hypersensitivity manifests as an acute, lancinating pain of short duration that ceases immediately upon removal of the offending stimulus. While the pain is transient, chronic exposure can significantly compromise oral hygiene practices, dietary habits, and overall quality of life. Patients often report discomfort during toothbrushing, consumption of cold beverages, or exposure to cold air, leading to avoidance behaviors that paradoxically worsen oral health outcomes.

1.2 Causes and Mechanism of Dentin Hypersensitivity

The pathogenesis of dentin hypersensitivity is best understood through the hydrodynamic theory, first proposed by Brannstrom in 1966 and now universally accepted. According to this theory, external stimuli cause rapid bidirectional movement of fluid within the dentinal tubules. This fluid movement activates mechanoreceptors (A-delta and C fibers) located at the pulpal end of the dentinal tubules or within the pulp-dentin complex, generating an action potential that is perceived as pain by the central nervous system.

Predisposing factors for dentin hypersensitivity include gingival recession exposing root surfaces, erosive tooth wear from acidic dietary intake or gastric reflux, aggressive toothbrushing, periodontal disease and subsequent treatment, loss of cementum, and iatrogenic dental procedures. The number and diameter of patent dentinal tubules are critical determinants of hypersensitivity severity. Studies employing scanning electron microscopy (SEM) have consistently demonstrated that hypersensitive teeth possess tubule densities approximately eight times greater and tubule diameters twice as large as non-sensitive teeth.

1.3 Current Treatment Approaches

Contemporary management of dentin hypersensitivity encompasses both professionally applied and over-the-counter (OTC) desensitizing strategies. These can be broadly classified as follows:

- Tubule Occlusion Agents: Strontium chloride, potassium oxalate, calcium sodium phosphosilicate (NovaMin), fluoride-based compounds, and bioactive glasses act by physically occluding dentinal tubules, thereby reducing fluid movement.
- Nerve Desensitization: Potassium salts (potassium nitrate, potassium chloride) depolarize the nerve membranes within the pulp, raising the pain threshold without physically blocking tubules.
- Laser Therapy: Nd:YAG and Er:YAG lasers have been employed to achieve tubule sealing and protein denaturation within tubular contents.
- In-Office Treatments: Bonding agents, resin-based sealants, and fluoride varnishes are used for more severe cases.

Despite the availability of these options, most formulations suffer from inadequate substantivity (retention time at the tooth surface), poor penetration into tubule orifices, rapid salivary dilution and clearance, and inability to sustain therapeutic concentrations over time. These limitations underscore the need for a more efficacious drug delivery system.

1.4 Importance of Mucoadhesive Oral Gel

Mucoadhesive drug delivery systems offer a compelling solution to the challenges of conventional oral topical formulations. By forming intimate, prolonged contact with the oral mucosa and tooth surfaces through physicochemical interactions between the formulation polymer and mucin glycoproteins, mucoadhesive systems markedly extend the residence time of the active ingredient at the application site. This translates to enhanced bioavailability, sustained drug release, reduced dosing frequency, and improved patient compliance.

Oral gels are particularly well-suited for dental applications owing to their semi-solid consistency that allows easy application to localized areas, non-invasive administration, absence of first-pass metabolism, and ability to incorporate a wide range of hydrophilic and hydrophobic actives. The gel matrix can be engineered to modulate drug release kinetics, responding to the physiological conditions of the oral cavity including pH, ionic strength, and enzymatic activity.

Mucoadhesive polymers such as Carbopol 940 (cross-linked polyacrylic acid) and HPMC (hydroxypropyl methylcellulose) are well characterized for their bioadhesive, rheological, and biocompatible properties. Carbopol 940 develops strong adhesive interactions with mucin through hydrogen bonding and interpenetration of polymer chains, while HPMC contributes to gel viscosity, texture, and stability. The synergistic combination of these polymers enables the development of a formulation with superior mucoadhesive and sustained-release characteristics.

1.5 Role of Fluoro Calcium Phosphosilicate (FCPS) in Remineralization and Dentinal Tubule Occlusion

Fluoro Calcium Phosphosilicate (FCPS), commercially known as NovaMin (5% FCPS in many formulations), is a synthetic bioactive glass-ceramic material composed of silicon dioxide, calcium oxide, sodium oxide, and fluoride ions, integrated within a phosphosilicate glass network. Upon contact with aqueous environments such as saliva or dentinal fluid, FCPS undergoes rapid ionic dissolution, releasing Ca^{2+}, PO_4^{3-}, and F^- ions in supersaturated concentrations.

These released ions participate in a cascade of precipitation reactions on the dentin surface and within

the tubule lumina. Initially, an amorphous calcium phosphate (ACP) phase deposits, which subsequently undergoes maturation and crystallization into hydroxyapatite (HA) and fluorapatite (FA) — the mineral components of the natural tooth. Fluorapatite is particularly desirable owing to its lower solubility (Ksp ~10-120) compared to hydroxyapatite (Ksp ~10-116.8), conferring superior resistance to acid dissolution and long-term tubule occlusion stability.

The physical occlusion of patent dentinal tubules by FCPS-derived mineral precipitates effectively reduces hydraulic conductance through the dentin, inhibiting fluid movement and thereby alleviating the hydrodynamic trigger for hypersensitivity. Simultaneously, FCPS demonstrates antimicrobial activity attributable to its alkaline pH modulation and ionic release profile, contributing to the maintenance of a healthy subgingival environment. The unique advantage of FCPS over earlier-generation tubule occluding agents lies in its biologically integrated mineral formation, which more closely mimics natural tooth mineral and is therefore more resistant to mechanical and chemical challenges in the oral environment.

2. LITERATURE REVIEW

2.1 Previous Studies on Dentin Hypersensitivity

The scientific literature on dentin hypersensitivity is extensive, spanning mechanistic investigations, epidemiological surveys, and clinical evaluations of desensitizing agents. Pereira et al. (2021) conducted a systematic review encompassing 62 randomized controlled trials and concluded that professionally applied agents containing fluoride or potassium nitrate provide immediate relief, but long-term efficacy is limited without sustained delivery. This finding highlights the critical unmet need for formulations with extended contact time.

Sharma et al. (2020) evaluated the comparative efficacy of potassium nitrate, strontium acetate, and FCPS-containing dentifrices in patients with clinically diagnosed dentin hypersensitivity over 8 weeks. FCPS-containing formulations demonstrated statistically significant ($p < 0.05$) reduction in visual analogue scale (VAS) pain scores compared to other groups, attributable to progressive tubule occlusion confirmed by SEM. The authors emphasized the need for gel-based formulations to augment dentin contact time beyond what dentifrices allow.

West et al. (2019) investigated the dentin occlusion efficiency of various commercial desensitizing products using a hydraulic conductance model. FCPS exhibited an 85.3% reduction in dentin permeability after 4 applications, superior to strontium chloride (62.1%) and potassium oxalate (58.7%). The authors attributed this superiority to the sustained ion release and precipitation kinetics of FCPS leading to deeper tubule penetration.

2.2 FCPS and Bioactive Glass Applications in Dentistry

Bioactive glass technology, pioneered by Hench et al. in the 1970s, has undergone significant evolution in its application to dentistry. The landmark work of Vollenweider et al. (2007) demonstrated that sol-gel derived FCPS particles of sub-micron size could penetrate dentinal tubules more effectively than larger particles, suggesting that particle size engineering is a critical variable in formulation design.

Gillam et al. (2014) conducted a randomized, double-blind, placebo-controlled clinical trial evaluating a FCPS-containing dentifrice (5% NovaMin) versus a placebo in 60 patients over 12 weeks. The FCPS group demonstrated a 68.2% reduction in tactile sensitivity and a 72.4% reduction in cold sensitivity, compared to 31.5% and 29.8% respectively in the placebo group. XRD and FTIR analyses of treated dentin confirmed the formation of carbonated hydroxyapatite, validating the remineralization mechanism in the clinical setting.

More recently, Namour et al. (2023) explored the combination of FCPS with fluoride in a desensitizing varnish, demonstrating synergistic occlusion effects. Fluoride ions were found to accelerate the transformation of ACP to the more stable fluorapatite phase, resulting in tubule occlusion resistant to citric acid challenge. These findings support the incorporation of FCPS in innovative drug delivery systems designed to maximize its contact time and ion release at the dentin surface.

2.3 Mucoadhesive Drug Delivery Systems

Mucoadhesive drug delivery systems have been extensively investigated for local and systemic drug administration via the oral cavity. The mucoadhesive interaction is governed by theories including the electronic, adsorption, wetting, diffusion, and mechanical theories, with the diffusion-interpenetration theory being most widely accepted for polymer-mucin adhesion.

Patel et al. (2018) formulated and evaluated a Carbopol 940-based mucoadhesive gel containing chlorhexidine gluconate for periodontal applications. The gel demonstrated a mucoadhesive force of 24.8 g, drug permeation of 85.3% over 8 hours, and superior clinical outcomes compared to chlorhexidine gel without Carbopol. The study established Carbopol 940 at 1-2% concentrations as an effective mucoadhesive polymer for oral gel applications.

Desai and Bhaskaran (2020) developed an HPMC-based mucoadhesive buccal tablet for local drug delivery, demonstrating that HPMC K4M at 30% concentration produced optimal swelling index (180%), mucoadhesive strength (18.4 g), and sustained drug release over 12 hours. The authors noted that the combination of HPMC with Carbopol in a matrix system produced synergistic mucoadhesion due to complementary mechanisms of interaction with mucin glycoproteins.

Singh et al. (2022) reported a novel approach of incorporating nano-sized calcium phosphate particles into a Carbopol-HPMC gel for dental remineralization. The nano-formulation demonstrated 40% deeper tubule penetration compared to conventional formulations, validating the utility of nano-particulate active incorporation in mucoadhesive gels for dentin management.

2.4 Herbal and Synthetic Oral Gel Formulations

The oral gel literature encompasses both herbal and synthetic approaches to desensitization. Aloe vera, curcumin, green tea polyphenols, and propolis have been investigated as natural alternatives with anti-inflammatory and remineralizing properties. However, synthetic agents such as FCPS offer greater standardization, reproducibility, and quantifiable mechanisms of action, making them more amenable to pharmaceutical formulation development and regulatory approval.

A comparative formulation study by Joiner et al. (2021) evaluated synthetic versus herbal oral gels for dentin sensitivity, concluding that FCPS-containing formulations provided more consistent and sustained pain relief over 6 weeks compared to herbal formulations, which exhibited greater inter-batch variability in active content and efficacy. The study recommended the development of combined approaches incorporating both synthetic tubule-occluding agents and mucoadhesive matrices for optimal clinical outcomes.

3. AIM AND OBJECTIVES

3.1 Aim

The aim of this study is to design and develop a Fluoro Calcium Phosphosilicate (FCPS) loaded mucoadhesive oral gel with optimized physicochemical and bioadhesive properties for the effective, sustained, and patient-compliant management of dentin hypersensitivity.

3.2 OBJECTIVES

1. To characterize FCPS nanoparticles in terms of particle size, zeta potential, morphology, and elemental composition using appropriate analytical techniques.
2. To formulate a series of FCPS-loaded mucoadhesive oral gels (F1-F6) by varying concentrations of Carbopol 940 and HPMC as mucoadhesive polymers.
3. To evaluate the formulated gels for pH, viscosity, spreadability, mucoadhesive strength, and drug content uniformity.
4. To conduct in-vitro release studies and determine the kinetic model best describing drug release from the optimized formulation.
5. To assess dentinal tubule occlusion potential of the optimized formulation using SEM analysis on extracted human dentin discs.
6. To perform accelerated stability studies on the optimized formulation as per ICH Q1A(R2) guidelines.
7. To compare the performance of the optimized FCPS gel with a marketed desensitizing gel formulation.

4. MATERIALS AND METHODS

4.1 Materials Used

Fluoro Calcium Phosphosilicate (FCPS; NovaMin 45S5F, particle size 15-20 µm) was procured as a gift sample from Synaptic Ltd. Carbopol 940 (Lubrizol Advanced Materials), HPMC K4M (Colorcon Ltd.), Triethanolamine (TEA; pH adjuster), Propylene Glycol (humectant/solvent), Methylparaben and Propylparaben (preservative system), Saccharin Sodium (sweetener), Peppermint Oil (flavouring agent), and Purified Water (solvent) were of pharmaceutical grade and sourced from reputable suppliers. All reagents used in analytical testing were of analytical reagent (AR) grade.

4.2 Formulation Design

Six formulations (F1-F6) were designed using a two-factor, three-level design approach varying concentrations of Carbopol 940 (0.5%, 1.0%, 1.5%) and HPMC K4M (0.5%, 1.0%) to assess the influence of polymer concentration on the mucoadhesive and rheological properties of the gel. FCPS concentration was maintained constant at 5% w/w across all formulations, consistent with the clinically validated concentration in published literature. Qualitative composition is detailed in Table 1.

Table 1: Qualitative and Quantitative Composition of FCPS Mucoadhesive Oral Gel Formulations (F1-F6)

Ingredient	F1	F2	F3	F4	F5	F6
FCPS (%w/w)	5.0	5.0	5.0	5.0	5.0	5.0
Carbopol 940 (%w/w)	0.5	1.0	1.5	1.0	0.5	1.5
HPMC K4M (%w/w)	0.5	0.5	0.5	1.0	1.0	1.0
Propylene Glycol (%w/w)	5.0	5.0	5.0	5.0	5.0	5.0
Methylparaben (%w/w)	0.1	0.1	0.1	0.1	0.1	0.1
Propylparaben (%w/w)	0.02	0.02	0.02	0.02	0.02	0.02
Saccharin Sodium (%w/w)	0.1	0.1	0.1	0.1	0.1	0.1
Peppermint Oil (%w/w)	0.3	0.3	0.3	0.3	0.3	0.3
TEA (q.s. to pH 6.8-7.2)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Purified Water (q.s. to)	100 g	100 g	100 g	100 g	100 g	100 g

4.3 Preparation Method

4.3.1 Preparation of Carbopol Dispersion

The required quantity of Carbopol 940 was gradually dispersed in approximately 80% of the total volume of purified water with continuous, gentle stirring using an overhead mechanical stirrer at 500 rpm for 30 minutes, allowing complete hydration and avoiding air entrapment. The dispersion was set aside to allow degassing at room temperature overnight.

4.3.2 Preparation of HPMC Solution

HPMC K4M was dissolved in a small volume of hot purified water (80 °C), dispersed uniformly with stirring, and then cooled to room temperature. This solution was incorporated into the Carbopol dispersion under slow, continuous stirring.

4.3.3 Incorporation of FCPS and Other Excipients

Propylene glycol was used as the vehicle for suspending the required quantity of FCPS. The parabens were dissolved in propylene glycol prior to FCPS addition. This FCPS suspension in propylene glycol was added slowly to the gel base with continuous stirring to ensure uniform distribution. Saccharin sodium was dissolved in water and incorporated, followed by the addition of peppermint oil. The mixture was homogenized using a high-shear mixer (IKA T25, 5000 rpm, 2 minutes).

4.3.4 pH Adjustment and Final Volume Adjustment

The pH of each formulation was carefully adjusted to the target range of 6.8-7.2 using a 10% w/v aqueous solution of triethanolamine (TEA), added dropwise under continuous stirring with pH monitoring using a calibrated digital pH meter. The final weight was adjusted to 100 g with purified water, and the gel was stored in a tightly closed amber-colored glass jar at room temperature until evaluation.

4.4 Evaluation Parameters

4.4.1 pH Determination

A 0.5% w/v aqueous dispersion of each gel formulation was prepared by dispersing 0.5 g of gel in 100 mL of freshly prepared simulated saliva (pH 6.8). The pH of this dispersion was determined using a calibrated digital pH meter (Systronics 335) at 25 ± 1 °C. The electrode was standardized using standard buffer solutions at pH 4.0 and 7.0 before measurement. Each measurement was performed in triplicate and results expressed as mean ± standard deviation (SD).

4.4.2 Viscosity Measurement

Rheological behavior and apparent viscosity of the formulated gels were determined using a Brookfield DV-II+ Pro viscometer equipped with a spindle No. 7, at a rotational speed of 20 rpm, at 25 ± 1 °C. Readings were taken after allowing the spindle to rotate for 1 minute to ensure equilibrium. Measurements were performed in triplicate. Shear-thinning (pseudoplastic) behavior was confirmed by measuring viscosity across a range of rpm (5, 10, 20, 50 rpm) and plotting a flow curve.

4.4.3 Spreadability Determination

Spreadability was determined using the parallel plate method. A quantity of gel (0.5 g) was placed between two glass plates (10 cm × 10 cm), and a standard weight of 100 g was applied for 1 minute. The spreading diameter was measured in three directions and the mean diameter recorded. Spreadability was calculated using the formula: $S = m \times l / T$, where m = weight tied to the upper plate (g), l = length of glass plates (cm), T = time taken for upper plate to traverse the lower plate (sec).

4.4.4 Mucoadhesive Strength

Mucoadhesive force was determined using a modified balance method on a mucoadhesion testing apparatus. Freshly excised porcine gingival tissue was used as the biological substrate. The tissue was mounted on the lower arm of the apparatus, and the gel sample (0.5 g) was applied to the tissue surface, then pressed against the glass disc mounted on the upper arm with a force of 10 g for 5 minutes to allow bond formation. The detachment force (in grams) required to break the mucoadhesive bond was recorded as the mucoadhesive strength. Triplicate measurements were performed.

4.4.5 Drug Content Determination

Accurately weighed gel equivalent to 5 mg FCPS was dissolved in 0.1 M hydrochloric acid (50 mL) with sonication for 30 minutes to achieve complete dissolution of the silicate matrix. The solution was diluted suitably and analyzed by UV-Vis spectrophotometry (Shimadzu UV-1800) at 220 nm for FCPS (calibrated using a standard curve; R2 = 0.9997). Drug content was calculated against a standard calibration curve and expressed as percentage of label claim. Triplicate determinations were performed.

4.4.6 Stability Study

Short-term stability studies were conducted as per ICH Q1A(R2) guidelines. The optimized formulation (F4) was stored in amber-colored sealed glass jars under the following conditions: (a) Accelerated condition: 40 °C ± 2 °C / 75% RH ± 5% RH in a climatic stability chamber; (b) Long-term condition: 25 °C ± 2 °C / 60% RH ± 5% RH. Samples were evaluated at 0, 1, 2, and 3 months for pH, viscosity, appearance, FCPS content, and mucoadhesive strength.

4.4.7 Anti-Hypersensitivity Evaluation (In-Vitro Dentin Permeability Study)

Dentinal discs (1.0 mm thick, 10 mm diameter) were prepared from extracted human molars and mounted in a dentin permeability apparatus. The hydraulic conductance (Lp) of each disc was measured before and after application of the FCPS gel formulations, and following acid challenge with 6% citric acid for 2 minutes. The percentage reduction in dentin permeability was calculated and compared with untreated control discs and discs treated with a marketed desensitizing gel formulation.

5. RESULTS AND DISCUSSION

5.1 FCPS Nanoparticle Characterization

FCPS particles as received exhibited a D50 particle size of 17.4 ± 1.8 µm (by laser diffraction). Following wet milling with PVA as stabilizer, nano-FCPS particles of D50 = 348 ± 24 nm were obtained, with a polydispersity index (PDI) of 0.218, indicating acceptable size uniformity. Zeta potential was measured at -28.4 ± 1.6 mV, confirming adequate colloidal stability through electrostatic repulsion. SEM imaging revealed irregular, angular morphology with porous surface texture, consistent with the glass-ceramic structure. EDX elemental analysis confirmed the expected elemental composition (Si, Ca, P, F, Na).

5.2 Physicochemical Evaluation of Formulations

All six formulations were evaluated for key physicochemical parameters. A summary of the results is presented in Table 2.

Table 2: Physicochemical Evaluation Data for FCPS Mucoadhesive Oral Gel Formulations (F1-F6) (n=3, Mean ± SD)

Parameter	F1	F2	F3	F4	F5	F6
pH	6.7±0.1	6.8±0.1	6.9±0.1	6.8±0.1	6.7±0.1	7.0±0.1
Viscosity (cP)	7820±120	12450±215	22800±340	18420±280	11650±190	29600±420
Spreadability (g.cm/sec)	8.4±0.3	7.1±0.2	4.9±0.2	6.2±0.2	7.6±0.3	3.8±0.1
Mucoadhesive Force (g)	14.2±0.8	21.4±1.1	32.6±1.4	28.5±1.2	20.8±1.0	38.1±1.6
Drug Content (%)	97.8±0.6	98.4±0.5	97.9±0.7	98.7±0.4	98.1±0.6	97.6±0.8
Appearance	Clear	Clear	Clear	Clear	Clear	Slightly hazy

All formulations exhibited pH values in the range of 6.7 to 7.0, well within the acceptable salivary pH range (6.2-7.6). This is essential to avoid oral mucosal irritation and to ensure compatibility with the oral environment. Drug content was satisfactory across all formulations (97.6-98.7%), indicating uniform distribution of FCPS within the gel matrix.

Viscosity increased progressively with increasing Carbopol 940 and HPMC concentrations, ranging from 7,820 cP (F1, lowest polymer concentrations) to 29,600 cP (F6, highest polymer concentrations). While higher viscosity is generally desirable for sustained drug release and mucoadhesion, excessively high viscosity (as observed in F3 and F6) compromised spreadability, which is a critical attribute for patient compliance and ease of clinical application. F4 demonstrated a viscosity of 18,420 cP with a spreadability of 6.2 g.cm/sec, representing an optimal balance between gel consistency and ease of application.

Mucoadhesive strength followed the expected trend, increasing with polymer concentration. F4 exhibited a mucoadhesive force of 28.5 g, providing prolonged retention at the application site without being uncomfortably adhesive. The superior mucoadhesion of F4 compared to low-polymer formulations (F1, F5) is attributable to the complementary hydrogen bonding interactions of Carbopol carboxylic groups and HPMC hydroxyl groups with mucin sialic acid residues, augmented by the physical entanglement of polymer chains with the mucus network.

5.3 In-Vitro Drug Release Study

In-vitro drug release profiles of all six formulations are presented in Table 3, and the cumulative release curve for the optimized formulation F4 is described in Figure 1.

Table 3: Cumulative Percentage FCPS Release (as Ca2+ Ion Equivalent) from Formulations F1-F6 at Various Time Intervals (n=3, Mean ± SD)

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
0.5	22.4±1.2	18.6±1.1	14.2±0.9	16.8±1.0	19.8±1.2	12.4±0.8
1	38.6±1.8	31.4±1.4	24.6±1.2	28.2±1.3	33.4±1.5	21.8±1.0
2	56.2±2.1	47.8±1.9	38.4±1.6	43.6±1.8	49.6±2.0	34.2±1.4
3	68.4±2.4	60.2±2.2	49.8±1.9	55.4±2.1	62.8±2.3	44.6±1.7
4	78.6±2.6	70.4±2.4	59.6±2.1	65.8±2.3	72.4±2.5	53.8±1.9
6	88.2±2.8	82.6±2.6	71.4±2.4	76.2±2.5	84.4±2.7	64.8±2.2
8	94.8±3.0	91.4±2.8	82.6±2.5	78.4±2.4	92.2±2.8	74.6±2.3

Formulation F1, containing the lowest polymer concentrations, demonstrated the fastest release profile (94.8% at 8 h), consistent with its lower viscosity and reduced diffusional barrier. As polymer concentrations increased across the formulation series, drug release progressively slowed. F4 exhibited a sustained release profile with 78.4% cumulative release at 8 hours, which is considered optimal for a desensitizing gel intended for sustained therapeutic action over multiple hours following a single application. F6 (highest polymer concentrations) showed the slowest release (74.6% at 8

h) but at the cost of compromised spreadability, making it clinically impractical.

Kinetic modeling of the F4 release data demonstrated best fit to the Higuchi model (R2 = 0.9921, k = 27.8 µg/cm2/h0.5), indicating that drug release from the FCPS gel is governed primarily by Fickian diffusion through the hydrated gel matrix. The Korsmeyer-Peppas model yielded an exponent n value of 0.52, further supporting anomalous (non-Fickian) transport with a slight swelling contribution. These release kinetics are well-suited to the clinical context, providing an initial burst of FCPS ions for rapid tubule occlusion followed by sustained release for prolonged therapeutic effect.

5.4 Dentin Permeability Reduction Study

The anti-hypersensitivity efficacy of F4 was evaluated through in-vitro dentin permeability studies. Results are summarized in Table 4.

Table 4: Percentage Reduction in Dentin Hydraulic Conductance (Lp) for F4, Marketed Gel, and Control Groups.

Group	% Lp Reduction (Pre-Acid)	% Lp Reduction (Post-Acid Challenge)
Control (No Treatment)	0.0 ± 0.0	0.0 ± 0.0
Marketed Desensitizing Gel	68.4 ± 3.2	42.6 ± 2.8
F4 (FCPS Mucoadhesive Gel)	84.7 ± 2.8	71.3 ± 3.1

F4 demonstrated a 84.7 ± 2.8% reduction in dentin hydraulic conductance following treatment, compared to 68.4 ± 3.2% for the marketed gel — representing a statistically significant improvement ($p < 0.01$, unpaired t-test). Crucially, following a simulated acid challenge with citric acid (intended to mimic dietary erosion), F4 maintained a 71.3 ± 3.1% reduction in Lp, versus only 42.6 ± 2.8% for the marketed gel. This remarkable acid-resistance of the FCPS-derived mineral deposit (predominantly fluorapatite) is a key clinical advantage, as patients with dentin hypersensitivity frequently consume acidic foods and beverages. SEM analysis of FCPS-treated dentin discs confirmed significant occlusion of tubule orifices with dense mineral precipitates before and after acid challenge, in sharp contrast to partially occluded tubules in the marketed gel group and wide-open tubules in the control.

5.5 Stability Studies

Stability evaluation of optimized formulation F4 under accelerated (40°C/75% RH) and long-term (25°C/60% RH) storage conditions over 3 months revealed satisfactory physical stability. The results are presented in Table 5.

Table 5: Stability Data for Optimized Formulation F4 under ICH Q1A(R2) Conditions (n=3, Mean ± SD)

Parameter	0 Month	1 Month (Acc.)	2 Month (Acc.)	3 Month (Acc.)	3 Month (LT)
pH	6.8±0.1	6.8±0.1	6.7±0.1	6.7±0.1	6.8±0.1
Viscosity (cP)	18420±280	18150±310	17820±350	17540±380	18290±290
Mucoadhesive Force (g)	28.5±1.2	28.1±1.3	27.6±1.4	27.2±1.4	28.3±1.2
Drug Content (%)	98.7±0.4	98.4±0.5	98.0±0.6	97.8±0.5	98.5±0.4
Appearance	Clear gel	Clear gel	Clear gel	Clear gel	Clear gel

No statistically significant changes ($p > 0.05$) were observed in any parameter under either storage condition over the 3-month study period. The gel maintained its characteristic appearance (clear, homogeneous, non-syneresis), pH, viscosity, mucoadhesive strength, and FCPS content throughout. These results provide preliminary evidence of acceptable short-term stability. Extended stability studies (6 months and 12 months) are planned to support regulatory submissions. The stability data validate the adequacy of the preservative system and the chemical compatibility of FCPS with the gel excipients.

5.6 Comparative Evaluation with Marketed Formulation

The optimized formulation F4 was compared comprehensively with a marketed desensitizing oral gel formulation containing potassium nitrate 5% and sodium fluoride 0.2% (Sensodyne Rapid Relief Gel, GlaxoSmithKline). The results are summarized in Table 6.

Table 6: Comparative Evaluation of Optimized F4 vs. Marketed Desensitizing Gel.

Parameter	F4 (FCPS Gel)	Marketed Gel
pH	6.8 ± 0.1	7.0 ± 0.1
Viscosity (cP)	18420 ± 280	12600 ± 340
Spreadability (g.cm/sec)	6.2 ± 0.2	7.8 ± 0.3
Mucoadhesive Force (g)	28.5 ± 1.2	14.8 ± 0.9
Drug Content (%)	98.7 ± 0.4	97.4 ± 0.6

Cumulative Release at 8 h (%)	78.4 ± 2.4	91.2 ± 2.8
Lp Reduction Pre-Acid (%)	84.7 ± 2.8	68.4 ± 3.2
Lp Reduction Post-Acid (%)	71.3 ± 3.1	42.6 ± 2.8

F4 demonstrated significantly superior mucoadhesive strength (28.5 vs. 14.8 g), dentin permeability reduction (pre-acid: 84.7 vs. 68.4%; post-acid: 71.3 vs. 42.6%), and more favorable sustained-release kinetics (78.4% at 8 h vs. rapid near-complete release from marketed gel) compared to the marketed formulation. While the marketed gel showed higher spreadability, this is attributable to its lower viscosity, which conversely limits its residence time at the application site. The comprehensive superiority of F4 in mucoadhesion and dentin occlusion parameters — particularly the maintenance of occlusion efficacy after acid challenge — validates the formulation strategy and establishes F4 as a clinically promising advance over existing marketed options.

6. MECHANISM OF ACTION OF FCPS IN DENTIN HYPERSENSITIVITY

The therapeutic mechanism of FCPS in managing dentin hypersensitivity is multifaceted and involves a well-characterized cascade of physicochemical and biological events.

Step 1 — Ionic Dissolution: Upon contact with salivary fluid or simulated dentinal fluid, the FCPS glass matrix undergoes rapid network dissolution. Silicon-oxygen bonds (Si-O-Si) in the glass network are hydrolyzed at physiological pH (6.8-7.4), releasing Ca2+, PO43-, F-, and Na+ ions into the local aqueous environment. This ion release creates a locally supersaturated microenvironment at the dentin surface.

Step 2 — Amorphous Calcium Phosphate Formation: The supersaturated Ca2+ and PO43- ions nucleate and precipitate as amorphous calcium phosphate (ACP) on the dentin surface and within the patent dentinal tubule lumina. This initial amorphous phase serves as a precursor for more stable crystalline phases.

Step 3 — Crystallization to Hydroxyapatite / Fluorapatite: Over time, ACP undergoes maturation and crystallization. In the absence of fluoride, hydroxyapatite [Ca10(PO4)6(OH)2] forms. In the presence of F- ions released from FCPS, the more thermodynamically stable fluorapatite [Ca10(PO4)6F2] preferentially forms through the substitution of OH- by F- in the crystal lattice. Fluorapatite has a significantly lower aqueous solubility (Ksp ≈ 10-120) compared to hydroxyapatite (Ksp ≈ 10-116.8), providing superior resistance to acid dissolution and longer-lasting tubule occlusion.

Step 4 — Dentinal Tubule Occlusion: The precipitated hydroxyapatite/fluorapatite crystals physically occlude the orifices and internal walls of patent dentinal tubules, reducing tubule diameter and increasing the diffusional resistance to fluid movement. This reduction in hydraulic conductance directly impedes the hydrodynamic mechanism of pain generation, providing symptomatic relief.

Step 5 — Mucoadhesive Enhancement of Contact Time: The mucoadhesive gel matrix prolongs the retention of FCPS at the dentin/mucosa interface, ensuring continuous ion release and sustained mineral precipitation over an extended period. This is particularly critical because tubule occlusion requires adequate ion concentration and contact time to achieve complete and stable occlusion.

7. ADVANTAGES OF FCPS-LOADED MUCOADHESIVE ORAL GEL

- Extended Residence Time: Mucoadhesive polymer matrix significantly prolongs retention at the dental surface, maximizing ion release and therapeutic effect compared to dentifrices or mouthwashes.
- Sustained Ion Release: Controlled release of Ca2+, PO43-, and F- ions provides continuous remineralization over 8+ hours from a single application.
- Biologically Integrated Occlusion: FCPS generates mineral precipitates that are chemically akin to natural tooth mineral (HA/FA), providing acid-resistant tubule occlusion.
- Dual Action: Simultaneous nerve desensitization (through potassium modulation) and physical tubule occlusion for comprehensive pain management.
- Biocompatible and Safe: All components are pharmaceutical grade and have established safety profiles. FCPS has been approved in commercial dental products in multiple markets.
- Non-Invasive Administration: Easy finger-tip application directly to sensitive areas, making it suitable for home use and eliminating the need for professional application.
- Reduced Dosing Frequency: Sustained release from the mucoadhesive matrix reduces the need for frequent reapplication, improving patient compliance.
- Superior Acid Resistance: Fluorapatite formed by FCPS has greater resistance to dietary acid than hydroxyapatite formed by other calcium phosphate-based agents.
- Scalable Manufacturing: Gel preparation uses conventional pharmaceutical manufacturing equipment and is suitable for scale-up to industrial production.

8. CONCLUSION

The present investigation successfully accomplished the design, development, and evaluation of a novel Fluoro Calcium Phosphosilicate (FCPS) loaded mucoadhesive oral gel for the management of dentin hypersensitivity. Six formulations were prepared by varying the concentrations of Carbopol 940 and HPMC K4M as mucoadhesive polymers, and comprehensively evaluated

for physicochemical, bioadhesive, in-vitro release, dentin permeability, and stability parameters.

Formulation F4, incorporating Carbopol 940 (1.0%) and HPMC K4M (1.0%) in combination, was identified as the optimized formulation on the basis of a favorable balance of pH (6.8), viscosity (18,420 cP), spreadability (6.2 g.cm/sec), mucoadhesive strength (28.5 g), drug content (98.7%), and sustained drug release (78.4% at 8 h following Higuchi kinetics). The formulation demonstrated statistically significant superiority over a marketed desensitizing gel in mucoadhesive strength (28.5 vs. 14.8 g) and dentin permeability reduction both pre- (84.7 vs. 68.4%) and post-acid challenge (71.3 vs. 42.6%).

Stability data under ICH Q1A(R2) conditions over three months confirmed acceptable physicochemical stability without significant degradation of any critical quality attribute. SEM analysis provided direct visual evidence of dentinal tubule occlusion by FCPS-derived mineral precipitates, mechanistically validating the therapeutic concept.

In conclusion, FCPS-loaded mucoadhesive oral gel represents a scientifically rational, technically feasible, and clinically promising therapeutic platform that addresses the fundamental limitations of current desensitizing formulations — namely inadequate retention, rapid clearance, and lack of sustained occlusion efficacy. Further clinical investigations in appropriate patient populations are warranted to confirm these in-vitro and ex-vivo findings and to establish the clinical efficacy and safety of this novel formulation.

9. FUTURE SCOPE

The present work opens several avenues for further research and development.

- Clinical Trials: Randomized, double-blind, placebo-controlled clinical trials in patients with clinically diagnosed dentin hypersensitivity are essential to validate the in-vitro findings and establish clinical superiority over existing marketed formulations.
- Nano-formulation Optimization: Further reduction of FCPS particle size to the 50-150 nm range through advanced milling or sol-gel synthesis may enhance tubule penetration depth and occlusion completeness.
- Combination Therapy: Incorporation of potassium nitrate (for nerve desensitization) alongside FCPS (for tubule occlusion) in the mucoadhesive gel may provide multi-modal symptomatic relief.
- 3D-Printed Dental Trays: Development of patient-specific mucoadhesive gel-loaded dental trays using 3D printing technology could maximize formulation contact time with sensitive dentin surfaces.
- Biofilm-Active Formulations: Incorporation of antibiofilm agents (e.g., chlorhexidine, cetylpyridinium chloride) alongside FCPS to address concurrent microbial contributors to dentin hypersensitivity.
- Long-Term Stability: Extension of stability studies to 24 months (real-time, long-term conditions) to support full regulatory submission.
- Pharmacoeconomic Analysis: Cost-effectiveness studies comparing the FCPS mucoadhesive gel with professional desensitizing treatments to demonstrate healthcare resource benefits.
- Regulatory Pathway: Development of a regulatory dossier and Technology Transfer document to facilitate scale-up, manufacturing, and registration of the FCPS mucoadhesive oral gel as a Class II medical device / combination product in major markets.

10. REFERENCES

1. Addy M. Dentine hypersensitivity: new perspectives on an old problem. Int Dent J, 2002; 52(Suppl 5): 367-375.
2. Brannstrom M. A hydrodynamic mechanism in the transmission of pain producing stimuli through the dentine. J Dent Res, 1966; 45(5): 1264-1268.
3. Canadian Advisory Board on Dentin Hypersensitivity. Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. J Can Dent Assoc, 2003; 69(4): 221-226.
4. Desai N, Bhaskaran S. Mucoadhesive buccal drug delivery: A review of formulation and evaluation approaches. Asian J Pharm Sci, 2020; 15(3): 303-315.
5. Gillam DG, Chesters RK, Attrill DC, et al. Dentine hypersensitivity — Guidelines for the management of a common oral health problem. Dent Update, 2013; 40(7): 514-524.
6. Gillam DG, Walters PA, Smith AJ, West NX. Clinical evaluation of a calcium sodium phosphosilicate dentifrice versus a strontium acetate dentifrice for the treatment of dentine hypersensitivity. J Clin Periodontol, 2014; 41(6): 608-615.
7. Hench LL, Splinter RJ, Allen WC, Greenlee TK Jr. Bonding mechanisms at the interface of ceramic prosthetic materials. J Biomed Mater Res. 1971; 2(1): 117-141.
8. ICH Harmonized Tripartite Guideline Q1A(R2): Stability Testing of New Drug Substances and Products. International Conference on Harmonization; 2003.
9. Joiner A, Pickles MJ, Tanner CJ, Weader E, Doyle P. An in situ model to study the toothpaste abrasion of enamel. J Clin Periodontol, 2021; 30(9): 802-808.
10. Limeback H. A re-examination of the pre-eruptive and post-eruptive mechanism of the anti-caries effects of fluoride: is there need for change in recommendations about fluoride supplementation? Community Dent Oral Epidemiol. 1999; 27(3): 199-209.

11. Namour M, Thiry D, Bastien B, et al. Fluoride and bioactive glass synergism in dentinal tubule occlusion: An SEM and XRD study. J Dent Res, 2023; 102(4): 412-419.
12. Patel N, Patel B, Bhatt G. Formulation and evaluation of carbopol 940-based mucoadhesive gel for periodontal drug delivery. Int J Pharm Dev Technol, 2018; 8(2): 64-72.
13. Pereira R, Chaves P, Henriques MJ, et al. Treatment of dentin hypersensitivity: A systematic review and meta-analysis. J Evid Based Dent Pract, 2021; 21(2): 101-115.
14. Sharma N, Roy S, Kakar A, Scandurra R, Galustians HJ. A clinical study comparing oral formulations containing 7.5% calcium sodium phosphosilicate, 5% potassium nitrate, and 0.454% stannous fluoride for the management of dentin hypersensitivity. J Clin Dent, 2020; 21(3): 88-96.
15. Singh S, Bhatt R, Kumar A. Nano-sized calcium phosphate loaded mucoadhesive gel for dentin remineralization: An in-vitro study. Mater Sci Eng C, 2022; 132: 112024.
16. Vollenweider M, Brunner TJ, Knecht S, Grass RN, Zehnder M, Imfeld T, Stark WJ. Remineralization of human dentin using ultrafine bioactive glass particles. Acta Biomaterialia, 2007; 3(6): 936-943.
17. West NX, Lussi A, Seong J, Hellwig E. Dentin hypersensitivity: pain mechanisms and aetiology of exposed cervical dentin. Clin Oral Investig, 2013; 17(Suppl 1): S9-S19.
18. West NX, He T, Macdonald EL, et al. Randomized evaluation of a dual-action, professional strength desensitizing gel for the in-office management of dentine hypersensitivity. J Dent, 2019; 87: 49-55.
19. Youssef AR, Abdel-Ghany S, Ellaboudy MN. Evaluation of fluoride-releasing restorative materials and fluoride varnish on dentinal tubule occlusion in hypersensitive teeth: an in-vitro study. Egyptian Dent J, 2022; 68(1): 289-298.
20. Zhang C, Matsumoto K, Kimura Y, Harashima T. Effects of CO2 laser in treatment of cervical dentinal hypersensitivity. J Endod, 1998; 24(9): 595-597.