World Journal of Pharmaceutical Science and Research

www.wjpsronline.com

Review Article

ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 5
Page: 941-956

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

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

[1]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.

[2]Assosiate Professor, Department of Pharmaceutical Analysis, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.

Article Received: 10 April 2026 | | ***Article Revised: 1 May 2026*** | | ***Article Accepted: 21 May 2026***

***Corresponding Author: Sujal Anil Jagnade**
Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.
DOI: https://doi.org/10.5281/zenodo.20363197

How to cite this Article: Sujal Anil Jagnade, Sagar Tambe Eknath, Jayesh Gangadhar Jadhav, Sahil Sonlal Janwale, Pratham Yogesh Bangar, Avishkar Suresh Kad (2026) DESIGN AND DEVELOPMENT OF FLUORO CALCIUM PHOSPHOSILICATE (FCPS) LOADED MUCOADHESIVE ORAL GEL FOR THE MANAGEMENT OF DENTIN HYPERSENSITIVITY. World Journal of Pharmaceutical Science and Research, 5(5), 941-956.

ABSTRACT

Dentin hypersensitivity (DH) remains one of the most frequently encountered and clinically challenging conditions in contemporary dental practice, affecting a significant proportion of adults globally. The condition is defined by a sharp, transient pain originating from exposed dentin in response to various external stimuli — thermal, evaporative, tactile, osmotic, and chemical — that cannot be attributed to any other dental pathology. While a number of therapeutic strategies have been employed over the years, achieving both immediate symptom relief and durable, long-term remineralization of exposed dentinal tubules continues to be an unmet clinical need. Fluoro Calcium Phosphosilicate (FCPS), commercially available as BioMin F, is a second-generation fluoride-incorporating bioactive glass that has demonstrated remarkable promise in the management of DH. Unlike its predecessor calcium sodium phosphosilicate (CSPS/NovaMin), FCPS incorporates fluoride directly into the glass matrix, enabling the sustained, pH-responsive release of calcium, phosphate, and fluoride ions over an extended 12-hour period after application. This ionic milieu fosters the in-situ crystallization of acid-resistant fluorapatite within dentinal tubules, offering superior and lasting tubule occlusion compared *to* conventional desensitizing agents. Despite these promising properties, the predominant delivery vehicle for FCPS remains toothpaste — a formulation that limits contact time with the dentin surface, reduces the depth of tubular penetration, and provides only transient therapeutic benefit. The development of a mucoadhesive oral gel incorporating FCPS represents a paradigm shift in the delivery of this bioactive material. Mucoadhesive gel systems extend residence time at the application site, allow for sustained and controlled ion release directly onto the exposed dentin, improve bioavailability of the active ingredient, and significantly enhance patient convenience. This review critically examines the pathophysiology of dentin hypersensitivity, the compositional and mechanistic attributes of FCPS, the rationale for adopting a mucoadhesive gel delivery platform, the pharmaceutical design and development considerations for FCPS-loaded oral gels, and the existing clinical and in-vitro evidence supporting this novel therapeutic approach. The review also highlights knowledge gaps and outlines directions for future research in this promising field.

KEYWORDS: Dentin hypersensitivity, fluoro calcium phosphosilicate, BioMin F, bioactive glass, mucoadhesive gel, oral drug delivery, fluorapatite, dentinal tubule occlusion, hydrodynamic theory.

1. INTRODUCTION

Dentin hypersensitivity is a common oral health concern affecting between 8% and 57% of the adult population worldwide, with notable variations depending on geographic region, assessment methodology, and the populations studied. The wide prevalence range reflects the subjective nature of pain reporting and the absence of a single universally adopted diagnostic test. What is consistent across studies, however, is that DH significantly impairs quality of life — patients often modify their dietary habits, oral hygiene routines, and social behaviors to avoid triggering painful stimuli.

The condition arises when dentin — the mineralized tissue underlying tooth enamel and cementum — becomes exposed due to enamel erosion, gingival recession, abrasion, erosive tooth wear, or dental procedures such as scaling and root planing. Once exposed, the patent dentinal tubules create a direct hydraulic communication pathway between the oral environment and the pulpal nerve endings. According to Brannstrom's widely accepted hydrodynamic theory, external stimuli produce rapid bidirectional fluid shifts within these tubules, mechanically activating the intradental nerve fibers (predominantly A-delta fibers) located at the pulp-dentin junction, generating pain.

Current therapeutic approaches broadly aim to either (a) occlude the dentinal tubules to physically block fluid movement, or (b) desensitize the neural component of the pain response. Tubule-occluding agents include potassium oxalate, arginine-calcium carbonate, nano-hydroxyapatite, stannous fluoride, and bioactive glass-based formulations, while potassium salts (nitrate and chloride) represent the primary nerve-desensitizing agents. Among all these options, bioactive glass-based desensitizers — particularly FCPS — have drawn considerable scientific interest owing to their dual capacity to provide physical occlusion and active remineralization through mineral ion release.

However, a critical limitation in the therapeutic translation of FCPS lies in its delivery. The toothpaste format, though widely accessible, suffers from short contact time with the tooth surface, dilution by saliva, and mechanical removal during rinsing. These factors collectively curtail the effective ion release period, reduce penetration depth into dentinal tubules, and necessitate twice-daily reapplication for sustained benefit. In this context, the development of a mucoadhesive oral gel as a delivery platform for FCPS represents a compelling pharmaceutical innovation.

Mucoadhesive formulations exploit specific polymeric interactions with mucosal glycoproteins to anchor the dosage form at or near the target site. When applied directly onto the exposed cervical dentin or gingival margins, a mucoadhesive gel containing FCPS would maintain prolonged contact with the tooth surface, facilitate deeper and more sustained ion diffusion into dentinal tubules, and allow controlled release of calcium, phosphate, and fluoride ions over an extended period.

2. DENTIN HYPERSENSITIVITY: PATHOPHYSIOLOGY AND EPIDEMIOLOGY

2.1 Definition and Diagnostic Criteria

Dentin hypersensitivity is formally defined as a short, sharp pain arising from exposed dentin in response to thermal, evaporative, tactile, osmotic, or chemical stimuli that cannot be explained as arising from any other form of dental defect or disease. This definition, proposed by Holland et al. (1997) and subsequently endorsed by international dental organizations, emphasizes two key features: the subjective and transient nature of the pain, and the requirement to exclude other conditions such as cracked teeth, carious lesions, or recently placed restorations before establishing the diagnosis.

Clinically, DH is diagnosed through a combination of patient history and provocation tests. The visual analog scale (VAS) is the most commonly employed patient-reported outcome measure for quantifying pain intensity, ranging from 0 (no pain) to 10 (worst imaginable pain). The Schiff Cold Air Sensitivity Scale (SCASS) provides a clinician-rated measure of sensitivity response to an air blast stimulus. A score of VAS ≥ 4 or SCASS ≥ 2 is typically considered clinically significant and is used as an inclusion threshold in most clinical trials.

2.2 Epidemiology and Prevalence

Epidemiological data consistently demonstrate a high global burden of dentin hypersensitivity, though precise figures are complicated by methodological heterogeneity across studies. A prevalence of 8–57% has been reported in adult populations, with peak incidence observed in the third and fourth decades of life. Women appear to report DH more frequently than men, possibly reflecting greater health-seeking behavior rather than a biological predisposition. Patients undergoing periodontal treatment — particularly scaling and root planing — represent a high-risk group, with post-procedural DH reported in up to 70% of cases.

The condition is particularly burdensome in patients with gingival recession, which is itself highly prevalent — affecting over 50% of individuals aged 18 and above in the general population. Erosive tooth wear, increasingly recognized as a growing concern due to dietary patterns rich in acidic foods and beverages, further expands the at-risk population. The social and functional impact of DH is substantial; avoidance of cold drinks, hot foods, sweet substances, and even breathing cold air are frequently reported behaviors that compromise nutritional intake and everyday well-being.

2.3 Etiology and Predisposing Factors

The development of dentin hypersensitivity requires two sequential events: dentin exposure and tubule patency. Dentin becomes exposed through various mechanisms, each with distinct etiological contributions. Gingival recession, whether localized or generalized, bares the root surface that is covered only by thin cementum rather than protective enamel. Erosive tooth wear from dietary acids or gastroesophageal reflux disease strips the overlying enamel from the coronal dentin. Abrasive tooth brushing — particularly with hard-bristled brushes and abrasive dentifrices — mechanically removes cervical tooth structure.

Once exposed, dentin must also exhibit patent (open) tubules for DH to manifest. The smear layer — a thin mineral deposit that forms on dentin surfaces from normal wear and dietary exposure — partially occludes tubules and reduces permeability. However, this layer is readily dissolved by acidic conditions, dietary acid intake, or vigorous brushing, restoring tubule patency and reinstating the hydrodynamic communication necessary for DH to occur.

2.4 Hydrodynamic Theory and Mechanisms of Pain

The hydrodynamic theory, first proposed by Brannstrom and Astrom in 1964 and now universally accepted, explains the mechanism of dentinal pain. Dentinal tubules are fluid-filled cylinders that traverse the dentin matrix from the pulp-dentin junction to the dentinoenamel junction (DEJ). Their diameter ranges from approximately 2.5 microns at the pulpal surface to 0.9 microns at the DEJ. External stimuli — cold, heat, drying, sweet substances, or mechanical touch — induce rapid movement of the dentinal fluid within these tubules, either outward (as with cold or drying) or inward (as with heat).

This rapid fluid movement mechanically activates mechanosensitive ion channels in odontoblastic processes and displaces the odontoblast cell bodies at the pulp-dentin interface, generating a deformation signal. A-delta nerve fibers, which are myelinated and fast-conducting, respond to this mechanical deformation by transmitting sharp, well-localized pain of short duration. A lesser contribution from unmyelinated C-fibers may explain the dull, lingering ache that sometimes follows the initial sharp sensation. Understanding this mechanism is foundational to appreciating why tubule occlusion — reducing or eliminating the hydrodynamic pathway — constitutes the most scientifically rational strategy for managing DH.

3. FLUORO CALCIUM PHOSPHOSILICATE (FCPS): CHEMISTRY, COMPOSITION, AND MECHANISM

3.1 Historical Context: The Bioactive Glass Family

The story of FCPS begins with the seminal work of Larry Hench at the University of Florida in 1969. Hench developed Bioglass 45S5, a silicate-based material composed of silicon dioxide (SiO2), sodium oxide (Na2O), calcium oxide (CaO), and phosphorus pentoxide (P2O5) in a specific molar ratio. This material was revolutionary because, unlike the biologically inert implants of the era that provoked fibrous encapsulation, it formed a strong chemical bond with living bone tissue by developing a surface layer of hydroxycarbonate apatite (HCA). The US Food and Drug Administration approved Bioglass 45S5 in 1985, and its application in dentistry soon followed.

In dentistry, the first major application of bioactive glass was calcium sodium phosphosilicate (CSPS), marketed under the name NovaMin by NovaBay Pharmaceuticals and later incorporated into Sensodyne Repair and Protect (GlaxoSmithKline). CSPS shares the basic compositional framework of Bioglass 45S5 and works by releasing calcium and phosphate ions in the oral environment, promoting the formation of HCA that physically occludes dentinal tubules. While CSPS demonstrated significant clinical efficacy over potassium-based desensitizers and plain fluoride dentifrices, it lacked intrinsic fluoride within the glass matrix, meaning the formed HCA layer was susceptible to acid dissolution.

The evolution from CSPS to FCPS represented a deliberate engineering solution to this limitation. Researchers at Queen Mary University of London, led by Robert Hill and colleagues, developed a modified glass composition that incorporates fluoride directly into the glass network as calcium fluoride (CaF2). This subtle but profound modification confers several advantages: the released fluoride ions promote the formation of fluorapatite (FAP) rather than hydroxyapatite (HAP), the higher phosphate content accelerates apatite nucleation kinetics, and the smaller engineered particle size enables deeper tubular penetration. The resulting material — FCPS — forms the basis of BioMin F toothpaste, launched commercially in 2016 in the United Kingdom, Germany, and India.

3.2 Compositional Characteristics of FCPS

FCPS differs from conventional CSPS in several key compositional and structural aspects. Most importantly, FCPS contains calcium fluoride (CaF2) directly within its glass matrix, distinguishing it from CSPS formulations where fluoride, if present at all, is added externally as a separate compound (such as sodium fluoride) and is not part of the glass structure. This structural incorporation ensures that fluoride is released in concert with calcium and phosphate as the glass dissolves, maintaining stoichiometric ratios favorable to FAP crystallization.

FCPS also has a significantly higher phosphate content compared to the original Bioglass 45S5 composition. Research by Mneimne et al. demonstrated that increasing phosphorus pentoxide (P2O5) content from 1 mol% to 6 mol%

dramatically accelerated FAP formation — from three days to as little as six hours. This concentration of phosphate lowers the energy barrier for apatite nucleation and promotes rapid crystallization at physiological pH. The higher phosphate content also accelerates dissolution of the glass matrix, which further increases the rate and duration of ionic release into the surrounding aqueous environment.

Additionally, FCPS particles are engineered to a smaller average diameter — approximately 6 microns (D50) — compared to CSPS particles. This reduced particle size, reportedly 60% smaller than NovaMin particles, has two important clinical implications. First, the smaller particle size enables physical entry into dentinal tubules whose openings average 2–3 microns in diameter, facilitating direct intra-tubular mineral deposition. Second, the increased surface area-to-volume ratio of smaller particles accelerates ionic dissolution, enhancing the rate of calcium, phosphate, and fluoride ion release.

Table 1: Comparative Characteristics of CSPS (NovaMin) and FCPS (BioMin F).

Parameter	CSPS (NovaMin)	FCPS (BioMin F)
Base Composition	SiO2, Na2O, CaO, P2O5	SiO2, CaO, P2O5, CaF2
Fluoride Source	External (NaF added separately)	Internal (CaF2 within glass matrix)
Apatite Formed	Hydroxycarbonate Apatite (HCA)	Fluorapatite (FAP)
Particle Size (D50)	~10–15 microns	~6 microns
Phosphate Content	Lower (~ 2.6 mol% P2O5)	Higher (up to 6 mol% P2O5)
Ion Release Duration	Shorter (flush with saliva)	Up to 12 hours post-application
Acid Resistance of Layer	Moderate (HCA dissolves under acid)	High (FAP highly acid-resistant)
Tubule Penetration Depth	Surface and superficial	Deep intra-tubular (up to 17 µm)
Fluoride Content (ppm)	None (glass); external NaF only	~530 ppm (slow, sustained release)

3.3 Mechanism of Action of FCPS

3.3.1 Dissolution and Ion Release

The therapeutic action of FCPS begins with its dissolution in the aqueous oral environment. When FCPS particles contact saliva or dentinal fluid, a cascade of surface reactions is initiated. Silicon-oxygen bonds at the glass surface undergo hydrolysis, releasing silicic acid and creating surface silanol groups (Si-OH). This creates a hydrated silica-rich layer on the glass surface, from which calcium (Ca2+), phosphate (PO43-), and fluoride (F-) ions are progressively released into the surrounding fluid. The rate of this dissolution — and consequently the rate of ion release — is pH-dependent: as oral pH drops below 5.5 following carbohydrate consumption, the glass dissolves more rapidly, providing a self-regulating, demand-responsive ion release mechanism.

3.3.2 Fluorapatite Crystallization

The released calcium, phosphate, and fluoride ions interact in the aqueous environment to nucleate and grow fluorapatite crystals [Ca10(PO4)6F2]. FAP formation is strongly favored over HAP formation in the presence of fluoride ions because fluoride substitutes for hydroxyl groups in the apatite lattice, producing a crystal that is thermodynamically more stable and chemically more resistant to acid dissolution. The critical distinction is significant: HAP begins to dissolve at oral pH below approximately 5.5, while FAP remains stable down to pH 4.5, providing substantially better protection against the acidic oral environment.

The crystallization of FAP occurs both on the exposed dentin surface and within the dentinal tubule lumen. Due to the smaller particle size of FCPS (D50 ~6 microns), FCPS particles can enter tubule openings directly, where they dissolve and nucleate FAP crystals from within. This intra-tubular mineral deposition creates tight, mechanically interlocking

plugs that resist both salivary dissolution and acid challenge — addressing the primary limitation of surface-only mineral deposition seen with older desensitizing agents.

3.3.3 Tubule Occlusion and Durability

SEM studies have confirmed the superior tubule occlusion achieved by FCPS compared to other desensitizing agents. In in-vitro studies using dentinal disc models, FCPS treatment produced greater percentages of fully or partially occluded tubules compared to CSPS, potassium nitrate dentifrices, and plain fluoride toothpastes. Critically, the FAP layer formed by FCPS showed significantly better resistance to an acid challenge with 6% citric acid compared to the HCA layer formed by CSPS, demonstrating that FAP tubule plugs endure acidic oral conditions that would dissolve conventional mineral deposits.

The gelatin-modified bioactive glass studies (MBG@PDA@Gel) further corroborated these findings, demonstrating that increasing the contact time between bioactive glass particles and dentin — as would be achieved by a mucoadhesive gel — allows mineral deposition to extend deeper into the tubule, with penetration depths of approximately 17 microns observed after 14 days of exposure. This finding provides compelling in-vitro evidence supporting the rationale for FCPS delivery in a mucoadhesive gel format that prolongs material contact with the dentin surface.

4. MUCOADHESIVE ORAL GEL: CONCEPT, RATIONALE, AND DESIGN PRINCIPLES

4.1 Concept of Mucoadhesion in Oral Drug Delivery

Mucoadhesion refers to the adhesive interaction between a synthetic or natural polymer and the mucous membrane lining the oral cavity. This adhesion is mediated by non-covalent attractive forces — hydrogen bonding, electrostatic interactions, van der Waals forces, and chain entanglement — between mucoadhesive polymer chains and the glycoprotein-rich mucin layer that coats oral mucosal surfaces. The result is a prolonged retention of the formulation at the target site, which translates directly into extended release of the active ingredient, improved local bioavailability, and reduced dosing frequency.

In the context of FCPS delivery for dentin hypersensitivity, the mucoadhesive gel concept offers a particularly elegant solution. Unlike transmucosal drug delivery aimed at systemic absorption, the target here is the exposed dentin surface itself — the cervical dentin at the gingival margin. When applied directly to this area, a mucoadhesive FCPS gel would adhere to the adjacent gingival mucosa and resist salivary dilution and mechanical removal, maintaining an intimate and prolonged contact between FCPS particles and the exposed dentin. This sustained contact allows for continuous, controlled ion release over several hours, enabling deeper FAP penetration and more complete tubule occlusion than achievable with toothpaste.

4.2 Polymeric Carriers for Mucoadhesive Oral Gel Formulation

The selection of appropriate polymeric carrier(s) is the most critical formulation decision in designing a mucoadhesive oral gel. Several polymers are well-established in this context, each with distinct mucoadhesive mechanisms, rheological profiles, and compatibility considerations when combined with mineral-rich actives such as FCPS.

4.2.1 Carbomer (Carbopol)

Carbomer — a polyacrylic acid polymer cross-linked with allyl sucrose or allyl ethers of pentaerythritol — is among the most widely used mucoadhesive polymers in oral formulations. Its mucoadhesive properties arise from the formation of hydrogen bonds between carboxyl groups (-COOH) in the carbomer chains and hydroxyl and amino groups in mucin glycoproteins. At neutral to slightly alkaline pH (above 6), carbomer chains unfold and expand, dramatically increasing their surface area for mucin interaction. Carbomer gels exhibit pseudoplastic (shear-thinning) rheological behavior — they are highly viscous at rest but flow readily upon application, enabling easy spreading followed by effective bioadhesion once the shear force is removed.

Carbomer is biocompatible, biodegradable, cost-effective, and thermostable up to 260°C. In oral gel formulations for dental applications, carbomer concentrations of 0.5%–2% w/w are typically used to achieve gel strengths appropriate for intraoral application. A carbomer-based FCPS gel would provide sustained mucoadhesion at the gingival margin, holding FCPS particles in close proximity to the exposed dentin for extended periods.

4.2.2 Hydroxypropyl Methylcellulose (HPMC)

Hydroxypropyl methylcellulose is a semi-synthetic cellulose derivative that forms clear, viscous aqueous gels. Its mucoadhesive behavior is primarily attributed to mechanical interlocking and hydrogen bonding with mucosal surfaces. HPMC is highly biocompatible, exhibits minimal systemic absorption, and is widely approved by regulatory agencies for oral use. It is particularly valued in dental formulations for its ability to form films that adhere to tooth and mucosal surfaces. HPMC can be used in combination with carbomer to modulate the overall rheology and mucoadhesion of the gel, providing complementary adhesion mechanisms.

4.2.3 Sodium Carboxymethylcellulose (SCMC)

Sodium CMC is an anionic water-soluble polymer derived from cellulose through carboxymethylation. It is particularly suitable for mucoadhesive formulations because its anionic carboxylate groups interact strongly with the positively charged domains of mucin glycoproteins. SCMC contributes to gel viscosity and cohesive strength, and its combination with carbomer has been shown to enhance overall mucoadhesive performance compared to either polymer alone.

Additionally, SCMC acts as a stabilizer in mineral-containing formulations, preventing agglomeration of FCPS particles.

4.2.4 Hyaluronic Acid

Hyaluronic acid (HA), a linear polysaccharide composed of alternating glucuronic acid and N-acetylglucosamine units, is an endogenous component of the extracellular matrix and oral mucosa. Its exceptional capacity to bind water — up to 1000 times its own mass — makes it a superb humectant and viscoelastic agent in oral formulations. HA interacts with specific cell surface receptors (CD44, RHAMM) present on gingival fibroblasts and keratinocytes, contributing to both mucoadhesion and tissue biocompatibility. HA also exhibits anti-inflammatory properties that may provide additional benefit in patients with concomitant gingival inflammation.

Table 2: Mucoadhesive Polymers for FCPS Oral Gel Formulation.

Polymer	Mucoadhesive Mechanism	Typical Conc. (%)	Key Advantage	Limitation
Carbomer	H-bonding via COOH	0.5–2.0	Excellent bioadhesion; pH-	May interact with

(Carbopol)	groups with mucin		responsive swelling	Ca2+ ions
HPMC	Mechanical interlocking; H-bonding	1.0–4.0	Film-forming; stable over wide pH range	Weaker mucoadhesion vs carbomer
Sodium CMC	Ionic interaction with mucin	0.5–2.0	Good viscosity; stabilizes mineral particles	Sensitive to high ionic strength
Hyaluronic Acid	CD44 receptor binding; H-bonding	0.1–2.0	Anti-inflammatory; tissue compatible	High cost
Chitosan	Ionic bonding with anionic mucin	0.5–2.0	Antibacterial; promotes mineral adhesion to dentin	Soluble only at low pH

4.3 Rationale for Gel Over Toothpaste as Delivery Platform

The limitations of toothpaste as a delivery vehicle for FCPS are well-recognized. The typical brushing duration is 2 minutes, during which FCPS particles contact the dentin surface for a brief period before being rinsed away. While some tubule occlusion occurs even within this short window, it is predominantly superficial. Furthermore, post-brushing rinsing accelerates the removal of FCPS particles from the oral cavity, dramatically curtailing the ion release window. The dilution effect of saliva further reduces local ion concentrations, diminishing the thermodynamic driving force for FAP crystallization within tubules.

A mucoadhesive gel applied directly to the cervical dentin region resolves each of these limitations. Applied post-brushing or as a stand-alone treatment, the gel adheres to the gingival mucosa and resists salivary washout. FCPS particles embedded within the gel matrix are presented to the dentin surface in sustained fashion, dissolving progressively and releasing calcium, phosphate, and fluoride ions over hours. The continuous local ion availability establishes a sustained supersaturation of FAP precursor ions in the dentinal fluid, promoting progressive inward crystallization of FAP within tubules and enabling the formation of deeper, more mechanically stable mineral plugs.

Additionally, the gel format enables site-specific application — the patient can apply the gel precisely to areas of known sensitivity without exposing the entire dentition to the material. This targeted delivery approach is not achievable with toothpaste and offers both therapeutic precision and economic efficiency in material use.

4.4 Gel Formulation Design and Excipients

Beyond the mucoadhesive polymer(s), the FCPS oral gel formulation incorporates several excipients that collectively ensure the physico-chemical stability of the product, patient palatability, microbial safety, and optimal rheological performance for intraoral application.

Humectants such as glycerin or propylene glycol serve a dual purpose: they prevent syneresis (water separation) within the gel matrix and maintain a moist environment at the dentin surface that is conducive to ion release and apatite crystallization. Flavoring agents — typically mint-based — improve patient acceptability and are critical for patient compliance in a gel intended for daily use. Sweeteners such as xylitol (which also exhibits anticariogenic properties) provide sweetness without cariogenic potential. Preservative systems incorporating sodium benzoate or parabens ensure microbiological stability across the product shelf life, though the selection must account for potential interactions with the mineral-rich FCPS glass.

The pH of the formulation requires careful optimization. A slightly acidic to neutral pH (5.5–7.0) is appropriate, as excessively alkaline conditions may prematurely initiate apatite crystallization within the gel bulk, compromising

particle distribution. The final pH should be biocompatible with oral mucosal tissue, which is most tolerant in the pH range of 5.5–8.0. Buffering agents such as sodium phosphate or citrate buffers can stabilize gel pH while simultaneously providing additional phosphate for FAP formation.

5. FORMULATION DEVELOPMENT AND EVALUATION PARAMETERS

5.1 Pharmaceutical Development Considerations

The design of an FCPS-loaded mucoadhesive oral gel demands a systematic pharmaceutical development process that begins with the establishment of target product profile (TPP). The TPP for this formulation would specify: a clear to translucent gel of appropriate viscosity (approximately 50,000–150,000 cPs at 25°C), a pH of 6.0–7.0, a minimum contact time with dentin of 4 hours, sustained release of calcium, phosphate, and fluoride ions with a maximum release period of 8–12 hours, acceptable organoleptic properties (mint flavor, smooth texture, neutral color), and microbiological compliance with Ph.Eur or USP specifications for non-sterile topical preparations.

5.2 Physico-Chemical Characterization of FCPS Particles

Prior to incorporation into the gel, FCPS particles must be thoroughly characterized to establish baseline properties.

Particle size distribution is measured using dynamic light scattering (DLS) or laser diffraction (Malvern Mastersizer), targeting a D50 of approximately 6 microns for optimal tubular penetration. Surface morphology is examined by scanning electron microscopy (SEM) to confirm particle shape, surface texture, and absence of agglomeration. X-ray diffraction (XRD) confirms the amorphous nature of the glass prior to dissolution — crystalline impurities could signal premature apatite formation during manufacturing.

Fourier-transform infrared spectroscopy (FTIR) establishes the characteristic absorption bands of FCPS (Si-O stretching at ~1000 cm-1; P-O bending at ~600 cm-1; Ca-F stretching at ~745 cm-1) and can be used to monitor ionic exchange reactions and FAP formation both in-vitro and post-formulation. Thermogravimetric analysis (TGA) confirms glass thermal stability and identifies any moisture content that could initiate premature dissolution within the gel matrix.

5.3 Gel Rheological Characterization

Rheological profiling is fundamental to ensuring that the gel possesses appropriate flow properties for intraoral application. The gel must be viscous enough to resist salivary dilution and remain at the application site, yet sufficiently fluid upon application to spread easily and conform to the irregular geometry of the tooth-gingiva interface.

Pseudoplastic (shear-thinning) behavior — decreasing viscosity with increasing shear rate — is the ideal flow profile for this purpose. Oscillatory rheological tests (frequency sweep, amplitude sweep) distinguish the viscoelastic character of the gel, with an elastic modulus (G') exceeding the viscous modulus (G") across the physiological frequency range indicative of a robust gel network.

Spreadability testing measures the area of gel spread under a defined load, providing a simple practical measure of application ease. Consistency and firmness measurements using texture analysis (TA.XT Plus) complement the oscillatory data, providing a comprehensive rheological picture.

5.4 Mucoadhesive Performance Evaluation

Mucoadhesive strength is evaluated using a modified texture analyzer method, measuring the maximum detachment force and work of adhesion when a gel sample is detached from a porcine or bovine mucosal tissue substrate. Ex-vivo residence time experiments quantify how long the gel formulation remains adherent to oral mucosal tissue under simulated salivary flow conditions, providing a direct measure of the formulation's capacity to maintain contact with the dentin surface over time.

Wash-off resistance — the gel's ability to remain at the application site following standardized salivary flow exposure — is determined gravimetrically or fluorometrically (using a fluorescent tracer incorporated in the gel). Formulations with superior wash-off resistance are expected to provide more consistent and prolonged FCPS-to-dentin contact, translating to better therapeutic outcomes.

5.5 In-Vitro Drug/Ion Release Studies

Ion release studies for FCPS gels differ fundamentally from conventional drug release testing because the therapeutic agents are inorganic ions rather than molecular drugs. Calcium ion release is quantified by atomic absorption spectroscopy (AAS) or inductively coupled plasma mass spectrometry (ICP-MS), phosphate by colorimetric phosphomolybdate assays, and fluoride by ion-selective electrode (ISE) potentiometry. Release profiles are generated by placing a defined mass of gel in simulated body fluid (SBF) or artificial saliva at 37°C under gentle agitation, with aliquot collection and analysis at defined time points (0, 15, 30, 60 min, 2h, 4h, 8h, 12h, 24h).

The ion release kinetics are modeled using mathematical equations — zero-order, first-order, Higuchi, and Korsmeyer-Peppas models — to understand the release mechanism. An anomalous or super-case II transport release mechanism (Korsmeyer-Peppas exponent $n > 0.45$) would indicate a combination of diffusion and matrix erosion controlling ion release, which is optimal for the intended prolonged therapeutic effect.

5.6 In-Vitro Tubule Occlusion Assessment

The ultimate measure of FCPS gel efficacy at the pre-clinical level is its ability to occlude dentinal tubules under conditions that simulate clinical use. Dentinal disc models, prepared from extracted human premolars by sectioning perpendicular to the long axis, are acid-etched to remove the smear layer and expose patent tubules. Gel is applied to the disc surface for a defined period (e.g., 2 minutes to simulate in-office application, or 8 hours to simulate sustained nocturnal use), followed by artificial saliva immersion at 37°C for up to 14 days.

Tubule occlusion is evaluated qualitatively by SEM imaging at standardized magnifications and quantitatively by calculating the percentage of occluded, partially occluded, and patent tubules across multiple microscopic fields. Elemental composition of the deposited material is confirmed by energy-dispersive X-ray spectroscopy (EDX), identifying calcium, phosphorus, and fluorine peaks consistent with FAP. Acid resistance of the deposit is assessed by exposing treated discs to 6% citric acid (pH 3.7) for 30–60 seconds and repeating SEM/EDX analysis.

6. CLINICAL EVIDENCE AND COMPARATIVE EFFICACY

6.1 Clinical Performance of FCPS in Toothpaste Format

The existing clinical evidence for FCPS in the management of dentin hypersensitivity, while predominantly derived from toothpaste-format studies, provides a compelling foundation for the development of the mucoadhesive gel. In a

landmark two-month randomized controlled clinical trial, Swatika et al. compared 5% FCPS dentifrice versus 5% CSPS dentifrice versus a standard fluoride toothpaste in 60 participants with confirmed DH (VAS ≥ 4). Sensitivity scores (VAS) were assessed at baseline, immediately after scaling and root planing, and at 15, 30, and 60 days. The 5% FCPS group demonstrated statistically significant reductions in VAS scores for both subjective and thermal sensitivity compared to both CSPS and the fluoride control across all evaluation time points. Notably, a clinically meaningful reduction in sensitivity in the FCPS group was observable even immediately after the first scaling and root planing visit, suggesting the rapid onset of tubule occlusion.

A subsequent comparative study by Aggarwal et al. evaluated FCPS, CSPS, and strontium chloride hexahydrate dentifrices in 93 participants over four weeks. This study similarly found that FCPS provided the most pronounced and rapid reduction in VAS scores from baseline, supporting the assertion that FCPS bioactive glass-containing dentifrices have an early onset of action in relieving hypersensitivity — an advantage attributed to the combination of rapid initial FAP crystallization and the acid-resistant nature of the deposited mineral layer.

The systematic review by Petrovic et al. (2023), which analyzed seven randomized controlled trials involving bioactive glass-based desensitizers conducted between 2018 and 2022, concluded that FCPS may represent the most effective long-term treatment option among bioactive glass-based agents, while CSPS showed performance comparable to positive control groups. This finding is particularly meaningful because long-term efficacy — sustained relief after weeks to months — reflects the ability of the formed mineral layer to withstand the acidic oral environment, a property uniquely conferred by fluorapatite.

A multicentric observational study conducted in India, evaluating Hydent Pro (a BioMin-based toothpaste) in patients with DH over 24 weeks, found statistically significant improvements in both Schiff Cold Air Sensitivity Scale (SCASS) scores and VAS pain scores from baseline, with improvements becoming progressively more pronounced across the 24-week observation period. Gingival health and plaque scores remained stable, and no safety concerns were identified, confirming the long-term safety profile of FCPS-based formulations.

6.2 Evidence from Gel-Based Bioactive Glass Formulations

While specific mucoadhesive gel formulations of FCPS have not yet been systematically reported in the peer-reviewed clinical literature, important insights can be drawn from studies on gel-based bioactive glass formulations more broadly. Research by Moussa et al. investigated polyethylene glycol (PEG)-based gels containing 45S5 biosilicate particles with and without hydrolyzed casein, evaluating their tubule occlusion capability over 7 days in an artificial saliva model. The gel formulations demonstrated substantially greater tubule occlusion compared to neat mineral application, confirming that the gel carrier enhances contact time and thereby improves mineral deposition.

The gelatin-modified mesoporous bioactive glass study (MBG@PDA@Gel) by Li et al. demonstrated penetration depths of FAP-like mineral into dentinal tubules of approximately 17.34 microns after 14 days — approximately twice the penetration depth observed with unmodified bioactive glass particles under otherwise identical conditions. The authors attributed this superior performance directly to the gel carrier's ability to maintain prolonged material-dentin contact and sustain ionic supersaturation within the tubule lumen over the extended observation period. These findings provide powerful in-vitro support for the hypothesis that a mucoadhesive gel delivery system for FCPS would outperform toothpaste in achieving deep, durable tubule occlusion.

The scoping review by Bidra et al. (2025), which comprehensively mapped clinical and in-vitro evidence on bioactive glass products for DH through March 2025, identified that among 72 studies included, gel-based formats accounted for only 6 studies compared to 39 toothpaste-based studies. This stark imbalance highlights the significant opportunity for original research specifically evaluating FCPS-loaded mucoadhesive gels, and underscores that the gel format remains substantially underexplored despite its mechanistic advantages.

6.3 Comparison with Other Desensitizing Modalities

To contextualize the anticipated benefits of an FCPS mucoadhesive gel, it is useful to compare FCPS's properties against major alternative desensitizing strategies. Potassium nitrate and potassium chloride act by depolarizing intradental nerve fibers — raising extracellular potassium concentration reduces the resting membrane potential of sensory neurons, diminishing action potential generation and pain transmission. However, potassium-based agents do not address the underlying exposed tubule and thus provide only temporary symptomatic relief without structural remediation of the dentinal surface.

Arginine-calcium carbonate (Pro-Argin technology) creates a positively charged complex that binds to the negatively charged dentin surface and physically occludes tubules. Clinical trials have demonstrated rapid, immediate relief with Pro-Argin, but the mineral plug formed is less acid-resistant than FAP and tends to demonstrate greater sensitivity rebound compared to bioactive glass-based agents. Nano-hydroxyapatite (nHAP) formulations mimic the natural mineral content of enamel and provide good tubule occlusion by direct deposition, but the formed HAP is susceptible to acid dissolution (critical pH 5.5), limiting durability.

Stannous fluoride and strontium-based formulations also occlude tubules through different chemical mechanisms, but each carries specific limitations — stannous fluoride can cause staining and taste issues, while strontium is incompatible with fluoride in combined formulations. Fluoride varnishes applied in-office provide high, short-duration fluoride exposure and tubule occlusion, but require professional application and have limited duration of action. In this comparative landscape, FCPS in a mucoadhesive gel format is uniquely positioned to combine the immediate tubule occluding capacity of physical particulate agents, the sustained ion release of second-generation bioactive glass, and the extended contact time advantage of mucoadhesive delivery — potentially exceeding the individual contributions of any single existing approach.

7. SAFETY AND BIOCOMPATIBILITY PROFILE

7.1 Biocompatibility of FCPS

The safety profile of FCPS is supported by its regulatory status and clinical use history. FCPS-containing products have received FDA clearance as safe and effective dental materials, and no systemic adverse effects have been reported in clinical studies involving twice-daily toothpaste use over periods ranging from four weeks to six months. The ions released by FCPS — calcium, phosphate, and fluoride — are endogenous constituents of the oral environment and are present in saliva, enamel, and dentin at comparable or higher concentrations than those achievable through FCPS dissolution. At the concentrations released during normal use, these ions are neither cytotoxic to oral epithelial cells, pulpal fibroblasts, nor systemic tissues.

Fluoride, while requiring careful management at high doses, is released by FCPS at approximately 530 ppm — a level well below the therapeutic fluoride varnish concentration (22,600 ppm) and the threshold associated with dental

fluorosis risk in young children. In adult use, this concentration is not associated with any fluoride toxicity and is comparable to or lower than the fluoride content of standard fluoride toothpastes (1,000–1,500 ppm). The sustained, low-level release over 12 hours from FCPS is in fact considered advantageous — it maintains a continuous remineralizing fluoride concentration at the tooth surface without the transient peak concentrations associated with soluble fluoride in conventional toothpastes.

7.2 Biocompatibility of Mucoadhesive Excipients

All mucoadhesive polymers proposed for the FCPS gel formulation — carbomer, HPMC, SCMC, hyaluronic acid, chitosan — have well-established safety and biocompatibility profiles in oral mucosal applications. Carbomer (Carbopol 940, 934) has been used in approved topical and mucosal products for decades, with no evidence of mucosal irritation at concentrations appropriate for dental gel use. Hyaluronic acid is an endogenous tissue component with an excellent tolerability profile and is approved for intraoral use in periodontal applications. Chitosan has demonstrated safety in oral mucosal applications and additionally confers antimicrobial activity against Streptococcus mutans and Porphyromonas gingivalis — pathogens relevant to caries and periodontal disease respectively.

The overall safety assessment of an FCPS-loaded mucoadhesive oral gel will require standard biocompatibility testing according to ISO 10993 standards, including cytotoxicity (ISO 10993-5), oral mucosal irritation (ISO 10993-10), and genotoxicity (ISO 10993-3) testing before clinical studies can be initiated. Given the established safety of individual components and the precedent from similar gel formulations approved for periodontal and mucosal applications, the likelihood of significant safety findings is considered low.

8. FUTURE RESEARCH DIRECTIONS AND CLINICAL TRANSLATION

8.1 Knowledge Gaps and Research Priorities

Despite the strong scientific rationale for FCPS-loaded mucoadhesive oral gels, several important knowledge gaps must be addressed through systematic research before clinical translation can be achieved. First and foremost, well-designed in-vitro studies specifically comparing FCPS gel versus FCPS toothpaste for dentinal tubule occlusion under standardized conditions are needed to quantitatively establish the advantage of the gel delivery system. These studies should assess not only the percentage of occluded tubules but also occlusion depth, mineral composition of the deposited layer, and acid resistance — parameters collectively needed to establish mechanistic equivalence or superiority.

Second, the formulation design space for FCPS gels requires systematic exploration. Factorial experimental designs — varying polymer type, polymer concentration, FCPS concentration (suggested range: 5%–15% w/w), particle size, and pH — with rigorous assessment of mucoadhesion, ion release kinetics, and tubule occlusion as response variables would define optimal formulation parameters. Response surface methodology can efficiently map the multi-dimensional formulation space and identify the formulation region that simultaneously maximizes mucoadhesion and ion release rate.

Third, animal studies using rodent or porcine dentin exposure models would provide in-vivo pharmacokinetic and pharmacodynamic data on tubule occlusion progression, mineral layer durability, and mucosal tolerability under conditions of realistic oral function (salivary flow, mechanical stress from occlusion, dietary acid exposure). These data are a regulatory prerequisite for human clinical trials.

Fourth, carefully designed randomized clinical trials comparing FCPS mucoadhesive gel against the FCPS toothpaste format and established comparators (8% arginine-calcium carbonate, 5% potassium nitrate) in participants with confirmed DH are ultimately required to establish clinical efficacy. These trials should incorporate patient-reported outcomes (VAS, DHEQ-15 quality of life score), clinician-rated outcomes (SCASS), and objective measures of tubule occlusion where feasible, with follow-up periods of at least 6 months to evaluate durability.

8.2 Emerging Innovations and Synergistic Approaches

Several emerging technologies could further enhance the therapeutic potential of FCPS mucoadhesive gels. Nano-encapsulation of FCPS particles within biopolymeric nanocapsules (chitosan, PLGA) could provide even more precisely controlled ion release and protect particles from premature dissolution during storage. The use of stimuli-responsive polymers that increase gel dissolution rate in response to reduced oral pH (following acidic food/drink consumption) could create an intelligent, demand-responsive FCPS delivery system that automatically reinforces tubule occlusion when the risk of mineral dissolution is highest.

Laser-assisted application represents another promising synergistic strategy. Studies combining bioactive glass application with low-power diode laser irradiation have demonstrated enhanced tubule penetration and mineral deposition compared to bioactive glass alone. The thermal energy imparted by the laser may increase dentin permeability and accelerate ion diffusion, while simultaneously helping to seal the top of the tubule with the mineral deposit. Combining FCPS gel application with adjunctive laser therapy in a clinical protocol could further maximize the depth and durability of tubule occlusion.

Finally, the incorporation of additional bioactive ions — strontium, magnesium, zinc, or silver — into the FCPS glass composition opens the possibility of multifunctional formulations that simultaneously provide desensitization, enhanced remineralization, and antimicrobial protection. Chitosan-modified FCPS particles, for example, could contribute antibacterial effects against biofilm-associated pathogens, reducing the risk of secondary caries at the exposed cervical dentin — a risk that is not addressed by conventional desensitizing agents alone.

9. CONCLUSION

Dentin hypersensitivity is a multifactorial, prevalent, and quality-of-life-impairing condition that demands formulation strategies capable of delivering both immediate relief and durable, structural remediation of the exposed dentin surface.

Fluoro Calcium Phosphosilicate (FCPS), as the active ingredient in BioMin F, represents the most scientifically advanced bioactive glass for this purpose — distinguished by its intrinsic fluoride content, superior phosphate concentration, small particle size, and the resultant capacity to form deeply penetrating, acid-resistant fluorapatite within dentinal tubules over an extended ion release period of up to 12 hours.

The development of FCPS-loaded mucoadhesive oral gels addresses the principal therapeutic limitation of the current toothpaste delivery format: insufficient contact time with the dentin surface. By harnessing the bioadhesive properties of carefully selected polymeric carriers — particularly carbomer, HPMC, and hyaluronic acid — a mucoadhesive gel can extend the residence time of FCPS at the gingival margin for several hours, enabling sustained, deep FAP crystallization within dentinal tubules, superior mineral plug durability, and a clinically meaningful reduction in DH symptoms.

While definitive clinical evidence specifically for FCPS mucoadhesive gels remains to be established, the scientific rationale is robust, supported by extensive mechanistic data, in-vitro evidence from gel-based bioactive glass systems, and a strong clinical track record for FCPS in toothpaste form. A systematic research program — spanning particle characterization, formulation optimization, in-vitro tubule occlusion studies, biocompatibility assessment, and ultimately randomized clinical trials — would provide the evidentiary scaffold required for regulatory approval and clinical adoption.

In an era where biomaterial science, pharmaceutical delivery technology, and dental therapeutics are converging, the FCPS-loaded mucoadhesive oral gel exemplifies a rational, patient-centered innovation poised to meaningfully advance the clinical management of dentin hypersensitivity. It holds the promise not merely of symptomatic relief, but of a sustained, self-reinforcing remineralization of exposed dentin — a true structural solution to a condition that has long been managed only symptomatically.

REFERENCES

1. Brannstrom M, Astrom A. A study on the mechanism of pain elicited from the dentin. Journal of Dental Research, 1964; 43(4): 619–625.
2. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R. Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. Journal of Clinical Periodontology, 1997; 24(11): 808–813.
3. Hench LL. The story of Bioglass. Journal of Materials Science: Materials in Medicine, 2006; 17(11): 967–978.
4. Petrovic D, Galic D, Seifert D, Lesic N, Smolic M. Evaluation of bioactive glass treatment for dentin hypersensitivity: a systematic review. Biomedicines, 2023; 11(7): 1992.
5. Swatika K, Ashwini S, Kamala DN. Comparative evaluation of desensitizing efficacy of dentifrice containing 5% fluoro calcium phosphosilicate versus 5% calcium sodium phosphosilicate: a randomized controlled clinical trial. Contemporary Clinical Dentistry, 2018; 9(3): 329–334.
6. Aggarwal S, Borkar AC, Borse AN, Acharya A. Comparative evaluation of fluoro calcium phosphosilicate, calcium sodium phosphosilicate, and strontium chloride hexahydrate containing dentifrice for the treatment of dentin hypersensitivity: a randomized single-blind study. Journal of Indian Society of Periodontology, 2022.
7. Mneimne M, Hill RG, Bushby AJ, Brauer DS. High phosphate content significantly increases apatite formation of fluoride-containing bioactive glasses. Acta Biomaterialia, 2011; 7(4): 1827–1834.
8. Patel VR, Shettar L, Thakur S, Gillam D, Kamala DN. A randomised clinical trial on the efficacy of 5% fluorocalcium phosphosilicate-containing novel bioactive glass toothpaste. Journal of Oral Rehabilitation, 2019; 46(12): 1121–1126.
9. Al-Haddad A, Alarami N, Alshammari AF, Madfa AA. Efficacy of bioactive glass-based desensitizer compared to other desensitizing agents or techniques in dentin hypersensitivity: a systematic review. BMC Oral Health, 2025; 25(1): 899.
10. Gowda RA, Ahmed S, Yoganatha HN, Gowda MCB, Joseph NJM, Raju RM. A scanning electron microscope analysis on the effect of bleaching gel in combination with fluoro calcium phosphosilicate-based dentifrice on whitening of teeth and dentinal tubule occlusion — an in vitro study. Journal of Conservative Dentistry and Endodontics, 2024; 27(8): 878–883.

11. Mishra A, Suryawanshi V, Thaper R. A multicentric observational single arm study to evaluate the effectiveness of toothpaste containing fluoro calcium phosphosilicate (Biomin) in the long-term relief of dentine hypersensitivity. International Journal of Community Medicine and Public Health, 2025; 12(12): 5747–5752.
12. Li XD, Wang YN, Zhao H, et al. Gelatin-modified bioactive glass for treatment of dentin hypersensitivity. International Journal of Molecular Sciences, 2024; 25(22): 11867.
13. Moussa M, Alsherbiny MA, Ibrahim KA. Dentine tubule occlusion effect of hydrolyzed casein in a bioactive glass-based dental desensitizing gel. Journal of Dentistry, 2023; 136: 104868.
14. Bidra AS, Gharpure GJ, Mehta SR, et al. Bioactive glass products for the treatment of dentin hypersensitivity: a scoping review. Clinical Oral Investigations, 2025.
15. Patel J, Gillam D. Efficacy of a BioMin F toothpaste compared to conventional toothpastes in remineralisation and dentine hypersensitivity: an overview. Journal of Dental and Maxillofacial Research, 2025; 8(1): 4–8.
16. Bartold PM. Dentinal hypersensitivity: a review. Australian Dental Journal, 2006; 51(3): 212–218.
17. Liu XX, Tenenbaum HC, Wilder RS, Quock R, Hewlett ER, Ren YF. Pathogenesis, diagnosis and management of dentin hypersensitivity: an evidence-based overview for dental practitioners. BMC Oral Health, 2020; 20(1): 220.
18. Gillam DG. Current diagnosis of dentin hypersensitivity in the dental office: an overview. Clinical Oral Investigations, 2013; 17(Suppl 1): S21–S29.
19. West NX, Lussi A, Seong J, Hellwig E. Dentin hypersensitivity: pain mechanisms and aetiology of exposed cervical dentin. Clinical Oral Investigations, 2013; 17(Suppl 1): S9–S19.
20. Boiko OV, Baker SR, Gibson BJ, et al. Construction and validation of the quality of life measure for dentine hypersensitivity (DHEQ). Journal of Clinical Periodontology, 2010; 37(11): 973–980.
21. Kahler B, Hu JY, Marriot RA, Idiyatullin D. Symmetry and asymmetry of pain from dentin hypersensitivity: comparative and mechanistic insights. Journal of Dental Research, 2021; 100(6): 580–588.
22. Frontiers in Dental Medicine. Synthesis and characterization of a highly stable mucoadhesive gel for oral drug delivery, 2025 (doi:10.3389/fdmed.2025.1696639).
23. Kaczmarek B, Nadolna K, Owczarek A. The physicochemical and biological activity of sodium alginate/tannic acid hydrogels. Materials, 2020; 13(5): 1041.
24. Kanwal N, Hill RG, Gillam D, Bushby A. In vitro formation of fluoride-containing apatite in fluoride bioactive glass in tris buffer solution. Journal of Materials Science: Materials in Medicine, 2018; 29(7): 100.
25. Skallevold HE, Rokaya D, Khurshid Z, Zafar MS. Bioactive glass applications in dentistry. International Journal of Molecular Sciences, 2019; 20(23): 5960.