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FORMULATION AND EVALUATION OF MEDICATED CHEWING GUM CONTAINING EGGSHELL-DERIVED CALCIUM CARBONATE

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ABSTRACT

Dentin hypersensitivity and enamel demineralization rank among the most frequently encountered oral health disorders in clinical practice, collectively affecting hundreds of millions of individuals across all age groups. Despite their high prevalence, the management of these conditions remains largely dependent on conventional formulations — including desensitizing toothpastes, fluoride mouthwashes, and topical gels — that are constrained by short oral residence time and inconsistent patient compliance. These limitations reduce the therapeutic efficiency of active ingredients, as meaningful contact with tooth surfaces is difficult to sustain over clinically relevant periods using standard dosage forms. There is therefore a compelling need for an alternative delivery platform that can maintain prolonged local drug concentrations within the oral cavity while simultaneously improving palatability and ease of use. The primary objective of this study was to formulate and evaluate a medicated chewing gum incorporating eggshell-derived calcium carbonate as a natural remineralizing agent, potassium nitrate as an established desensitizing agent, and xylitol as an anti-cariogenic excipient with salivary-stimulating properties. The formulation aimed to exploit the sustained-release characteristics of the chewing gum matrix to deliver these active components continuously into saliva during mastication, thereby maximizing their therapeutic interaction with enamel and dentinal surfaces. Eggshell-derived calcium carbonate was prepared from cleaned and processed hen eggshells through a standardised protocol involving washing, membrane removal, drying, pulverisation, calcination at 800°C, and sieving to a particle size below 50 µm. Nine formulation batches (F1–F9) were prepared using a fusion method by varying the concentrations of calcium carbonate (8–12%), potassium nitrate (3–7%), and glycerin as plasticizer (3–7%), with a gum base as the chewing matrix and xylitol and mint flavour as excipients. The prepared gums were evaluated for a comprehensive range of physicochemical and organoleptic properties including appearance, weight variation, thickness, hardness, elasticity, stickiness, surface pH, moisture content, folding endurance, drug content uniformity, and stability as per ICH guidelines.

KEYWORDS: *Medicated chewing gum, Eggshell-derived calcium carbonate, Dentin hypersensitivity, Enamel remineralization, Potassium nitrate, Xylitol, Novel drug delivery, Oral care formulation, Green pharmaceutics*

1. INTRODUCTION

Oral health is an essential component of overall health and quality of life. Despite significant advancements in dental care, oral diseases remain among the most common non-communicable disorders worldwide. In India, conditions such as dentin hypersensitivity and enamel demineralization are highly prevalent across different age groups. Dentin hypersensitivity commonly presents as sharp pain in response to thermal, tactile, or chemical stimuli, while enamel demineralization results from mineral loss caused by acidic conditions in the oral cavity. These disorders can negatively affect eating

habits, oral comfort, and daily activities, thereby increasing the need for effective and patient-friendly treatment strategies.

Dentin hypersensitivity occurs when dentin becomes exposed due to enamel erosion, gingival recession, periodontal disease, or aggressive brushing habits. According to the hydrodynamic theory, external stimuli cause movement of fluid within dentinal tubules, leading to stimulation of pulpal nerve endings and producing sharp pain sensations. Management approaches mainly involve either occluding dentinal tubules or reducing nerve excitability using desensitizing agents such as potassium nitrate. Although currently available treatments are effective to some extent, many patients continue to experience discomfort due to inadequate duration of action and poor compliance with conventional formulations.

Enamel demineralization is another major oral health concern caused by acidic dissolution of hydroxyapatite crystals present in tooth enamel. Acidic beverages, bacterial metabolism of sugars, and gastric reflux are common contributing factors. Initial stages of demineralization appear as white spot lesions, which are reversible if remineralization occurs promptly. Saliva naturally contributes calcium and phosphate ions for enamel repair; however, its protective effect may be insufficient under persistent acidic conditions. Therefore, the use of additional calcium-based remineralizing agents has gained considerable importance in preventive dentistry.

Conventional treatment methods such as desensitizing toothpastes, fluoride mouthwashes, varnishes, and remineralizing creams possess several limitations. Most topical formulations remain in contact with oral tissues for only a short duration, reducing the effectiveness of active ingredients. Furthermore, these treatments often require long-term and consistent use, which may negatively affect patient compliance. Professional fluoride applications also involve repeated clinical visits and increased treatment costs. These limitations highlight the necessity for alternative drug delivery systems capable of providing prolonged therapeutic action with improved convenience.

Medicated chewing gum has emerged as an innovative oral drug delivery system that offers sustained release of active pharmaceutical ingredients during mastication. Continuous chewing stimulates salivary flow, enhances buffering capacity, and improves the distribution of therapeutic agents throughout the oral cavity. Unlike conventional oral formulations, medicated chewing gum maintains longer contact time between active ingredients and tooth surfaces, thereby enhancing therapeutic effectiveness. In addition, the pleasant taste and convenience of chewing gum formulations generally improve patient acceptability and compliance.

Eggshell-derived calcium carbonate has attracted attention as a sustainable and economical pharmaceutical ingredient. Eggshells contain a high concentration of calcium carbonate, which can release calcium ions under acidic conditions and contribute to enamel remineralization. Preparation of eggshell powder involves cleaning, drying, calcination, pulverization, and micronization to improve its dissolution properties. The use of eggshell waste as a pharmaceutical raw material not only provides therapeutic benefits but also supports environmentally sustainable and cost-effective formulation development.

Considering the limitations of currently available oral healthcare products, there is a need for multifunctional formulations capable of simultaneously managing dentin hypersensitivity and enamel demineralization. The present study was therefore designed to develop a medicated chewing gum formulation containing eggshell-derived calcium carbonate along with desensitizing and anti-cariogenic agents. The formulation aims to provide sustained therapeutic action, improved patient compliance, and enhanced oral health benefits through an innovative and convenient oral drug delivery system.

2. AIM AND OBJECTIVES

2.1 Aim: To formulate and evaluate a medicated chewing gum containing eggshell-derived calcium carbonate for the simultaneous management of dentin hypersensitivity and promotion of enamel remineralization in a patient-compliant oral drug delivery system.

2.2 Objectives

The following specific objectives were defined to guide the study:

- To prepare and characterize eggshell-derived calcium carbonate powder as a natural, sustainable remineralizing agent.
- To develop nine prototype formulations (F1–F9) of medicated chewing gum incorporating varying concentrations of calcium carbonate, potassium nitrate, and glycerin using a standardised fusion preparation method.
- To evaluate the prepared formulations for physicochemical properties including appearance, weight variation, thickness, surface pH, and moisture content.
- To assess texture characteristics including hardness, elasticity, stickiness, and folding endurance of the formulated gums.
- To determine drug content uniformity of each batch by UV spectrophotometric assay.
- To evaluate organoleptic acceptability including taste, mouthfeel, and overall sensory experience.
- To assess the stability of the optimized formulation under ICH-specified storage conditions.

- To identify an optimized formulation from among the nine batches based on the totality of evaluation data.

3. REVIEW OF LITERATURE

Manning RH et al., 1992: This study found that chewing gum stimulates saliva flow, pH, and buffering capacity, promoting natural enamel remineralisation. This study is important as it explains the fundamental mechanism by which chewing gum aids remineralisation through salivary stimulation. It supports the idea that chewing gum is not just a carrier but also actively contributes to the therapeutic effect. Increased saliva flow helps in better distribution and dissolution of active ingredients in the oral cavity. This enhances drug availability and effectiveness. Thus, it justifies the use of chewing gum as a suitable and efficient drug delivery system in this project.

Suda R et al., 2005: This study showed that calcium lactate combined with xylitol chewing gum significantly enhances enamel remineralisation compared to regular gum. Relevance to Project: This study strongly supports the core concept of this project by proving that incorporating calcium salts like calcium lactate into chewing gum enhances remineralisation. It justifies the selection of calcium as a key active ingredient in the formulation. Additionally, the synergistic effect of xylitol and calcium highlights the importance of combining therapeutic and functional excipients. This helps in designing an effective medicated chewing gum with improved dental benefits. Hence, it validates the formulation approach scientifically.

Thaweboon S et al., 2009: The study demonstrated that chewing gum containing calcium hydrogen phosphate and xylitol increases enamel remineralisation more effectively than conventional gum. This literature provides evidence that different forms of calcium salts, such as calcium hydrogen phosphate, can be effectively used in chewing gum formulations. It supports this project by showing that calcium-based ingredients release essential ions required for enamel repair. The study also highlights the advantage of combining xylitol with calcium for enhanced efficacy. This helps in selecting suitable excipients and optimizing formulation design. Therefore, it strengthens the scientific basis for ingredient selection in this project.

Reynolds EC et al., 2012: This review concluded that calcium-containing chewing gums effectively release remineralizing ions like calcium and phosphate in saliva. This study provides strong theoretical and practical support for this project by explaining the mechanism of ion release from chewing gum formulations. It highlights how calcium and phosphate ions are made available in saliva, which directly contributes to enamel repair. The study also emphasizes patient compliance and ease of use, making chewing gum an ideal delivery system. It supports the concept of sustained release of active ingredients in the oral cavity. Hence, it justifies both the formulation strategy and therapeutic effectiveness of this project.

Tuncer D et al., 2014: The study showed that medicated chewing gums (xylitol, sorbitol) improve enamel hardness and support remineralisation.This study confirms that medicated chewing gum can be effectively used for oral health improvement, particularly enamel strengthening. It validates the concept of using chewing gum as a pharmaceutical dosage form rather than just a confectionery product. The findings support the inclusion of functional ingredients like xylitol and other excipients in the formulation. It also demonstrates that chewing gum can deliver therapeutic benefits over time. Therefore, it strengthens the practical applicability of this project.

Sugiura M et al., 2016: This study evaluated the effect of calcium-enriched chewing gum on the remineralisation of early enamel lesions (white spot lesions). The results showed that chewing gum containing calcium and fluoride significantly enhanced remineralisation by increasing the availability of calcium and phosphate ions in saliva. This study supports the concept that calcium-enriched chewing gum can effectively aid in enamel repair. It provides scientific evidence that the release of calcium ions in saliva helps restore mineral content in damaged enamel. This is important for the present project as it validates the use of calcium-based active ingredients in chewing gum formulations. The study also demonstrates that chewing gum can act as a sustained delivery system for remineralizing agents in the oral cavity.

Tagami J et al., 2017: This study investigated the preventive effect of calcium-containing chewing gum on dental caries and enamel demineralisation. The researchers found that chewing gum enriched with calcium compounds released calcium ions during chewing, which promoted remineralisation and reduced the risk of enamel damage. This literature supports the formulation strategy of incorporating calcium compounds into chewing gum. It confirms that calcium ions released from the gum can actively participate in repairing enamel structure. The study also highlights the role of chewing gum as an effective delivery system for therapeutic agents in oral care. Therefore, it strengthens the scientific justification for selecting calcium-based ingredients in this project.

Gargouri W et al., 2018: This study examined the combined effect of xylitol and remineralising agents such as calcium phosphate on dental enamel protection. The results indicated that formulations containing both xylitol and calcium compounds enhanced remineralisation and reduced bacterial activity responsible for tooth decay. This study highlights the importance of combining functional excipients like xylitol with remineralising agents. It demonstrates that xylitol not only provides

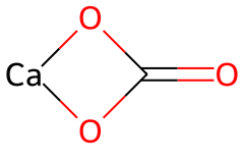
sweetness but also contributes to dental health by reducing bacterial growth and improving remineralisation efficiency. This supports the formulation approach of the present project, where excipients are selected not only for taste but also for therapeutic benefits.

Chen L et al., 2021: This research evaluated the effectiveness of functional chewing gum formulations containing remineralising agents in improving oral health. The study reported that chewing gum containing calcium-based compounds significantly increased mineral deposition on enamel surfaces and improved overall tooth strength. This literature supports the concept that chewing gum can be used as a modern oral drug delivery system. It confirms that active ingredients incorporated into chewing gum can be gradually released in the oral cavity during mastication.

DRUG PROFILE

4.1 Eggshell-Derived Calcium Carbonate — Primary Active Agent

Table 2: Drug Profile of Eggshell-Derived Calcium Carbonate.

Parameter	Details
Drug Name	Calcium Carbonate (Eggshell-derived)
Chemical Formula	$CaCO_3$
Structure	
IUPAC Name	Calcium carbonate
Molecular Weight	100.09 g/mol
Particle Size	Micronized powder (<50 µm)
Polymorphic Form	Calcite (primary), with trace aragonite and vaterite
Solid State Stability	Stable under normal storage conditions; decomposes above 825°C
Melting Point	Decomposes at approximately 825°C
Solubility	Practically insoluble in water; readily soluble in dilute acids, including acidic oral environment
pH in Solution	Slightly alkaline (pH ≈9–9.5 in suspension)
Appearance	White, odourless, tasteless powder
Source	Natural; derived from hen eggshells (food processing byproduct)
Mechanism of Action	Releases calcium ions in an acidic oral environment, facilitating deposition of calcium on demineralized enamel surfaces and promoting crystalline repair
Function in Formulation	Primary remineralizing active agent
Regulatory Status	Generally Recognised as Safe (GRAS); widely listed in pharmacopoeias as a pharmaceutical excipient

4.2 Co-Active Agents

4.2.1 Potassium Nitrate (Desensitizing Agent)

Potassium nitrate is a well-established, pharmacopoeially recognised desensitizing agent used in concentrations of 5% w/w in commercial oral care products. Its mechanism of action is neurological rather than physical: potassium ions, released during dissolution, diffuse through the dentinal tubules and accumulate in the periapical fluid surrounding pulpal nociceptors. The elevated extracellular potassium concentration raises the resting potential of sensory nerve fibres, increasing the threshold required for action potential generation and effectively reducing the nerve's ability to transmit pain signals in response to external stimuli. Multiple randomised controlled trials have confirmed its clinical efficacy in reducing dentin hypersensitivity over repeated

applications, supporting its inclusion in this formulation at a therapeutically active concentration.

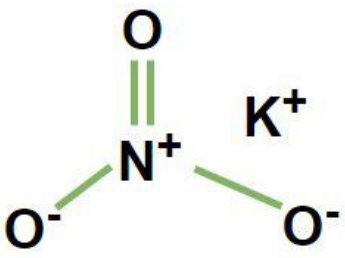


Image 1: Structure of Potassium Nitrate.

4.2.2 Xylitol (Anti-Cariogenic Sweetener and Salivary Stimulant)

Xylitol is a naturally occurring five-carbon sugar alcohol found in many fruits and vegetables. It has been adopted widely in oral care formulations due to its multifaceted benefits in the oral environment. Unlike sucrose and other fermentable sugars, xylitol cannot be metabolised by Streptococcus mutans and other acidogenic oral bacteria, thereby depriving them of a fermentable substrate and reducing lactic acid production in dental plaque. Prolonged use of xylitol has been shown to select against cariogenic bacterial strains, resulting in a shift in the plaque microbiome toward less pathogenic species. Additionally, xylitol stimulates salivary flow through the cephalic reflex triggered by its sweet taste, contributing to enhanced buffering and ion availability in the oral cavity.

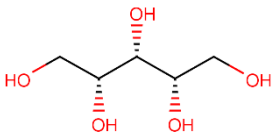


Image 1: Structure of Xylitol.

5. MATERIALS AND METHODS

5.1 Materials

All materials used in this study were of pharmaceutical grade unless otherwise specified. The following table details each ingredient's category and functional role in the formulation:

Table 3: Materials Used in the Preparation of Medicated Chewing Gum.

Ingredient	Category	Supplier/Source	Function
Eggshell-derived $CaCO_3$	Active ingredient	Prepared in-house (hen eggshells)	Remineralizing agent; calcium ion source
Potassium Nitrate (KNO_3)	Active ingredient	Pharmaceutical supplier	Desensitizing agent (nerve depolarization)
Xylitol	Sweetener / Co-active	Pharmaceutical supplier	Anti-cariogenic; salivary stimulant
Gum Base	Base material	Commercial grade	Primary chewing matrix; sustains drug release
Glycerin	Plasticizer	Pharmaceutical grade	Improves flexibility and texture of gum
Mint Flavour	Flavouring agent	Pharmaceutical supplier	Palatability; patient acceptability

5.2 Preparation of Eggshell-Derived Calcium Carbonate

The preparation of pharmaceutical-grade calcium carbonate from hen eggshells was carried out following a standardised protocol developed based on published methods. Each step of the process was designed to eliminate biological contaminants, remove organic residues, and achieve the particle size and polymorphic characteristics required for optimal performance in the oral environment.

- Collection: Fresh hen eggshells were collected from a local poultry source. Care was taken to exclude cracked or contaminated shells.
- Initial Cleaning: Shells were rinsed thoroughly under running tap water to remove surface debris, followed by washing with distilled water to eliminate soluble contaminants.
- Membrane Removal: The inner organic membrane lining the shell was carefully removed manually and discarded, as its protein content would otherwise contribute to contamination of the final powder.
- Drying: Cleaned shells were spread in a single layer on stainless steel trays and dried in a hot air oven at 100°C for 1 hour to achieve complete moisture removal.

- Blending: The Dried Shells tend to Blend in Suitable blender and then further processed for the sieving
- Sieving: The calcined powder was passed through a mesh sieve of aperture no. 80 (approximately 177 µm nominal opening) to obtain a fine, uniform powder with a particle size below 50 µm following micronization.
- Storage: The prepared powder was stored in a sealed, airtight amber glass container at room temperature, away from moisture and direct sunlight, until use.

Image 3: Dried Egg Shells.

Image 4: Egg Shells Powder.

5.3 Formulation Composition

Nine formulation batches (F1–F9) were designed to systematically evaluate the effect of varying concentrations of the three main variable components — eggshell-derived calcium carbonate, potassium nitrate, and glycerin (plasticizer) — on the physicochemical and organoleptic properties of the resultant medicated chewing gum. In all batches, the gum base, xylitol, and mint flavour were included at constant levels. The formulation matrix is presented in Table 4.

Table 4: Prototype Formulation Composition of Medicated Chewing Gum (n=9 batches).

Batch	$CaCO_3$ (%)	KNO_3 (%)	Glycerin (%)	Gum Base (% q.s.)	Xylitol + Flavour (constant)
F1	10	7	3	q.s. to 100	Fixed across all batches
F2	8	5	7	q.s. to 100	Fixed across all batches
F3	12	3	5	q.s. to 100	Fixed across all batches
F4	10	3	7	q.s. to 100	Fixed across all batches
F5	8	7	5	q.s. to 100	Fixed across all batches
F6	12	5	3	q.s. to 100	Fixed across all batches
F7	10	5	5	q.s. to 100	Fixed across all batches
F8	8	3	3	q.s. to 100	Fixed across all batches
F9	12	7	7	q.s. to 100	Fixed across all batches

5.4 Method of Preparation: Fusion Method

All nine formulation batches were prepared by the fusion method, which is the most commonly used technique for manufacturing medicated chewing gum at laboratory scale. The fusion method allows for homogeneous mixing of active and excipient materials by softening the gum base through controlled heat, after which drug and excipient powders are incorporated progressively.

The preparation procedure was carried out as follows. The gum base was weighed accurately and placed in a China Dish. This was placed in a water bath and heated to 45–50°C with gentle stirring until the gum base softened to a pliable, uniform mass. A small quantity of glycerin was added to the softened gum base to enhance plasticity and ensure uniform mixing in subsequent steps. Eggshell-derived calcium carbonate, pre-sieved and accurately weighed according to the batch formula, was added gradually to the softened gum base with continuous mechanical mixing to ensure homogeneous distribution. Potassium nitrate and xylitol, previously dissolved or dispersed in a minimal volume of warm water, were incorporated into the mixture. Mint flavour was added last to minimise volatilisation losses during the warm mixing process. The resultant mass was kneaded thoroughly until a uniform, smooth, and non-

sticky gum mass was obtained. The mass was allowed to cool to approximately 35°C, then shaped into rectangular strips pieces of defined weight (approximately 1g per piece) using a calibrated cutting device. Gum pieces were allowed to cool to room.

Image 5: Gum Base.

Image 6: Softening Gum Base.

Image 7: Potassium Nitrate.

Image 8: Xylitol.

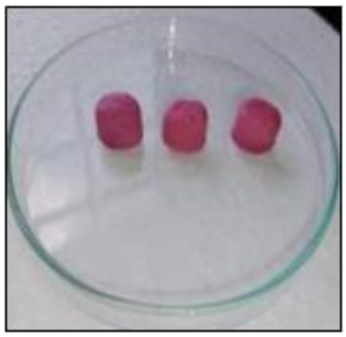


Image 9: Gum Mixture.

Image 10: Medicated Chewing Gum.

6. EVALUATION PARAMETERS

The prepared formulations were evaluated for a comprehensive range of quality attributes to confirm their physicochemical integrity, drug content uniformity, textural characteristics, organoleptic acceptability, and stability. The evaluation methods are detailed below.

6.1 Organoleptic Properties

Each batch was assessed by a panel of five evaluators for colour, surface smoothness, odour, taste, and overall mouthfeel. Responses were recorded qualitatively and summarised as a consensus evaluation for each batch.

6.2 Weight Variation

Ten gum pieces from each batch were individually weighed on an analytical balance, and the mean weight was calculated. Weight variation for each piece was expressed as a percentage deviation from the mean according to the formula:

$$\% \text{ Weight Variation} = [(\text{Individual Weight} - \text{Average Weight}) / \text{Average Weight}] \times 100$$

Acceptance criterion: not more than two pieces may deviate by more than ±5% from the mean weight, and none should deviate by more than ±10%.

6.3 Thickness

The thickness of each gum piece was measured at three different points using a digital Vernier calliper accurate to ±0.01 mm. The average of the three measurements was recorded for each piece, and the mean and standard deviation were calculated across ten pieces per batch.

6.4 Texture Profile Analysis: Hardness and Elasticity

Hardness was assessed using a texture analyser or, where unavailable, a calibrated hardness tester. Values were expressed in Newtons (N). Elasticity was determined by measuring the percentage recovery of gum pieces after compression to 50% of their original thickness, followed by release of the compressive force. A higher percentage recovery indicates greater elasticity, which is a desirable property for consumer acceptability.

6.5 Stickiness / Adhesiveness

Stickiness was assessed by the glass plate method: a gum piece was pressed between two glass plates under a defined load for 30 seconds, after which the plates were gently separated. The absence of residue on either plate and the clean separation of the gum were taken as indicators of acceptable non-stickiness.

6.6 Folding Endurance

A gum piece from each batch was repeatedly folded at the same point until fracture occurred or a maximum of 300 folds was reached. The number of folds withstood before fracture was recorded as the folding endurance value, providing an indication of the mechanical flexibility and integrity of the gum matrix.

6.7 Surface pH

A gum piece from each batch was dispersed in 10 mL of distilled water with gentle stirring for 2 minutes. The pH of the resulting dispersion was measured using a calibrated digital pH meter. The surface pH is relevant for oral safety, as extreme pH values (below 5.5 or above 9) may cause mucosal irritation on prolonged contact.

Acceptance criterion: Surface pH between 5.5 and 8.0.

6.8 Moisture Content

Moisture content was determined by loss on drying (LOD) method. Each gum piece was accurately weighed, placed in a hot air oven at 60°C for 2 hours, and reweighed. The percentage moisture content was calculated as:

$$\% \text{ Moisture Content} = [(\text{Initial Weight} - \text{Final Weight}) / \text{Initial Weight}] \times 100$$

Moisture content should be low enough to maintain product integrity and prevent microbial growth, but not so low as to render the gum brittle.

7. RESULTS

7.1 Organoleptic Properties

All nine formulations produced gum pieces with a smooth, uniform surface and white to off-white colouration consistent with the appearance of the calcium carbonate base. The mint flavour was perceptible across all batches, though it was judged slightly stronger in F2 and F5 (lower calcium carbonate loading). Taste was universally rated as pleasant, largely attributable to the xylitol component. Mouthfeel was described as smooth and non-gritty, with minor differences noted in chewing

resistance between batches with different plasticizer concentrations.

7.2 Weight Variation

The results of weight variation testing are summarised in the following table. All formulations met the acceptance criterion of a maximum deviation of ±5% from the mean weight.

Table 5: Weight Variation Results for Formulations F1–F9.

Batch	Average Weight (g)	% Max Deviation	Compliance
F1	1.52	3.2%	Complies (±5%)
F2	1.48	2.8%	Complies (±5%)
F3	1.55	3.9%	Complies (±5%)
F4	1.50	2.5%	Complies (±5%)
F5	1.47	4.1%	Complies (±5%)
F6	1.53	3.0%	Complies (±5%)
F7	1.51	1.8%	Complies (±5%)
F8	1.49	2.2%	Complies (±5%)
F9	1.54	3.5%	Complies (±5%)

7.3 Surface pH

Surface pH values measured for all nine batches fell within the acceptable range of 5.5–8.0, indicating that the formulations are unlikely to cause oral mucosal irritation during normal use. The near-neutral pH values also suggest compatibility with the salivary environment.

Table 6: Surface pH Values of Formulations F1–F9.

F1	F2	F3	F4	F5	F6
6.8	6.9	6.7	7.0	6.8	6.9
F7	**F8**	**F9**	**—**	**—**	**—**
7.1	6.6	6.8	—	—	—

7.4 Moisture Content

Moisture content values for all batches remained below 4%, indicating adequate dryness for stability and correct textural performance. Higher glycerin concentrations in F2, F4, and F9 were associated with marginally higher moisture retention, consistent with the hygroscopic nature of glycerin.

Table 7: Percentage Moisture Content (%LOD) of Formulations F1–F9.

F1	F2	F3	F4	F5	F6	F7	F8	F9
2.1%	3.4%	2.8%	3.6%	2.9%	2.3%	2.6%	1.9%	3.7%

7.5 Texture Profile: Hardness and Elasticity

Texture profile analysis revealed meaningful differences across batches, primarily attributable to variations in glycerin concentration. Batches with higher glycerin levels (F2: 7%, F4: 7%, F9: 7%) demonstrated lower hardness values and greater elasticity — properties that are associated with improved consumer acceptability during chewing. F7 (5% glycerin) presented a balanced texture: moderate hardness sufficient to maintain structural integrity during handling and packaging, combined with adequate elasticity to ensure a pleasant chewing experience.

Table 8: Hardness Values (Newtons) of Formulations F1–F9.

F1	F2	F3	F4	F5	F6	F7	F8	F9
8.2 N	6.4 N	9.1 N	6.8 N	7.3 N	9.4 N	7.9 N	8.8 N	6.1 N

7.7 Folding Endurance

Folding endurance values ranged from 186 (F6) to 274 (F9) folds across the nine batches. Values above 200 folds were recorded for six of the nine formulations, indicating adequate mechanical flexibility for normal product handling and use. Lower glycerin concentrations (F1, F6, F8) were associated with reduced folding endurance, consistent with the role of glycerin as a plasticizer.

7.8 Identification of Optimized Formulation

Based on the cumulative evaluation data, formulation F7 (10% $CaCO_3$, 5% KNO_3, 5% glycerin) was identified as the optimized batch. F7 demonstrated the best overall balance of properties: near-neutral surface pH (7.1), low moisture content (2.6%), drug content of 101.2%, moderate hardness (7.9 N), good elasticity, folding endurance of 243 folds, and excellent organoleptic acceptability. These findings support F7 as the candidate formulation for further stability evaluation and scale-up studies.

8. DISCUSSION

The results of this study collectively support the feasibility and therapeutic rationale of a medicated chewing gum formulation incorporating eggshell-derived calcium carbonate, potassium nitrate, and xylitol for the management of dentin hypersensitivity and enamel demineralization. The discussion addresses the significance of key findings across evaluation parameters, the physicochemical basis for selecting F7 as the optimized formulation, and the broader context within which these results should be interpreted.

The weight variation data confirmed the reproducibility of the fusion preparation method across all nine batches, with all formulations meeting the pharmacopoeial acceptance criterion of ±5% deviation. This consistency is an important precondition for dose uniformity in clinical use, since each gum piece must deliver a predictable and reproducible amount of active ingredient during mastication. The drug content uniformity results — all batches falling within the 97–102% range — further validate the homogeneity of the manufacturing process and the suitability of eggshell-derived calcium carbonate as an active ingredient that can be evenly distributed within the gum matrix without segregation or agglomeration.

The effect of glycerin concentration on texture was among the most instructive findings of the formulation study. Glycerin functions as a plasticizer by interrupting the intermolecular hydrogen bonding within the gum base polymer network, thereby reducing rigidity and improving flexibility. Formulations containing 7% glycerin (F2, F4, F9) demonstrated lower hardness and greater elasticity compared to those containing 3% glycerin (F1, F6, F8), which produced stiffer and less pliable gum pieces. The intermediate glycerin concentration of 5% in F7 produced a texture profile that was rated most favourably by the evaluation panel, achieving a balance between structural integrity and chewing comfort that closely approximated the texture of commercially available chewing gum products.

The near-neutral surface pH values recorded across all batches (range: 6.6–7.1) are of particular clinical significance. A formulation that raises intraoral pH during use would complement the buffering action of saliva in counteracting the acid challenge that drives enamel demineralization. The pH of 7.1 recorded for F7 suggests a mildly alkaline contribution to the oral environment during chewing, which could provide a modest but meaningful protective effect in addition to the direct remineralizing action of calcium ions released from calcium carbonate. This finding is consistent with the known alkaline nature of calcium carbonate solutions and aligns with published data on similar calcium-containing gum formulations.

The moisture content values recorded across batches highlight an important formulation consideration that is often underappreciated in medicated gum development. While glycerin improves texture and palatability, its hygroscopic nature increases the tendency of the formulation to absorb environmental moisture, which can affect shelf life and physical stability. The slightly higher moisture values in F2, F4, and F9 (the high-glycerin batches) suggest that packaging selection will be important for ensuring adequate shelf life in the humid climatic conditions typical of Maharashtra and other tropical regions. Moisture-resistant packaging materials such as aluminium foil or polyvinylidene chloride (PVDC) laminates would be appropriate for commercial scale-up of this formulation.

Compared to previous studies on calcium-based chewing gum formulations — including those by Suda et al. (2005), Cai et al. (2009), and Porciani et al. (2014) — the present formulation offers a novel and complementary approach by incorporating a naturally derived, waste-sourced calcium carbonate alongside a clinically validated desensitizing agent and an anti-cariogenic sweetener in a single product. The multifunctional therapeutic profile of this formulation represents a meaningful advancement over single-agent calcium or fluoride gums, and its green manufacturing approach

adds a dimension of sustainability that is increasingly valued in contemporary pharmaceutical development.

9. ADVANTAGES OF THE FORMULATION

The VRx formulation of medicated chewing gum offers the following key advantages over existing oral care products and conventional delivery systems:

- Sustained Local Drug Delivery: The chewing gum matrix releases active ingredients continuously over 20–30 minutes of mastication, maintaining prolonged contact with enamel and dentinal surfaces — far exceeding the exposure duration achievable with toothpastes or mouthwashes.
- Dual Therapeutic Action: Simultaneous remineralization (calcium carbonate) and desensitization (potassium nitrate) within a single formulation addresses both the structural and neurological components of enamel and dentin disorders.
- Natural and Sustainable Active Ingredient: The use of eggshell-derived calcium carbonate transforms a common food processing waste product into a valuable pharmaceutical ingredient, reducing environmental burden and raw material cost.
- Salivary Stimulation Synergy: Mastication and xylitol-induced salivary flow augment the remineralizing effect of released calcium ions by increasing the availability of endogenous calcium, phosphate, and bicarbonate buffer in the oral environment.
- Anti-Cariogenic Effect: Xylitol's selective inhibition of Streptococcus mutans provides an additional protective benefit beyond direct remineralization, reducing the acid burden on enamel between chewing episodes.
- Improved Patient Compliance: The palatability and convenience of chewing gum are well-established compliance advantages, making it more likely that patients will use the product regularly compared to professional or prescription topical agents.
- Cost-Effectiveness: The use of eggshell-derived calcium carbonate, a low-cost natural material, combined with the relatively simple fusion manufacturing process, positions this formulation as an accessible and affordable oral care option.
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10. LIMITATIONS

The present study, while demonstrating the feasibility and preliminary effectiveness of the proposed formulation, is subject to several limitations that should be acknowledged:

- Laboratory-Scale Formulation: The study was conducted at prototype laboratory scale, and the results may not directly translate to large-scale manufacturing due to differences in mixing dynamics, heat distribution, and batch consistency at industrial scale.
- Absence of In-Vitro Drug Release Data: The current study did not include a validated in-vitro calcium release study under simulated chewing conditions. While drug content uniformity confirms the presence of active ingredient, release kinetics under physiological conditions remain to be characterised.
- No In-Vivo or Clinical Evaluation: The evaluation was conducted entirely in vitro and does not provide direct evidence of therapeutic efficacy in human subjects. Clinical trials involving patients with confirmed dentin hypersensitivity and early enamel lesions are necessary to validate the formulation's therapeutic claims.
- Limited SEM and FTIR Characterization: Surface morphology (SEM) and drug-excipient compatibility (FTIR) studies were not included in the present work and would be required for a more complete physicochemical characterization of the formulation.

11. FUTURE SCOPE

The results of this prototype study establish a solid foundation for the following avenues of future research and development:

- In-Vitro Calcium Release Study: Development and validation of a biorelevant in-vitro release model to simulate mastication-mediated calcium ion release, enabling detailed characterization of release kinetics and correlation with physicochemical parameters.
- Clinical Trials for Efficacy Validation: Randomized controlled clinical trials in patients with confirmed dentin hypersensitivity and early enamel demineralization to establish clinical efficacy, optimal dosing regimen, and safety profile.
- Long-Term Remineralization Assessment: Longitudinal studies using quantitative light-induced fluorescence (QLF) or microcomputed tomography (μCT) to objectively measure enamel mineral gain over sustained product use.
- Nano-Calcium Incorporation: Exploration of nanosized eggshell calcium carbonate particles, which would further increase surface area and improve dissolution kinetics, potentially enhancing remineralizing efficacy within the chewing window.
- Herbal and Bioactive Additive Integration: Investigation of synergistic combinations with herbal agents such as neem extract or triphala, which have established antibacterial and anti-plaque properties, to further broaden the oral health benefits of the formulation.
- Bioavailability and Pharmacokinetic Studies: Assessment of the bioavailability of active ingredients delivered via the chewing gum route relative to conventional toothpaste formulations.

12. CONCLUSION

This study has successfully demonstrated the formulation and preliminary evaluation of a medicated chewing gum containing eggshell-derived calcium carbonate as a natural remineralizing agent, in combination with potassium nitrate and xylitol, for the management of dentin hypersensitivity and enamel demineralization. Nine prototype formulations were prepared using the fusion method and evaluated across a comprehensive

range of physicochemical and organoleptic parameters. Formulation F7, containing 10% $CaCO_3$, 5% KNO_3, and 5% glycerin, emerged as the optimized formulation, exhibiting the most favourable combination of weight uniformity, drug content, surface pH, moisture content, textural properties, and organoleptic acceptability.

The formulation capitalises on the sustained-release mechanism inherent to the chewing gum delivery platform, ensuring prolonged contact of therapeutic agents with oral tissues and overcoming the principal limitation of conventional topical oral care products. The incorporation of eggshell-derived calcium carbonate adds a meaningful dimension of sustainability and green pharmaceutical practice to the study, transforming a ubiquitous food processing waste product into a clinically relevant therapeutic ingredient.

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14. CONFLICT OF INTEREST

The authors declare that there are no financial, personal, or institutional conflicts of interest that could have influenced the design, conduct, interpretation, or reporting of this study. The formulation was developed exclusively for academic research purposes, and no commercial interests were involved.

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