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CALCIUM CARBONATE–VITAMIN D_3 GUMMY LOZENGES: FORMULATION STRATEGIES, PHARMACEUTICAL CHARACTERIZATION, STABILITY CHALLENGES AND FUTURE PERSPECTIVES—A CRITICAL REVIEW

Aftab Khan*, Dr Tara Chand, Ashish Jain, Nehal Sharma

Regional College of Pharmacy, ISI-17, RIICO Institutional Area, Sitapura, Jaipur, Rajasthan-302022, India.

***Corresponding Author: Aftab Khan**

Regional College of Pharmacy, ISI-17, RIICO Institutional Area, Sitapura, Jaipur, Rajasthan-302022, India.

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ABSTRACT

Gummy dosage forms have progressed from confectionery products to increasingly sophisticated oral delivery platforms for pharmaceuticals, vitamins and minerals. Their chewability, portability, water-free administration and potential for taste masking make them attractive for populations who may experience difficulty with conventional tablets or capsules. Calcium carbonate and vitamin D_3 represent a particularly relevant combination because calcium carbonate is a high-density, poorly water-soluble mineral salt, whereas vitamin D_3 is a lipophilic and chemically sensitive micronutrient. The simultaneous incorporation of these components into a gummy matrix therefore requires control of particle dispersion, matrix rheology, texture, moisture, dose uniformity, release and chemical stability. This critical review examines the scientific basis of calcium carbonate–vitamin D_3 gummy lozenges, with emphasis on active-ingredient properties, hydrocolloid selection, gelatin–pectin systems, sweetener and acidulant effects, manufacturing approaches, taste and mouthfeel, analytical characterization, release testing, stability, quality-by-design (QbD), emerging technologies and regulatory considerations. Recent literature indicates that gummy quality is multidimensional: hardness, adhesiveness, chewiness, cohesiveness, springiness, moisture, mass uniformity and intraoral dissolution can all contribute to product performance. Vitamin D_3 stability represents a particular challenge because temperature, light, oxygen, pH and metal ions can affect degradation. The review also identifies important gaps in the current literature, including limited standardization of pharmaceutical gummy specifications, inadequate reporting of analytical methods, limited comparative studies of calcium salts, and a scarcity of validated calcium carbonate–vitamin D_3 gummy studies linking formulation attributes with in vivo performance. Future development should integrate QbD, multivariate experimental design, validated stability-indicating assays, protective packaging, texture profiling and, where appropriate, pharmacokinetic or bioavailability studies.

KEYWORDS: Calcium Carbonate; Cholecalciferol; Vitamin D_3; Gummy Lozenge; Chewable Dosage Form; Gelatin; Pectin; Texture Analysis; Content Uniformity; Stability; Quality By Design; Oral Drug Delivery.

1. INTRODUCTION

Oral dosage forms remain central to pharmaceutical and nutritional delivery because of their convenience, patient familiarity and manufacturing scalability. Nevertheless, conventional tablets and capsules may present acceptability and swallowing challenges for children, older adults and individuals with dysphagia or aversion to solid dosage forms. Gummy dosage forms have consequently attracted increasing interest as chewable matrices capable of incorporating active pharmaceutical ingredients, vitamins, minerals and other bioactive compounds. Recent work has emphasized that the appeal of gummies is not simply their shape or flavour; their performance depends on a complex relationship between hydrocolloid structure, water activity, sugar solids, active-ingredient distribution, texture and storage conditions.[1–4]

The development of pharmaceutical gummies is moving beyond simple confectionery adaptation. Recent research

has demonstrated the feasibility of medicated gummies containing conventional drugs, including pediatric formulations and controlled-release systems, while semi-solid extrusion 3D printing has opened opportunities for individualized dose and shape.[5–8] A 2024 study of prototype gummies demonstrated the importance of quantitative micromechanical and physicochemical characterization and proposed measurable quality attributes that could contribute to future specification development.[1] A 2026 perspective on gummy dietary supplements similarly emphasized formulation, manufacturing and analytical-testing challenges and the need for improved product consistency and stability.[9]

Calcium and vitamin D are frequently combined in nutritional supplementation because calcium is required for skeletal and physiological functions while vitamin D contributes to calcium homeostasis and intestinal calcium absorption. Calcium carbonate is widely used because of its high elemental-calcium content and established availability. However, it is practically insoluble in water, and its dissolution is strongly influenced by the acidic environment of the stomach.[10,11] Its high particle density also creates a formulation challenge in a viscous gummy matrix: inadequate suspension or mixing may produce sedimentation, nonuniform dosing and a gritty mouthfeel.

Vitamin D_3, or cholecalciferol, presents a contrasting formulation problem. It is lipophilic and susceptible to degradation under several environmental conditions. A systematic stability study demonstrated that vitamin D_3 stability in aqueous systems can be affected by temperature, light, oxygen, pH, concentration and metal ions, with acidic conditions and metal ions among the important destabilizing factors.[12] Therefore, the combination of calcium carbonate and vitamin D_3 in one gummy requires simultaneous management of a dense particulate mineral and a low-level, chemically sensitive lipophilic component.

The objective of this critical review is to integrate current evidence concerning the formulation and pharmaceutical characterization of calcium carbonate–vitamin D_3 gummy lozenges. Particular attention is given to the formulation–process–quality relationship, including polymer selection, active dispersion, texture, taste masking, release, analytical methods, stability, QbD and emerging manufacturing technologies. The review also identifies knowledge gaps that should be addressed before these systems can be developed into robust pharmaceutical or nutraceutical products.

2. Review Methodology

A structured narrative literature review was undertaken to identify evidence relevant to calcium carbonate–vitamin D_3 gummies and the broader pharmaceutical science of gummy dosage forms. Literature was identified through searches of PubMed/MEDLINE and publisher-indexed scientific literature, supplemented by official regulatory and scientific sources. Search concepts included combinations of the terms “gummy”, “gummy dosage form”, “medicated gummy”, “chewable gummy”, “calcium carbonate”, “calcium supplement”, “vitamin D3”, “cholecalciferol”, “gelatin”, “pectin”, “texture analysis”, “content uniformity”, “drug release”, “stability”, “3D printing”, “quality by design” and “dietary supplement manufacturing”. Priority was given to peer-reviewed literature, recent reviews, primary formulation studies and official guidance. Older studies were retained where they provided foundational evidence on calcium absorption, gummy composition or dosage-form principles.

This article is a critical/narrative review rather than a registered systematic review or meta-analysis. Consequently, no numerical claim of comprehensive database retrieval or PRISMA study selection is made. The objective was to synthesize formulation science and identify research priorities rather than estimate a pooled clinical effect.

3. Scientific Rationale for Combining Calcium Carbonate and Vitamin D_3

3.1 Calcium carbonate as an active mineral

Calcium carbonate is a commonly used calcium salt in nutritional supplementation. Its principal formulation advantages include high calcium density, established availability and comparatively low material cost. Its major pharmaceutical limitations are its low aqueous solubility and dependence on acidic conditions for efficient dissolution. The physiological literature indicates that gastric acidity can markedly improve calcium carbonate dissolution, and absorption is influenced by the meal context and individual physiological conditions.[10,11]

In a gummy, however, the relevant formulation problem begins before gastrointestinal dissolution. Calcium carbonate must be dispersed uniformly in a polymeric/sugar matrix during manufacture. Because the particles are dense relative to the continuous phase, prolonged processing or insufficient viscosity can permit sedimentation. Conversely, excessive viscosity may complicate mixing, filling and deaeration. Particle size distribution is therefore an important critical material attribute. Finer particles may improve sensory characteristics and suspension but can also modify rheology, surface area and dissolution behaviour.

3.2 Vitamin D_3 as a lipophilic micronutrient

Vitamin D_3 has poor aqueous solubility and is sensitive to environmental stress. Its incorporation into an aqueous or semi-aqueous gummy system is therefore fundamentally different from the incorporation of calcium carbonate. Direct addition of crystalline vitamin D_3 may result in poor dispersion, low-dose segregation and analytical recovery problems. Lipid carriers, emulsified systems, pre-dissolved concentrates,

encapsulated vitamin D_3 and other solubilization approaches may improve dispersion and protection, but each introduces additional formulation and regulatory considerations.

The stability of vitamin D_3 is particularly important because potency loss can occur without obvious changes in gummy appearance. Temova Rakuša et al. systematically investigated vitamin D_3 stability and showed that temperature, pH, light, oxygen and metal ions can affect degradation.[12] This evidence supports the use of light-protective packaging, controlled processing temperature, appropriate antioxidants or chelators where justified, and stability-indicating analytical methods.

4. Gummy Dosage Forms as Pharmaceutical Delivery Systems

Gummies are structured semisolid or soft-solid matrices formed through gelation and/or concentration of hydrocolloids and other structural ingredients. Their performance differs from that of conventional compressed tablets because mechanical properties, water mobility, chewing behaviour and dissolution are interdependent. A gummy can exhibit acceptable appearance while having unacceptable stickiness, insufficient structural strength, poor active uniformity or inadequate stability.

A recent characterization study of prototype gummies measured hardness, adhesiveness, chewiness, cohesiveness, springiness, resilience, firmness, rupture behaviour, moisture, weight uniformity and intraoral dissolution pH, demonstrating the breadth of quality attributes relevant to gummy products.[1] Texture analysis has also become an established tool for pharmaceutical oral dosage forms, although differences in instruments, probes and test conditions make direct comparison between studies difficult.[13]

Gummy quality domain	Representative critical quality attributes	Why it matters
Physical	Appearance, dimensions, mass, shape, surface integrity	Manufacturing consistency and consumer acceptability
Mechanical	Hardness/firmness, adhesiveness, chewiness, cohesiveness, springiness	Mastication, handling and dose-form integrity
Chemical	Assay, degradation products, pH	Potency and stability
Uniformity	Mass and active-content uniformity	Dose accuracy
Performance	Disintegration, dissolution/release profile	Availability of active ingredient
Microbiological	Total microbial quality and specified organisms as applicable	Product safety
Stability	Assay, texture, moisture, appearance, release	Shelf-life and packaging suitability

5. Formulation Components and Their Functional Roles

5.1 Gelatin

Gelatin is a widely used gummy-forming polymer because it can generate elastic, cohesive gels and contributes strongly to chewiness and mouthfeel. Gelatin concentration, bloom strength, hydration conditions, temperature and cooling history can affect the final network. Increasing gelatin concentration generally increases structural strength, but excessive gel strength can reduce chewability and alter dissolution. Gelatin is animal-derived, which may also influence source selection, religious or dietary acceptability, allergen considerations and product labeling.

5.2 Pectin

Pectin is a natural polysaccharide with established pharmaceutical and food applications. Its gelation behaviour depends on molecular characteristics, degree of esterification, soluble-solids concentration, pH and ionic environment. Recent reviews describe pectin as a versatile material for oral and other drug-delivery systems and highlight the influence of crosslinking and environmental conditions on release.[14–16] In gummy formulations, pectin can provide a useful alternative or complement to gelatin and may support vegetarian/vegan product concepts depending on the complete formulation.

5.3 Gelatin–pectin combinations

Combining gelatin and pectin can allow independent tuning of elasticity, firmness and gel structure. However, the optimum ratio cannot be generalized because it depends on polymer grade, solids content, acidification, processing temperature and active loading. For calcium carbonate–vitamin D_3 systems, polymer selection should be considered together with mineral suspension, moisture and release requirements rather than as an isolated variable.

5.4 Sugars and glucose syrup

Sucrose and glucose syrup contribute sweetness, total soluble solids, viscosity, body and water-binding characteristics. They also influence crystallization,

moisture migration and texture during storage. High sugar levels can improve palatability but may be undesirable for some consumer groups and may complicate positioning as a health-oriented product. Sugar-reduced or sugar-free systems require alternative bulking agents and sweeteners, which can substantially change gel structure and water activity.

5.5 Acidulants and pH modifiers

Citric acid and related acidulants contribute flavour and pH control. Acidification can influence pectin gelation, gelatin behaviour, calcium carbonate dissolution and vitamin D_3 stability. Because acidic conditions can destabilize vitamin D_3 in aqueous systems while also favouring calcium carbonate dissolution, pH optimization represents a particularly important formulation trade-off.[12]

5.6 Flavours, colours and sensory modifiers

Flavour systems should not be treated only as cosmetic components. Calcium salts may produce chalky, mineral or undesirable aftertastes. Experimental work with calcium-containing gummies has demonstrated that calcium carbonate can negatively affect taste and that sweetness and flavour strategies may be required to reduce undesirable sensory effects.[17] Taste masking should therefore be integrated into formulation development rather than performed only after the formulation has been finalized.

6. Formulation Strategies for Calcium Carbonate–Vitamin D_3 Gummies

The formulation strategy should begin with identification of the critical material attributes (CMAs) of the active ingredients and excipients. For calcium carbonate, relevant attributes include particle size, particle-size distribution, density, purity and surface characteristics. For vitamin D_3, concentration, physical state, carrier system, oxidative status and light sensitivity are important. For hydrocolloids, grade, molecular characteristics, gel strength and hydration behaviour are critical.

Development variable	Potential effect on calcium carbonate	Potential effect on vitamin D_3	Potential quality consequence
Polymer concentration	Suspension/viscosity; sedimentation control	May affect dispersion and release	Texture, uniformity, release
Particle size	Surface area, grit, suspension	Usually indirect	Mouthfeel, dissolution
Sugar solids	Viscosity and matrix density	Can alter water activity	Firmness, stickiness, stability
Acidulant/pH	Improves carbonate dissolution under acidic conditions	May influence degradation	Taste, release, stability
Processing temperature	Controls polymer dissolution and viscosity	Thermal exposure may promote degradation	Assay, texture
Mixing time/speed	Controls particulate distribution	Controls low-dose distribution	Content uniformity
Moisture	Controls matrix plasticity	May affect chemical stability	Texture, shelf life
Packaging	Limited direct effect	Strong protection against light/oxygen/moisture	Stability

7. Manufacturing Approaches

Conventional gummy manufacturing generally involves hydration of the hydrocolloid, preparation of the sugar phase, controlled heating, blending, active incorporation, moulding and cooling/setting. For calcium carbonate–vitamin D_3 systems, the order of addition is critical. Calcium carbonate should be incorporated under conditions that maintain adequate viscosity and minimize sedimentation, while vitamin D_3 should be exposed to the lowest practical thermal and oxidative stress.

Process scale-up can be challenging because heat transfer, mixing intensity and residence time change with batch size. A formulation that performs well at laboratory scale may develop nonuniformity or texture defects during scale-up. Process parameters such as temperature, mixing speed, hold time, deaeration, filling rate and cooling rate should therefore be treated as potential critical process parameters.

Emerging manufacturing technologies provide new opportunities. Semisolid extrusion 3D printing has been used to produce personalized gummy chewable tablets, with formulation variables such as gelatin and carrageenan affecting printability, mastication and thermal stability.[5] Pectin-based 3D-printed gummies have also been explored for personalized dosing[7], while recent pediatric work has demonstrated 3D-printed chewable gummies containing ondansetron.[8] These approaches are particularly relevant when dose personalization or complex geometries are desired.

8. Taste Masking and Patient Acceptability

Sensory acceptability is one of the principal reasons for developing gummy dosage forms, but it should be evaluated scientifically. Calcium carbonate may introduce chalkiness and mineral aftertaste, while high levels of acids, sweeteners or flavouring agents can alter texture and stability. Taste masking can involve flavour optimization, sweetness enhancement, particle-size

reduction, microencapsulation, lipid coating or incorporation into a structured matrix.

Sensory evaluation should ideally be conducted using a validated or well-designed protocol with appropriate ethical oversight when human participants are involved. Instrumental texture data should complement rather than replace sensory information. The relationship between instrumental hardness/adhesiveness and perceived chewability is not necessarily linear, making combined instrumental and sensory characterization preferable.

9. Pharmaceutical Characterization

9.1 Mass and dimensional uniformity

Individual gummy mass and dimensions should be measured using a predefined sampling plan. Mass uniformity is useful for assessing manufacturing consistency but cannot substitute for active-content uniformity, particularly when one component is present at a much lower concentration.

9.2 Texture profile analysis

Texture analysis should include, where relevant, hardness/firmness, adhesiveness, cohesiveness, springiness, resilience and chewiness. The test method must report instrument model, probe geometry, compression percentage or distance, test speed, trigger force, sample temperature and number of replicates. The 2024 gummy characterization study demonstrates the value of such standardized measurements but also illustrates the broad range of parameters that may require harmonization.[1]

9.3 Moisture and water activity

Moisture strongly influences gummy plasticity, stickiness, microbial stability and chemical degradation. Water activity can provide additional information beyond total moisture because it better describes the fraction of water available for chemical and microbiological processes. Moisture migration between the gummy and packaging environment can also alter texture during storage.

9.4 pH

The pH of the gummy matrix should be measured using a validated procedure appropriate to the semisolid sample. The selected pH must balance flavour, polymer behaviour, calcium carbonate dissolution and vitamin D_3 stability.

9.5 Assay and content uniformity

Separate validated analytical methods may be necessary for calcium carbonate and vitamin D_3 because of their markedly different chemical properties and concentrations. Calcium carbonate can be quantified using acid-base/complexometric approaches or suitable instrumental methods, whereas vitamin D_3 is commonly determined using chromatographic methods. Validation should address specificity, linearity/range, accuracy, precision, robustness and solution/sample stability. Stability-indicating capability is particularly important for vitamin D_3.

9.6 Disintegration and in vitro release

Unlike conventional tablets, gummy disintegration may involve swelling, softening, erosion and mastication. The method should therefore be clearly defined rather than simply adopting a tablet disintegration test without justification. Release testing should specify apparatus, medium, volume, temperature, agitation, sampling schedule and analytical method. For calcium carbonate, medium acidity has major implications for apparent dissolution; for vitamin D_3, solubilization and recovery require careful consideration.

9.7 Release kinetics

Mathematical models such as zero-order, first-order, Higuchi and Korsmeyer–Peppas may be useful for comparing profiles. However, model fitting should be based on sufficiently dense time-point data and reported with appropriate goodness-of-fit statistics. A high correlation coefficient alone does not establish a mechanism. Mechanistic interpretation should consider matrix swelling, erosion, diffusion, dissolution and experimental conditions.

10. Stability of Calcium Carbonate–Vitamin D_3 Gummies

Stability is arguably the most challenging aspect of the dual-active gummy system. Calcium carbonate is relatively chemically robust, whereas vitamin D_3 is considerably more sensitive. The systematic study by Temova Rakuša et al. demonstrated the influence of pH, temperature, light, oxygen and metal ions on vitamin D_3 degradation.[12] These factors can interact with the gummy matrix and packaging environment.

Stability stress	Potential impact	Recommended control
Temperature	Vitamin D_3 degradation; texture changes	Controlled processing and storage
Light	Vitamin D_3 photodegradation	Opaque/light-protective packaging
Oxygen	Oxidative degradation	Low-oxygen headspace/appropriate packaging where justified
Moisture/RH	Softening, stickiness, microbial risk	Moisture-barrier packaging
pH	Polymer and vitamin D_3 stability; calcium carbonate dissolution	Controlled formulation pH
Metal ions	Potential catalytic degradation of vitamin D_3	Raw-material control and justified chelation
Time	Cumulative chemical/physical changes	Long-term stability program

Stability studies should monitor appearance, mass, moisture, texture, pH, active assay and relevant degradation products at predefined intervals. The final container-closure system should be used because packaging can substantially influence moisture and oxygen exposure. For pharmaceutical development, stability design should be aligned with applicable ICH principles; for dietary supplements, applicable regional food/supplement GMP and stability expectations must also be considered.

11. Quality by Design and Risk-Based Development

A QbD approach is particularly appropriate for gummy formulations because multiple formulation and process variables interact. ICH Q8 describes an enhanced development approach based on understanding relationships among material attributes, process parameters and critical quality attributes rather than relying solely on one-factor-at-a-time experimentation.[18] ICH Q9 provides a framework for systematic quality-risk management across development and manufacturing[19], while ICH Q10 links pharmaceutical development with a lifecycle pharmaceutical quality system.[20]

QbD element	Application to calcium carbonate–vitamin D_3 gummy
QTPP	Chewable, stable, uniform, acceptable taste, intended dose and release
CQAs	Assay, content uniformity, hardness, adhesiveness, moisture, pH, release, stability
CMAs	$CaCO_3$ particle size, vitamin D_3 form, polymer grade, sugar solids, acidulant
CPPs	Hydration temperature, heating time, mixing speed, active-addition temperature, cooling
Risk assessment	Sedimentation, vitamin D_3 degradation, stickiness, microbial risk, dose nonuniformity
DoE	Multivariable optimization of polymer, solids, acidulant and processing parameters
Design space	Defined multidimensional region producing acceptable CQAs
Control strategy	Raw-material controls, in-process controls, finished-product testing and packaging

For a calcium carbonate–vitamin D_3 gummy, a response-surface design could evaluate polymer concentration, solids content and acidulant level as independent variables, with responses such as hardness, adhesiveness, active-content uniformity, moisture and release. This would provide a stronger scientific basis for calling a formulation 'optimized' than simple screening of a small number of batches.

12. Analytical and Quality-Control Challenges

Analytical control is a major gap in gummy research. Many published formulation reports provide assay percentages without adequate information regarding extraction efficiency, method validation, recovery, specificity or matrix interference. This is particularly problematic for vitamin D_3 because its low concentration and lipophilicity can produce incomplete extraction or adsorption losses.

A robust analytical strategy should include matrix-matched validation, recovery studies from placebo gummies, system suitability, sample stability and stress studies. Chromatographic methods should distinguish vitamin D_3 from degradation products where stability claims are made. Calcium carbonate quantification should likewise account for complete extraction and potential interference from mineral or excipient components.

Standardization of texture testing is another important need. A 2023 review noted that texture-analysis results can vary substantially with experimental conditions and that standardized pharmacopoeial approaches remain limited for many oral products.[13] Future gummy research should therefore report sufficient methodological detail to allow interlaboratory comparison.

13. Regulatory and Manufacturing Considerations

The regulatory classification of a calcium–vitamin D gummy depends on jurisdiction, composition, intended use and claims. A product marketed as a dietary supplement is subject to a different regulatory framework from a medicinal product. In the United States, FDA identifies gummies among common dietary-supplement dosage forms and provides separate regulatory information concerning dietary supplements and their manufacturing.[21,22] Manufacturers of dietary supplements must comply with applicable current good manufacturing practice requirements, including specifications and production controls.

For pharmaceutical products, development and quality systems should be aligned with applicable regional requirements and relevant ICH quality guidance. The distinction is important because a product cannot be described as a pharmaceutical dosage form merely because it contains an active ingredient; its regulatory pathway depends on intended use, claims and applicable legislation.

Regardless of classification, a robust product should have defined specifications for identity, strength, composition, microbial quality where applicable, physical attributes, active uniformity and stability. Recent regulatory enforcement activity involving gummy dietary supplements illustrates the practical importance of establishing and following appropriate product specifications and GMP controls.[23]

14. Current Evidence on Calcium–Vitamin D Gummies

Commercial calcium–vitamin D gummies demonstrate the practical feasibility of delivering these nutrients in a chewable format. Product-label databases include formulations combining calcium salts and vitamin D_3 with sugar, glucose syrup, gelatin or pectin, citric acid and flavouring systems.[24–26] However, the existence of commercial products should not be interpreted as evidence that all formulations are pharmaceutically equivalent or clinically interchangeable.

Human bioequivalence research provides useful context for vitamin D gummy delivery. A crossover study compared a vitamin D gummy with a tablet in healthy adults and demonstrates that gummy formulations can be evaluated using pharmacokinetic approaches rather than relying solely on in vitro release.[27] Such studies are important when the scientific question concerns bioavailability or systemic exposure.

Direct evidence specifically examining calcium carbonate–vitamin D_3 gummies remains much less developed than the broader literature on calcium supplementation, vitamin D stability and gummy technology. This creates an important research opportunity: future studies should compare calcium–vitamin D gummy formulations with established dosage forms using validated pharmaceutical and, where justified, pharmacokinetic or calcium-absorption endpoints.

15. Emerging Technologies and Future Directions

15.1 Personalized gummy dosage forms

3D printing can potentially individualize dose, shape and composition. Semisolid extrusion has been demonstrated for propranolol gummy chewable tablets and other pediatric formulations.[5,8] For calcium and vitamin D, personalized dosing could be relevant when nutrient requirements differ among age groups or clinical populations. However, dose flexibility must be accompanied by rigorous content-uniformity and process-control strategies.

15.2 Microencapsulation and nanostructured delivery

Encapsulation can potentially protect vitamin D_3 from light, oxygen and adverse interactions while improving dispersion in the gummy matrix. Lipid-based carriers, polymeric particles and other delivery systems may also improve the apparent aqueous dispersibility of vitamin D_3. However, additional excipients can influence texture, release, stability and regulatory acceptability and should therefore be assessed using QbD principles.

15.3 Sugar-reduced and functional gummies

Reducing added sugar is an important formulation challenge because sugar contributes strongly to solids, sweetness, water activity and texture. Alternative sweeteners and bulking agents may reduce sugar content but can change gelation, crystallization and moisture migration. Future formulations should evaluate nutritional composition alongside pharmaceutical performance rather than treating sugar reduction as an isolated formulation variable.

15.4 Sustainable and plant-based matrices

Pectin and other plant-derived hydrocolloids can support vegan or vegetarian product concepts and may reduce dependence on animal-derived gelatin. However, plant-based matrices are not automatically equivalent to gelatin systems. Polymer source, degree of esterification, molecular weight and ionic environment can produce substantial differences in texture and stability.

15.5 Digital quality control

Machine vision, process analytical technology, near-infrared spectroscopy and data-driven process monitoring could eventually support real-time assessment of colour, shape, moisture, mass and potentially active distribution. Integration of these tools with QbD and continuous improvement could reduce batch variability and facilitate lifecycle management.

16. Critical Knowledge Gaps

- Limited standardized quality specifications exist specifically for pharmaceutical gummies.
- Published studies frequently use different texture-analysis protocols, making direct comparison difficult.
- Validated analytical methods for low-dose vitamin D_3 in complex gummy matrices are not consistently reported.
- Direct comparative evidence for calcium carbonate versus alternative calcium salts in gummy matrices is limited.
- Few studies integrate formulation variables, process parameters, texture, active uniformity, release and stability within a single QbD framework.
- Long-term stability and packaging studies specifically addressing vitamin D_3 in mineral-containing gummies remain limited.
- Clinical or pharmacokinetic evidence for calcium–vitamin D gummy formulations is considerably less extensive than the formulation literature.
- Microbiological quality, water activity and packaging interactions deserve greater emphasis in future pharmaceutical gummy studies.
- Human sensory acceptability should be integrated with instrumental texture analysis when claims concerning palatability or acceptability are made.

17. Proposed Development Framework

Based on the evidence reviewed, an integrated development pathway for calcium carbonate–vitamin D_3 gummy lozenges can be organized into eight stages: (1) define the target product profile; (2) characterize calcium carbonate and vitamin D_3; (3) select and characterize hydrocolloids; (4) conduct risk assessment and DoE-based formulation screening; (5) optimize processing and active dispersion; (6) validate analytical and performance

methods; (7) establish packaging and stability; and (8) confirm reproducibility using independent batches. This framework moves development from empirical formulation toward a scientifically justified control strategy.

Stage	Key activities	Primary outputs
1. QTPP	Dose, dosage form, sensory and performance targets	Target product profile
2. Preformulation	Solubility, particle size, compatibility, stability	CMAs and formulation constraints
3. Excipient selection	Gelatin/pectin/sugar/acid/flavour screening	Candidate matrix
4. DoE/QbD	Multivariate formulation/process studies	Design space
5. Process development	Mixing, temperature, filling, cooling	Robust manufacturing process
6. Analytical validation	Assay, uniformity, release, degradation	Reliable analytical package
7. Stability	Long-term/accelerated studies and packaging	Shelf-life evidence
8. Confirmation	Independent batches and, where relevant, in vivo studies	Reproducibility and performance evidence

18. CONCLUSION

Calcium carbonate–vitamin D_3 gummy lozenges represent a scientifically interesting intersection of nutritional supplementation, hydrocolloid science and patient-centric oral dosage-form design. The formulation challenge is intrinsically multidimensional: calcium carbonate requires efficient particulate dispersion and management of its mineral mouthfeel and dissolution behaviour, whereas vitamin D_3 requires protection against environmental and chemical degradation. The gummy matrix must simultaneously provide adequate mechanical integrity, chewability, dose uniformity, acceptable sensory properties and reproducible release.

Current evidence supports the feasibility of gummies as oral delivery systems and demonstrates increasingly sophisticated approaches to their characterization, including texture profiling, controlled release, personalized 3D printing and systematic stability assessment.[1,5,7–9] Nevertheless, the specific evidence base for calcium carbonate–vitamin D_3 gummy lozenges remains comparatively limited. Future studies should prioritize validated dual-component analytical methods, standardized texture and release testing, QbD/DoE-based optimization, packaging development, microbiological quality, long-term stability and appropriate in vivo evaluation where claims concerning bioavailability are intended.

The most important research opportunity is to connect formulation variables with measurable critical quality attributes through mechanistic and statistically supported development. Such an approach can transform calcium–vitamin D gummies from empirically optimized consumer products into reproducible, quality-controlled oral delivery systems suitable for rigorous pharmaceutical and nutraceutical development.

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