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(REVIEW ARTICLE)

LIPOSOMAL VITAMIN C CHEWABLE TABLETS: FORMULATION STRATEGIES, BIOAVAILABILITY, STABILITY, QUALITY ATTRIBUTES, AND COMPARATIVE ADVANTAGES

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ABSTRACT

Liposomal vitamin C chewable tablets represent a combined dosage-form strategy in which the patient-friendly attributes of a chewable tablet are integrated with a phospholipid-based delivery system. Conventional vitamin C chewable tablets provide portability, swallowing convenience, and opportunities for taste masking, but free L-ascorbic acid remains susceptible to oxidative and moisture-related degradation and exhibits dose-dependent, saturable intestinal absorption. Researchers have investigated liposomal encapsulation to protect vitamin C and modify its gastrointestinal delivery. Commercial development of liposomal vitamin C has also progressed through platforms such as WBCIL's Lipoedge™ technology, which includes a dry, water-dispersible liposomal vitamin C format intended for oral dosage forms such as tablets, capsules, sachets, and gummies. Human studies of oral liposomal vitamin C formulations have reported higher systemic exposure than matched non-liposomal vitamin C in several experimental settings, including a 2024 randomized double-blind crossover trial of a powdered liposomal product and earlier controlled studies. However, the evidence is formulation-specific, doses and liposomal compositions vary substantially, and direct clinical evidence for compressed liposomal vitamin C chewable tablets remains limited. This review therefore distinguishes demonstrated advantages of liposomal oral vitamin C from formulation hypotheses that require product-specific validation. It discusses liposome composition, encapsulation, drying and rehydration, conversion to a chewable solid dosage form, excipient selection, critical quality attributes, analytical characterization, stability, taste and dental considerations, and comparative development against non-liposomal vitamin C chewables. Particular emphasis is placed on preserving vesicle integrity and vitamin C potency during drying, blending, compression, storage, and gastrointestinal exposure. A development framework is proposed in which bioavailability, rehydrated liposome size, polydispersity, encapsulation efficiency, dissolution/release, chewability, moisture, oxidation, and sensory performance are evaluated together.

Keywords: LipoEdge™ technology; WBCIL; Liposomal vitamin C; L-ascorbic acid; Chewable tablets; Liposomes

1 INTRODUCTION

Vitamin C (L-ascorbic acid) is an essential water-soluble nutrient that humans must obtain from the diet or supplements. It acts as a reducing agent and enzyme cofactor and contributes to collagen formation, carnitine and neurotransmitter synthesis, antioxidant defence, immune function, wound healing and non-heme iron absorption. The same redox chemistry that makes vitamin C biologically useful also makes it vulnerable to oxidation during processing and storage [1-3].

From a nutritional and pharmacokinetic perspective, oral vitamin C has a clear dose-response pattern. Intestinal uptake is saturable and plasma and tissue concentrations are tightly regulated.

According to the U.S. National Institutes of Health, about 70–90% of vitamin C is absorbed at intakes of 30–180 mg/day, whereas the fraction absorbed falls below 50% at doses above 1 g/day. Thus, simply increasing the dose of a conventional product does not lead to a proportional increase in systemic exposure, and excess unmetabolized ascorbate is eliminated in urine. Controlled pharmacokinetic work has also shown that the incremental rise in plasma vitamin C becomes progressively smaller as the oral dose increases [2,3].

These pharmacokinetic features matter when designing convenient, higher-strength oral products. A chewable tablet has obvious practical advantages: it can be taken without water, is portable, and can be made more acceptable with sweeteners and flavours. It must nevertheless perform well as a tablet, with appropriate hardness, friability, chewability, disintegration, dissolution, dimensions, palatability and moisture control. Because L-ascorbic acid is acidic, both taste masking and the extent of dental acid exposure also deserve attention. The formulation has to be strong enough to survive manufacturing and handling while remaining pleasant to chew [4-10].

The convenience of a chewable format does not remove the chemical sensitivity of vitamin C. Oxygen, light, temperature, moisture, pH and trace metal ions can all contribute to ascorbic acid degradation. In practice, stability depends on the whole formulation rather than on the active ingredient alone: excipients, water activity, processing conditions and packaging all play a part. Earlier tablet studies and reviews of vitamin C delivery have consequently focused on controlling moisture and oxygen exposure and on using formulation strategies that reduce the direct exposure of vitamin C to destabilizing conditions. This provides a reasonable basis for exploring a carrier system in which vitamin C is not continuously exposed as free ascorbic acid [1,6,11].

Liposomes offer one such carrier-based strategy. They are vesicles formed when amphiphilic phospholipids organize into bilayer membranes around an aqueous phase. Since vitamin C is highly water-soluble, it is generally located in the aqueous interior or near the lipid-water interface, depending on the formulation and manufacturing conditions. Encapsulation can create a different local environment for the vitamin and may reduce its immediate exposure to some chemical or biological stresses. Liposomes have consequently been studied for a wide range of delivery applications because their composition can be adjusted and they can accommodate both water-soluble and lipid-soluble compounds [12,13].

The oral route also makes the problem more complicated. After ingestion, a liposome encounters acidic gastric conditions, bile salts, digestive enzymes, dilution and mechanical forces. Depending on its composition and stabilization, a vesicle may aggregate, leak, lose membrane integrity or be digested before it reaches the intestinal surface. The success of an oral liposomal system therefore depends on more than achieving a high encapsulation efficiency at the time of manufacture. Lipid composition, membrane properties, surface characteristics, stabilization and the final dosage form all influence what happens to the vesicles after administration. For vitamin C, the practical goal is to obtain a carrier that is reproducible during manufacture and storage and behaves predictably after rehydration and gastrointestinal exposure [12-14].

An industry example that illustrates this translational pathway is the liposomal vitamin C technology reported by West Bengal Chemical Industries Ltd. (WBCIL), Kolkata, India. Within WBCIL's broader liposomal portfolio, Lipoedge™ is its branded liposomal technology platform, which includes Lipoedge™ Liposomal Vitamin C for nutraceutical and oral-delivery applications. WBCIL describes the vitamin C system as using non-GMO, sunflower-derived phosphatidylcholine and nano-encapsulation and reports a dry, water-dispersible material intended for oral formats such as tablets, capsules, sachets and gummies. Its product information lists a particle-size range of about 100–220 nm, PDI ≤0.25 and encapsulation efficiency above 90%, together with a reported three-year shelf life under the stated storage conditions. These are relevant development parameters because particle size and PDI are useful indicators of dispersion quality, while encapsulation efficiency describes how much vitamin C is associated with the carrier. A separate 2025 publication from the WBCIL research group reported a mean particle size of 184 nm, zeta potential of −33.7 mV, PDI of 0.334 and encapsulation efficiency of 91.98% for a sunflower-phosphatidylcholine formulation characterized by HPLC, DLS, FTIR

and XPS. These numbers are specific to the reported formulations and illustrate the range of physicochemical measurements needed to describe a liposomal intermediate [15-17].

The dry form of the WBCIL Lipoedge™ Liposomal Vitamin C system is particularly relevant to chewable-tablet development. A liquid liposomal dispersion cannot simply be compressed into a tablet, so a solid intermediate must first be produced and made suitable for powder processing. WBCIL reports that its liposomal vitamin C is water-dispersible and suitable for tablet-oriented applications, which provides a useful commercial example of this transition. It is important, however, to distinguish a tablet-compatible dry material from a finished chewable tablet whose liposomal properties have been independently demonstrated. Drying, milling, powder handling, excipient blending, compression, moisture exposure and storage can all affect vesicle recovery, vitamin C potency and leakage. A robust development program should therefore compare the liposomal system before and after solid-state processing using assay, encapsulation efficiency, particle size, PDI, zeta potential and leakage or rehydration measurements. In this sense, WBCIL's Lipoedge™ platform can be viewed as an industry example of translational development rather than as proof that every liposomal vitamin C chewable will perform in the same way [15,17].

Human pharmacokinetic studies provide the clearest evidence that liposomal delivery can change the behaviour of orally administered vitamin C. Gopi and Balakrishnan reported higher bioavailability with a liposomal preparation than with a non-liposomal comparator [18].

A later randomized, double-blind, placebo-controlled crossover study in 27 healthy adults found greater plasma and leukocyte exposure after 500 mg of liposomal vitamin C than after the corresponding conventional dose [19]. Another study by Żmuda and colleagues evaluated a spray-dried liposomal powder in healthy adults given 1000 mg. The liposomal product produced about 30% higher AUC and a 30% higher 24-hour vitamin C concentration than the non-liposomal comparator. Importantly for solid-dose development, the investigators also examined the powder after rehydration and found measurable preservation of its liposomal characteristics [20]. Together, these studies make a useful case for further development, but they do not remove the need to test the final chewable tablet itself [19,20].

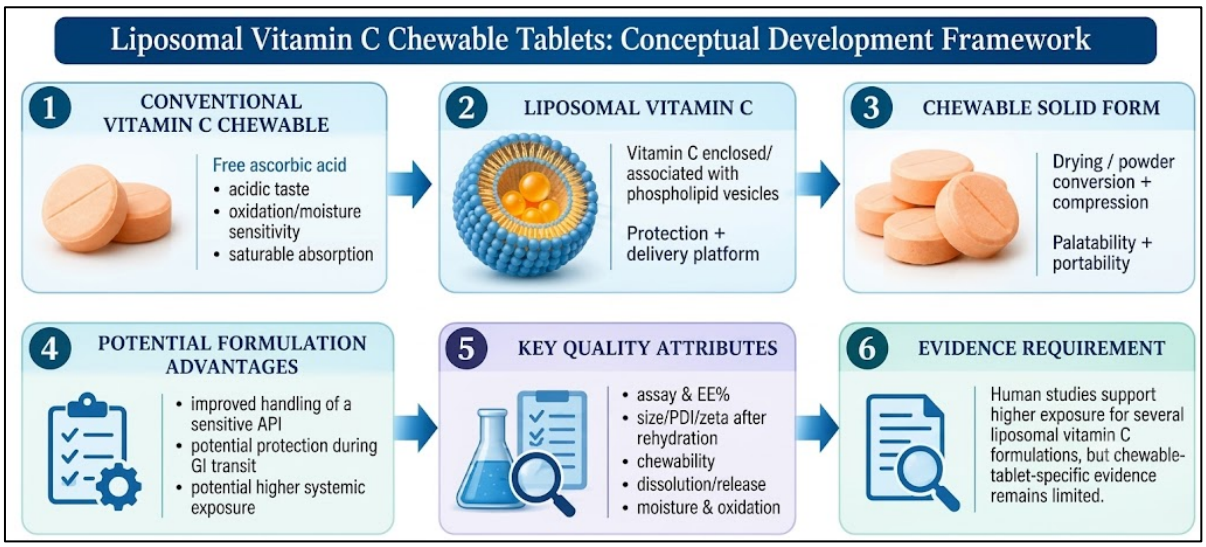


Figure 1*:* Conceptual development framework for liposomal vitamin C chewable tablets, showing the relationship between the conventional chewable platform, liposomal delivery, solid-dose conversion, quality attributes, and evidence requirements.

The overall evidence is promising, although the findings are not entirely consistent across studies. A 2025 scoping review of 10 studies comparing liposomal and non-liposomal ascorbate found that nine reported higher bioavailability with liposomal formulations, although the magnitude of the increase varied substantially. The studies differed in several important aspects, including liposomal composition, vitamin C dose, study design, and duration of blood sampling. In addition, outcomes such as urinary excretion, cellular uptake, and the resulting biological effects were not consistently evaluated, making it difficult to draw definitive conclusions about the clinical significance of the observed improvements in bioavailability [4]. Therefore, the current literature supports the proposition that some liposomal vitamin C formulations can increase systemic exposure, but it does not establish a universal magnitude of benefit for all liposomal products. This distinction is particularly important when moving from liquid or powdered liposomal preparations to a compressed chewable tablet.

A liposomal vitamin C chewable has to satisfy two sets of formulation requirements at the same time. The lipid carrier needs controlled particle size, PDI, encapsulation efficiency, surface characteristics and chemical stability, while the tablet matrix needs good flow and compression behaviour together with acceptable hardness, friability, chewability, taste, dissolution and moisture protection. The transition from a liquid dispersion to a dry intermediate is therefore a major development step. Spray drying, lyophilization and other solid-state approaches can be used, but dehydration may cause aggregation, leakage, lipid oxidation or incomplete recovery of the original vesicle population. Published work on liposome drying shows that the outcome depends strongly on lipid composition, protectant selection, freezing and drying conditions, and storage. The overall development framework is summarized in Figure 1.

Tabletting adds another possible source of stress. Before and during compression, the liposomal powder may experience shear, pressure, heat and interactions with excipients or lubricants. A tablet can therefore meet ordinary pharmacopoeial specifications and still fail to preserve the carrier. For this reason, the liposome recovered from the finished tablet should be compared with the starting dispersion. Hydrodynamic diameter, PDI, zeta potential, encapsulation efficiency and leakage can reveal whether the carrier has changed, while vitamin C assay and degradation testing show whether the active has remained chemically intact. Tablet hardness or dissolution on their own cannot answer these questions.

The purpose of this review is to bring the established formulation science of vitamin C chewables together with the more recent literature on liposomal delivery. The combination raises questions that are not encountered with a conventional chewable alone, including how the carrier behaves during drying, tabletting and rehydration and whether the reported pharmacokinetic advantages of liposomal vitamin C survive conversion into a solid dosage form. The review therefore considers formulation, processing, analytical and performance issues alongside the evidence for bioavailability. It also proposes a practical development framework in which the final product is treated as one formulation-process-package system and compared at the same vitamin C dose with a conventional chewable [5,12,13].

2 VITAMIN C: PHYSICOCHEMICAL AND BIOLOGICAL CONSIDERATIONS

L-ascorbic acid is a strong reducing agent, and that chemistry is central to both its biological activity and its formulation challenges. Its degradation can be accelerated by oxygen, heat, moisture, light, pH and the surrounding formulation environment. For chewable tablets, moisture and temperature are especially important because even relatively small changes in the solid-state environment can affect vitamin C retention during storage [1,3,11].

It is also useful to keep two questions separate during development: how much vitamin C remains chemically intact, and how much of it ultimately reaches the systemic circulation. A product can retain a satisfactory assay yet behave differently during gastrointestinal release, while higher plasma exposure does not automatically mean a proportionally greater clinical effect. For this reason, development should combine stability-indicating analytical methods with appropriate pharmacokinetic or comparative performance studies rather than relying on a single physical measurement [1,3]. The key physicochemical, biopharmaceutical, sensory, and processing differences are summarized in Table 1.

Table 1: Comparison of key physicochemical, biopharmaceutical, sensory, and processing characteristics of conventional and liposomal vitamin C chewable tablets.

Property	Conventional vitamin C chewable	Implication for liposomal chewable
Active form	Usually free L-ascorbic acid or mineral ascorbate	Vitamin C is encapsulated/associated with phospholipid vesicles before solid-dose conversion
Water solubility	High; rapid dissolution is generally expected after tablet breakup	The final product must release or reconstitute the liposomal vitamin C without compromising vesicle integrity
Oxidation sensitivity	Important formulation concern	Vitamin C is readily susceptible to oxidation. Liposomal encapsulation may help protect it from degradation, but this protective effect needs to be confirmed by monitoring potency during processing and storage.
Absorption	Dose-dependent and saturable	Vitamin C absorption is dose-dependent and can become saturated at higher doses. Human studies of several liposomal formulations have reported greater systemic exposure, although the extent of this benefit appears to depend on the specific formulation.

Taste	Strong sourness can be prominent with L-ascorbic acid	Liposome preparation may alter sensory exposure, but sweetening/flavouring remains necessary for a chewable product
Solid-state processing	Direct compression/dry granulation/wet granulation may be considered	Drying, carrier selection, blending and compression must preserve the liposomal system or its ability to reconstitute

3 WHAT IS A LIPOSOMAL VITAMIN C SYSTEM?

A liposome is essentially a small vesicle built from amphiphilic lipids, most commonly phospholipids. In water, these molecules arrange themselves into bilayer membranes that enclose an aqueous compartment. Water-soluble compounds can be held within the aqueous region, whereas more lipophilic compounds can associate with the membrane. For vitamin C, the hydrophilic nature of the molecule means that the aqueous core or the interfacial region is the main location of interest, depending on the composition and preparation method [12,13].

In practical formulation terms, a liposomal vitamin C system requires a phospholipid source, vitamin C and an aqueous phase, with cholesterol or other membrane modifiers added when needed. When the system is converted to a dry powder, stabilizers and cryo- or lyoprotectants may also be required. The choice and purity of the lipid, vesicle size, surface charge, pH, ionic strength and processing history all influence the final product, so these variables need to be considered together rather than optimized in isolation [12-14].

The 2024 spray-dried vitamin C study is particularly useful here because it connects liposome preparation with a dry oral intermediate. The investigators converted the dispersion into a powder and, in a randomized double-blind crossover study of 10 healthy adults given 1000 mg, reported about 30% higher AUC and 30% higher 24-hour vitamin C concentration than with non-liposomal vitamin C. The study also found that the liposomal characteristics could be measured after rehydration. Because only a small number of participants were studied, the authors appropriately noted that the findings need confirmation in larger trials [20]. WBCIL's Lipoedge™ Liposomal Vitamin C provides a commercial example of this dry-intermediate concept, but the performance of a compressed chewable still requires product-specific confirmation after rehydration and tabletting [15,17].

These findings support the feasibility of making a dry liposomal vitamin C product, but they should not be taken as direct evidence that a compressed chewable tablet will behave identically. Compression force, lubricant exposure, moisture, excipient interactions and the conditions used for rehydration can all influence vesicle structure. These factors therefore need to be treated as development variables and not as fixed assumptions [20]. The basic structural organization of the liposomal vitamin C system is illustrated in Figure 2.

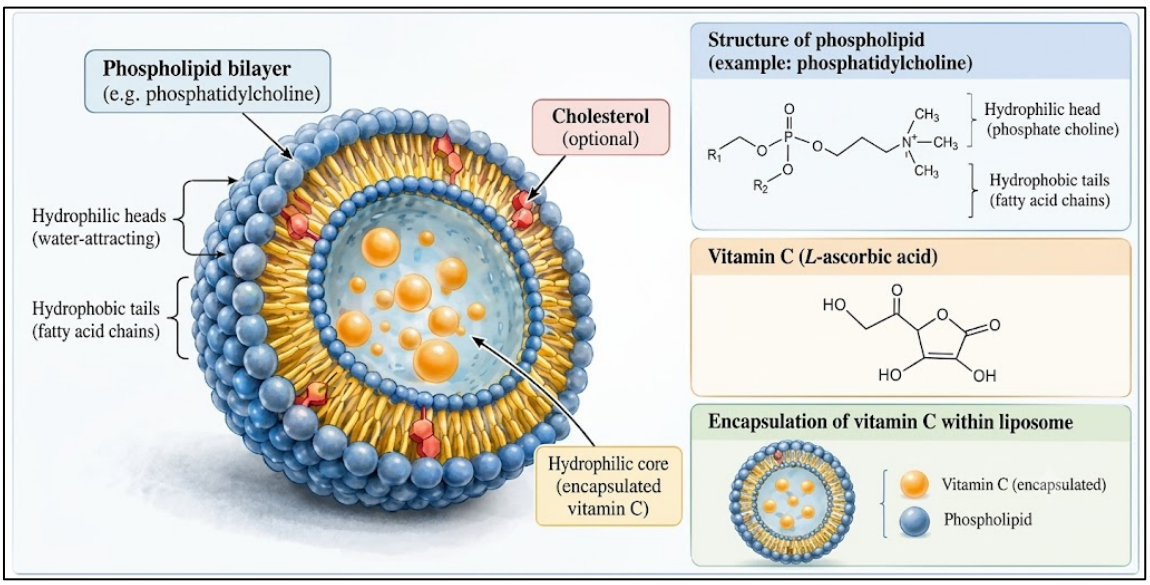


Figure 2: Schematic representation of a liposomal vitamin C vesicle showing the phospholipid bilayer, optional cholesterol component, aqueous core, and encapsulated hydrophilic vitamin C.

4 RATIONALE FOR LIPOSOMAL VITAMIN C CHEWABLE TABLETS

Table 2: Comparative development objectives, potential advantages, and evidence status of conventional and liposomal vitamin C chewable tablets.

Development objective	Non-liposomal chewable	Liposomal chewable: potential advantage	Evidence status
Convenient oral administration	Yes	Retained	Established dosage-form attribute
Taste masking	Requires sweeteners/flavors or alternative vitamin C form	May reduce direct exposure of free acid, but still requires sensory optimization	Formulation hypothesis; product-specific testing needed
Protection of vitamin C	Depends on solid formulation and packaging	Phospholipid vesicles may provide an additional microenvironmental barrier	Supported mechanistically and by liposomal stability literature; must be validated in final tablet
Systemic exposure	Dose-dependent and saturable	Several human studies report higher AUC/C_{max} with specific liposomal formulations	Human evidence exists, but not specifically for compressed chewable tablets
GI delivery	Free vitamin C dissolves and is available for absorption	Liposomal structures may alter release, interaction with GI fluids and uptake	Mechanistically plausible; formulation-specific
Portability	Excellent	Excellent if successfully converted to a dry powder/tablet	Solid-dose development principle
Manufacturing complexity	Relatively simple	Higher because liposome preparation, drying, tabletting are required	Established formulation consideration

A schematic comparison of conventional and liposomal vitamin C following oral administration is presented in Figure 3.

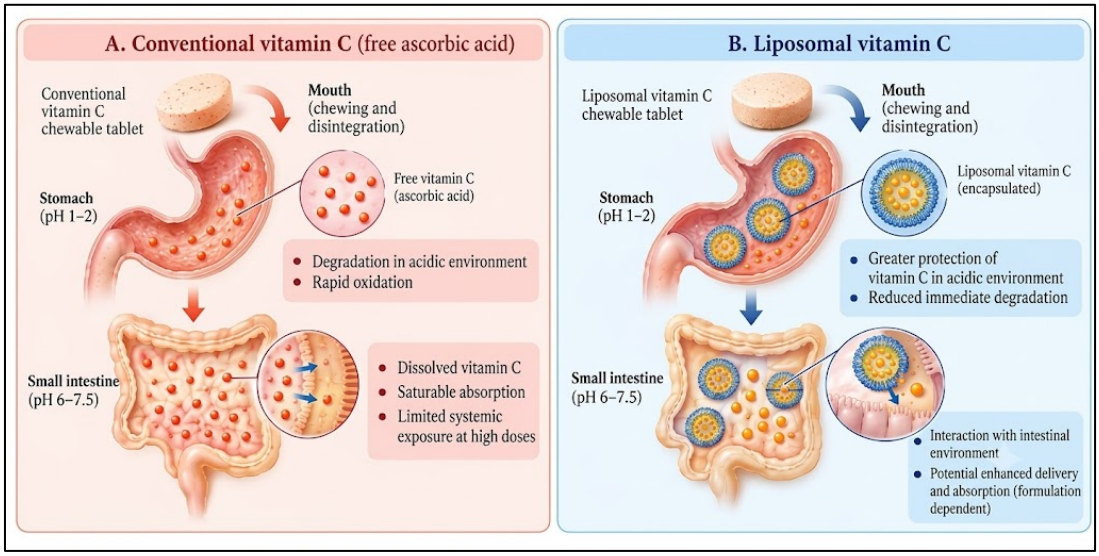


Figure 3: Schematic comparison of conventional and liposomal vitamin C following oral administration, highlighting differences in gastrointestinal exposure, protection of vitamin C, and potential systemic delivery.

The proposed product is a combination of two technologies. The chewable tablet solves a practical administration problem by offering a portable, water-free and generally easy-to-use dosage form, while the liposome is intended to change how vitamin C is presented to the gastrointestinal environment. The two components should therefore be evaluated separately as well as together: the tablet must be acceptable to the consumer, and the liposomal carrier must

retain the properties needed for its intended delivery function [4,5]. The principal development objectives and evidence status are summarized in Table 2.

The most cautious comparison is that a liposomal chewable may offer delivery-related benefits in addition to the established convenience of a conventional chewable. The strongest human evidence so far concerns systemic exposure with particular liposomal formulations; possible benefits related to protection, gastrointestinal handling and sensory exposure remain more dependent on the formulation and need to be demonstrated in the final product [18-20].

5 EVIDENCE FOR ENHANCED BIOAVAILABILITY OF LIPOSOMAL VITAMIN C

Controlled human studies provide the most useful evidence for assessing whether liposomal vitamin C changes systemic exposure. In a randomized crossover study, Gopi and Balakrishnan reported approximately 1.77-fold higher bioavailability with their liposomal formulation than with the non-liposomal comparator. The formulation had an encapsulation efficiency of about 65.9% and a particle size below 100 nm [18].

In a 2016 controlled study involving 11 participants who received 4 g of oral vitamin C, the liposomal preparation produced higher circulating vitamin C concentrations than unencapsulated vitamin C. The study also included an intravenous comparator, so the findings are useful for understanding pharmacokinetic behaviour but should not be interpreted as a direct comparison between two finished chewable tablets.

The 2024 randomized, double-blind crossover study of a spray-dried liposomal powder provides another relevant example. Ten healthy adults received 1000 mg, and the liposomal formulation produced approximately 30% higher AUC and 30% higher 24-hour vitamin C concentration than non-liposomal vitamin C. The investigators also reported higher bioavailability in a Caco-2 model. These results are consistent with the possibility of improved systemic exposure, although the small clinical sample and formulation-specific nature of the study should be kept in mind [21,22].

A separate 2024 randomized, double-blind, placebo-controlled crossover study included 27 adults and compared 500 mg of conventional vitamin C with 500 mg of liposomal vitamin C. Both treatments increased plasma and leukocyte vitamin C relative to placebo, with the study designed to examine whether the liposomal formulation could increase absorption. The findings add to the human evidence base, but again relate to a specific liposomal formulation rather than to a generic liposomal chewable tablet [19].

A 2025 scoping review identified 10 studies comparing liposomal and non-liposomal ascorbate, and nine reported higher bioavailability with liposomal products. The review also highlighted substantial differences in formulation, dose, sampling duration and study design, as well as gaps in urinary elimination, cellular uptake and biological outcomes. The literature therefore supports a potential pharmacokinetic advantage, but not a single universal value for the expected increase in bioavailability [19].

Taken together, the studies make liposomal vitamin C an interesting delivery strategy, but the size of the benefit clearly depends on the formulation and the study conditions. A reported increase in AUC or C_{max} should be treated as evidence for that particular product and dose, not as a blanket claim for every liposomal vitamin C preparation.

6 FORMULATION DESIGN OF LIPOSOMAL VITAMIN C

6.1 Phospholipid selection

Phosphatidylcholine-rich materials such as soybean and sunflower lecithin are widely used because they readily form bilayers and are available in grades suitable for pharmaceutical and nutraceutical development. Hydrogenated phosphatidylcholine can produce a more rigid membrane and may improve physical robustness, but the phase-transition behaviour of the lipid must be considered during processing. Lipid purity and composition can influence particle size, surface charge, encapsulation and storage stability, making raw-material characterization an important early step [12,13].

6.2 Cholesterol and membrane modifiers

Cholesterol is commonly added to liposomal membranes to change lipid packing, fluidity and permeability. There is no single lipid-to-cholesterol ratio that is optimal for every vitamin C formulation. Too much membrane rigidification can slow release or interfere with rehydration, whereas insufficient membrane stabilization may increase leakage or aggregation [12,13].

6.3 Vitamin C loading

Vitamin C is hydrophilic, so its loading is strongly influenced by the aqueous volume, lipid composition, hydration conditions, concentration gradient and preparation method. Encapsulation efficiency should be measured experimentally rather than inferred from the amount initially added. Increasing the starting vitamin C concentration may improve nominal loading, but it can also change osmotic conditions and affect particle size, PDI and physical stability [12,13,23].

6.4 pH and oxidation control

Vitamin C oxidation needs to be considered from the beginning of formulation development. Oxygen exposure, temperature, light, pH and trace metals should be controlled as far as practical, and the choice of any antioxidant or chelating agent should be justified by compatibility, safety and regulatory requirements. Because the carrier itself contains lipids that may oxidize, vitamin C stability and lipid stability should be monitored carefully [23].

7 METHODS FOR PREPARING LIPOSOMAL VITAMIN C

The principal liposome preparation and solid-state conversion methods are compared in Table 3.

Table 3: Comparison of liposome preparation and solid-state conversion methods for the development of liposomal vitamin C chewable tablets.

Method	General principle	Advantages	Key development concern for a chewable tablet
Thin-film hydration	Lipids form a dry film and are hydrated with vitamin C-containing aqueous phase	Widely used; flexible composition control	Residual solvent, multilamellarity, scale-up and need for size reduction
Ethanol injection	Lipid-containing ethanolic phase is injected into aqueous vitamin C phase	Simple and scalable in principle	Solvent removal and vesicle size control
Microfluidization/high-pressure processing	High shear reduces vesicle size and improves dispersion	Suitable for nanoscale systems and scale-up	Heat generation, processing pressure and equipment optimization
Extrusion	Preformed vesicles pass through membranes to narrow size distribution	Good size control	Membrane fouling and processing time
Sonication	Ultrasonic energy reduces vesicle dimensions	Simple laboratory method	Potential oxidation/heating and scale-up limitations
Spray drying	Liposomal dispersion is converted into a dry powder	Relevant to solid oral dosage forms; 2024 vitamin C study demonstrated feasibility [20]	Rehydration, lipid oxidation, carrier selection and thermal stress
Lyophilization	Water is removed by freezing and sublimation	Can improve storage stability with suitable protectants	Cost, cycle optimization and preservation of vesicle structure

Work on liposome lyophilization shows that successful drying depends on mechanisms such as water replacement and vitrification, as well as on the lipid composition, vesicle size, protectant and freezing/drying cycle. Proliposome and lipid-enriched powder approaches have also shown that lipid systems can be converted into solid carriers using materials such as mannitol or sorbitol. These findings are relevant to chewable-tablet development because the dry intermediate has to survive handling and still produce a reproducible liposomal system when exposed to water [24-26].

8 CONVERSION OF LIPOSOMAL VITAMIN C INTO A CHEWABLE TABLET

The key difference between a liquid liposomal product and a liposomal chewable tablet is the conversion from a dispersion into a solid intermediate. In a practical development sequence, the liposomes are first prepared and, if necessary, reduced in size or homogenized. The dispersion may then be purified or adjusted before being dried or otherwise converted into a powder. After conditioning, the powder is blended with chewable excipients, compressed and packaged in a way that limits exposure to moisture, oxygen and other stability risks. [24-26] WBCIL's Lipoedge™ Liposomal Vitamin C illustrates the relevance of a dry, water-dispersible liposomal intermediate for this type of solid-dose development [15,17].

The finished tablet is therefore the end point of several linked operations rather than simply a compressed liposome. Each step - from liposome preparation and size control through drying, powder conditioning and compression - can affect the final carrier. This is why process development and product characterization need to be considered together [26].

The proposed conversion pathway from a liposomal dispersion to a chewable tablet is illustrated in Figure 4.

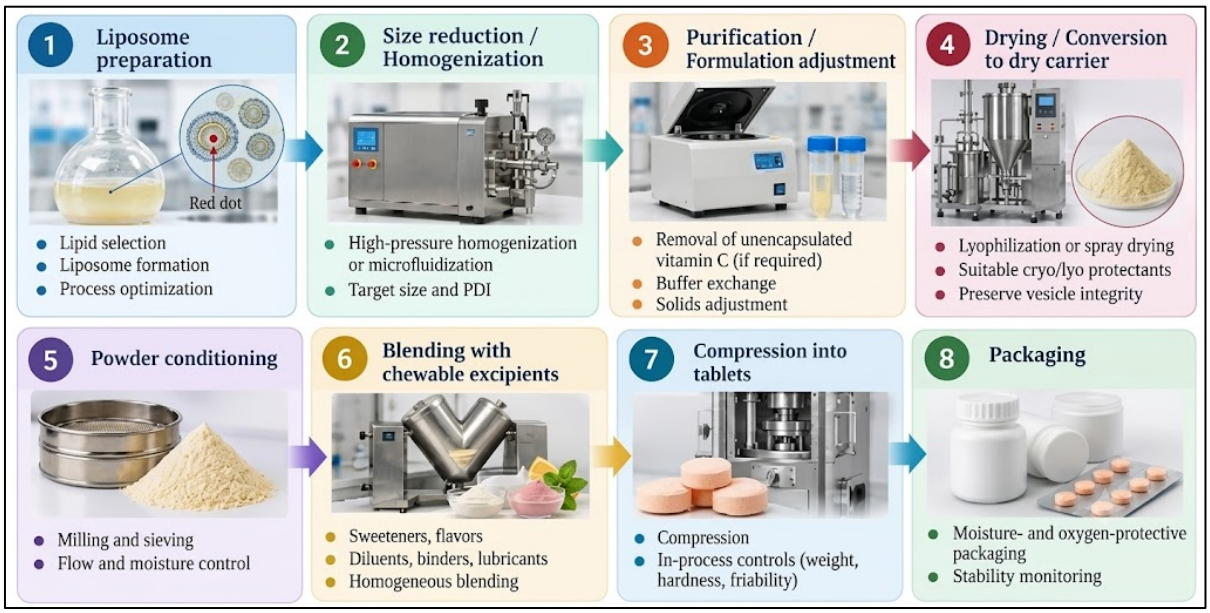


Figure 4: Development pathway for conversion of a liquid liposomal vitamin C dispersion into a chewable tablet, including size reduction, purification or formulation adjustment, drying or solid-state conversion, powder conditioning, excipient blending, compression, and packaging.

The drying method should be chosen with a clear recovery criterion: either the vesicles remain sufficiently intact during drying, or they must reproducibly re-form a defined liposomal population when the powder is rehydrated. Spray drying is attractive when scale-up and continuous processing are important, whereas lyophilization can provide a gentler dehydration route but usually requires a longer and more complex cycle. The choice should ultimately be based on post-drying particle characteristics, encapsulation and stability rather than on the drying method alone [20,24,26].

Compression deserves the same level of attention. High compression force, prolonged blending, heat or excessive lubricant can change the powder and may affect subsequent rehydration. A useful development experiment is to compare the starting liposome with the material recovered from the finished tablet and to follow hydrodynamic diameter, PDI, zeta potential, encapsulation efficiency and leakage before and after tabletting [26].

A 2022 study on lyophilized liposomes provides a useful proof of principle: liposome-containing powder was compressed into tablets while retaining a liposome-release function in a sublingual delivery system. Although the study did not involve vitamin C or a chewable tablet, it demonstrates that solid-state processing and tabletting of a liposomal powder can be feasible when the formulation and process are designed together [27].

9 EXCIPIENT SELECTION FOR LIPOSOMAL VITAMIN C CHEWABLE TABLETS

The principal excipient categories and their functional roles are summarized in Table 4.

Table 4: Key excipient categories and their functional roles in the formulation of liposomal vitamin C chewable tablets.

Excipient category	Possible examples	Function	Liposomal-specific consideration
Diluent/chewable base	Mannitol, sorbitol, MCC, co-processed excipients	Bulk, flow, compression, mouthfeel	Avoid excessive moisture; assess impact on rehydration
Sweetener	Sucralose, aspartame or permitted alternatives	Taste masking	Sensory optimization should account for lipid and vitamin C aftertaste
Flavor	Orange, lemon, berry	Masks acidity	Check compatibility and oxidative stability
Disintegrant	Crospovidone, croscarmellose sodium, SSG	Tablet breakup	Rapid breakup may support rehydration but excessive levels may affect texture
Lubricant	Magnesium stearate, stearic acid	Ejection and processing	Hydrophobic coating can alter wetting/dissolution; optimize level and mixing
Glidant	Colloidal silicon dioxide	Flow improvement	Excess may alter compaction
Drying protectant/carrier	Mannitol, trehalose, sucrose or another validated protectant	Protects vesicles during dehydration	Must be selected with rehydration and tablet texture in mind
Antioxidant/chelating strategy	Only when justified and permitted	May reduce oxidative degradation	Compatibility and regulatory acceptability must be demonstrated

Mannitol, microcrystalline cellulose, co-processed excipients, polyols, sweeteners, flavours, disintegrants, lubricants and glidants all have established roles in chewable-tablet manufacture. In a liposomal product, however, the question is not only whether an excipient gives good tablets; it is also whether it changes moisture uptake, lipid stability, powder flow or the ability of the dry carrier to reconstitute. Excipients should therefore be screened with both tablet performance and liposomal recovery in mind [4-7,26].

10 CRITICAL QUALITY ATTRIBUTES

The critical quality attribute (CQA) profile of a liposomal chewable needs to cover the usual tablet requirements as well as the properties of the lipid carrier. FDA guidance for chewable tablets highlights attributes such as mechanical strength, chewability, disintegration, dissolution, dimensions, friability and palatability. For a liposomal product, these should be complemented by assay, encapsulation efficiency, particle size, PDI, zeta potential, leakage and rehydration measurements [4,28]. The key critical quality attributes and their suggested evaluation approaches are summarized in Table 5.

Table 5: Critical quality attributes (CQAs), their importance, and suggested evaluation methods for liposomal vitamin C chewable tablets.

CQA	Why it is important	Suggested evaluation
Vitamin C assay	Confirms labeled potency	Validated HPLC/appropriate stability-indicating method
Encapsulation efficiency	Shows fraction of vitamin C associated with liposomes	Separation of free vitamin C followed by validated assay
Loading capacity	Defines active-to-lipid relationship	Vitamin C mass relative to total formulation/lipid
Hydrodynamic diameter	Assesses vesicle size after rehydration	DLS; report Z-average
PDI	Assesses size distribution	DLS
Zeta potential	Provides electrokinetic surface characterization	Electrophoretic light scattering
Vesicle morphology	Confirms vesicular structure	Cryo-TEM/TEM where appropriate
Leakage after tabletting	Determines whether compression damages the carrier	EE% before and after compression/rehydration
Dissolution/release	Assesses vitamin C availability after administration	Discriminatory dissolution/release method
Hardness/chewability	Balances robustness and ease of mastication	Breaking force + sensory correlation
Friability	Assesses abrasion resistance	Pharmacopoeial method
Moisture	Controls oxidation and physical changes	Karl Fischer/LOD + package studies
Oxidation/degradation products	Confirms chemical stability	Stability-indicating HPLC
Taste/mouthfeel	Determines acceptance	Controlled sensory evaluation
Rehydration performance	Confirms recovery of liposomal characteristics	Size/PDI/EE% after reconstitution

11 COMPARATIVE ADVANTAGES OVER NON-LIPOSOMAL VITAMIN C CHEWABLE TABLETS

The comparison below is intended to distinguish genuine dosage-form advantages from benefits that are only potential. Both products are chewable tablets, so convenience is not unique to the liposomal version. The main question is whether the liposomal system adds a measurable improvement in chemical protection, systemic exposure, gastrointestinal handling or sensory performance without creating an unacceptable increase in manufacturing complexity and cost [4,26]. A comparative assessment of non-liposomal and liposomal vitamin C chewable tablets is provided in Table 6.

Table 6: Comparative evaluation of non-liposomal and liposomal vitamin C chewable tablets in terms of formulation, performance, stability, manufacturing, and analytical considerations.

Attribute	Non-liposomal vitamin C chewable	Liposomal vitamin C chewable	Interpretation
Dosage-form convenience	High	High	Both are portable, water-free solid dosage forms
Acidic taste exposure	Direct exposure to free vitamin C is likely	May be modified by encapsulation, but tablet still requires taste masking	Potential sensory advantage; must be measured
Chemical protection	Relies mainly on formulation and packaging	Lipid bilayer may add a protective microenvironment	Potential advantage; must be confirmed in final product
Systemic exposure	Constrained by dose-dependent absorption	Several human studies report higher AUC/C_{max} for specific liposomal products	Demonstrated for several liposomal formulations, not yet universal
Cellular delivery	Vitamin C enters cells after conventional absorption and transport	Liposome may alter interaction with biological membranes	Mechanistically plausible; clinical significance requires evidence
Dose efficiency	Higher dose does not necessarily mean proportional exposure	Potential to obtain greater exposure at an equivalent administered dose	Requires direct matched-dose comparison
Manufacturing simplicity	Simpler	More complex	Clear disadvantage of liposomal platform
Cost	Generally lower formulation complexity	Likely higher due to lipid materials and processing	Economic trade-off
Stability risk	Mainly vitamin C oxidation/moisture	Vitamin C + lipid oxidation + vesicle integrity	Liposomal product has additional CQAs
Analytical burden	Primarily assay/degradation + tablet CQAs	Adds EE%, size, PDI, zeta and rehydration testing	Higher development workload

Among the possible advantages, the best-supported finding in human studies is increased systemic exposure with several specific liposomal vitamin C formulations. The 2025 scoping review found higher bioavailability in nine of ten comparisons, although it also stressed the heterogeneity of the available evidence. Other proposed advantages-such as improved protection or taste masking are plausible but need to be demonstrated for the finished chewable [19,20].

12 DISINTEGRATION, DISSOLUTION AND GASTROINTESTINAL RELEASE

With conventional vitamin C, tablet breakup is followed by rapid dissolution because ascorbic acid is highly water-soluble. A liposomal chewable has a more complicated sequence: the tablet must first disintegrate, the dry carrier must hydrate or disperse, the vesicles must interact with gastrointestinal fluids, and vitamin C must then become available for absorption. The performance target is therefore not simply rapid release of vitamin C but controlled recovery of the intended delivery system [12-14,26].

For this reason, dissolution testing alone is not enough. A conventional dissolution test can show how quickly vitamin C appears in the medium, but it cannot tell whether the liposomes have remained intact or whether the vitamin was released prematurely. A more informative development program would combine dissolution or release measurements with rehydrated particle size, PDI and encapsulation efficiency [26].

Simulated gastric and intestinal fluids can be useful for comparing free and liposomal vitamin C under controlled laboratory conditions. Samples can be taken at selected time points to measure vitamin C concentration together with particle size, PDI and encapsulation efficiency. Such experiments are valuable for understanding formulation behaviour, but they should be treated as mechanistic or comparative studies rather than as direct substitutes for clinical bioavailability studies [12-14].

13 STABILITY OF LIPOSOMAL VITAMIN C CHEWABLE TABLETS

Stability becomes more demanding when vitamin C is placed inside a lipid carrier. The formulation has to protect the vitamin while also keeping the phospholipid membrane within an acceptable chemical and physical state. Vitamin C can oxidize, and phospholipids can undergo their own oxidative reactions. Moisture, oxygen, temperature, light, pH, lipid composition and mechanical stress can therefore affect both sides of the system and should be monitored during development [29]. The major stress factors affecting stability and their corresponding control strategies are summarized in Table 7.

Table 7: Potential effects of environmental, formulation, and processing stress factors on liposomal vitamin C chewable tablets and strategies for their control.

Stress factor	Possible effect on liposomal chewable	Control strategy
Moisture	Vitamin C degradation; changes in tablet texture; vesicle reconstitution changes	High-barrier packaging, moisture study, desiccant where justified
Oxygen	Vitamin C oxidation and possible lipid oxidation	Low-oxygen processing/packaging where appropriate; antioxidant strategy
Temperature	Accelerated vitamin C and lipid degradation; altered physical properties	Controlled manufacturing and stability storage
Light	May accelerate degradation depending on formulation	Light-protective packaging
Mechanical stress	Potential change in powder structure and rehydration	Compression-force optimization and post-compression rehydration testing
Lipid composition	Can affect membrane rigidity, leakage and oxidation	Select lipid grade and composition using stability data
Water activity	Can influence chemical and physical stability	Control moisture and packaging
Storage time	Cumulative loss of potency or carrier performance	Long-term and accelerated stability with multiple CQAs

The major factors influencing the stability of liposomal vitamin C chewable tablets are illustrated in Figure 5.

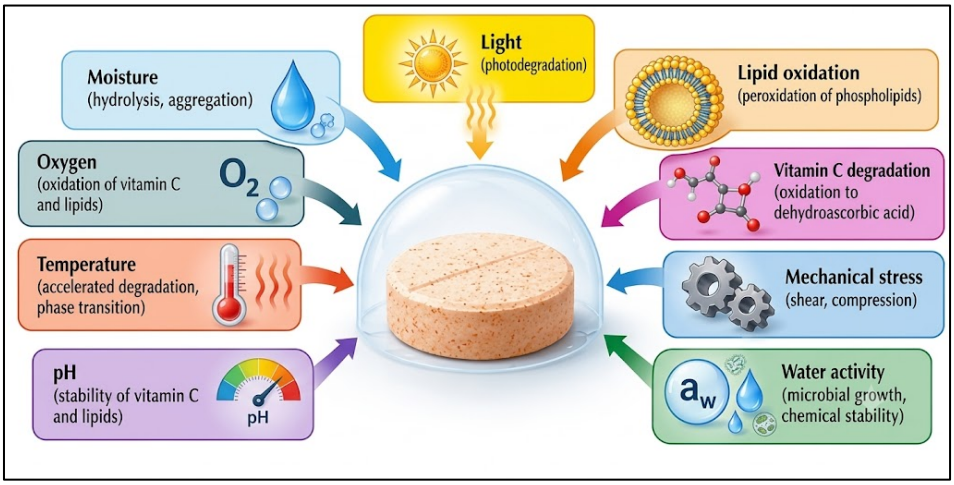


Figure 5: Major factors influencing the stability of liposomal vitamin C chewable tablets, including moisture, oxygen, temperature, light, pH, lipid oxidation, mechanical stress, and water activity.

Packaging should be selected from measured stability data rather than from the nominal barrier rating of a container. Moisture ingress, oxygen exposure and vitamin C retention should be monitored during stability studies so that the final pack is matched to the actual sensitivity of the product. High-barrier blisters or containers, with desiccants where justified, may be useful options when the data support their use [4,11,29].

14 TASTE, MOUTHFEEL AND DENTAL CONSIDERATIONS

The acidic taste of L-ascorbic acid is one of the practical difficulties of a vitamin C chewable. Polyols, high-intensity sweeteners and fruit flavors can help, but they also affect tablet mass, moisture sensitivity, compression and aftertaste. Taste masking therefore needs to be developed as part of the formulation rather than added as a final cosmetic step [4,6].

A liposomal carrier may reduce the immediate contact of free ascorbic acid with taste receptors if a meaningful fraction of the vitamin remains associated with the vesicles during chewing and early saliva exposure. That effect cannot be assumed, however. Tablet composition, vesicle rupture, saliva dilution and formulation pH will all influence what reaches the taste receptors, so sensory testing of the actual product is necessary [4,8-10].

Dental exposure deserves similar attention. Acidic vitamin C chewables can lower salivary pH and have been associated with enamel erosion under prolonged or repeated exposure. Whether liposomal delivery reduces that local acid exposure is an open formulation question. Product pH, free-acid concentration, residual acidity after chewing and the duration of oral contact should be measured rather than inferred from the presence of a liposomal carrier [8-10].

15 ANALYTICAL EVALUATION

Vitamin C assay and degradation monitoring should rely on a validated, stability-indicating HPLC method. The analytical procedure should demonstrate specificity, accuracy, precision, linearity, range and robustness. Because the final product contains both a vitamin and a lipid carrier, analytical development should also distinguish total vitamin C from the unencapsulated fraction and should include tests that describe the carrier after rehydration. [28,30] The WBCIL Lipoedge™ example also illustrates why these carrier-specific measurements are important when a liposomal ingredient is incorporated into a solid oral product [15,17].

Table 8: Analytical approaches for evaluating the physicochemical characteristics, chemical stability, liposomal integrity, tablet performance, and sensory attributes of liposomal vitamin C chewable tablets.

Test	Purpose	Recommended approach
Vitamin C assay	Potency	HPLC/validated stability-indicating method
Free vitamin C	Quantify unencapsulated fraction	Validated separation method followed by HPLC
Encapsulation efficiency	Determine fraction associated with vesicles	EE% = (total vitamin C − free vitamin C)/total vitamin C × 100
Loading capacity	Measure active-to-carrier relationship	Define clearly whether denominator is total formulation or lipid mass
Particle size	Characterize rehydrated vesicles	DLS hydrodynamic diameter
PDI	Assess size distribution	DLS
Zeta potential	Surface/electrokinetic characterization	Electrophoretic light scattering
Morphology	Confirm vesicles	TEM/cryo-TEM
Thermal behavior	Assess lipid/API interactions	DSC where relevant
Chemical interactions	Assess formulation compatibility	FTIR as supportive characterization
Lipid oxidation	Monitor carrier degradation	Peroxide value/another validated lipid oxidation marker
Tablet performance	Assess chewable quality	Hardness, friability, dimensions, disintegration, dissolution
Moisture	Monitor solid-state stability	Karl Fischer/LOD
Sensory performance	Taste and mouthfeel	Controlled sensory study

The recommended analytical approaches for evaluating liposomal vitamin C chewable tablets are summarized in Table 8.

An integrated analytical characterization framework is presented in Figure 6.

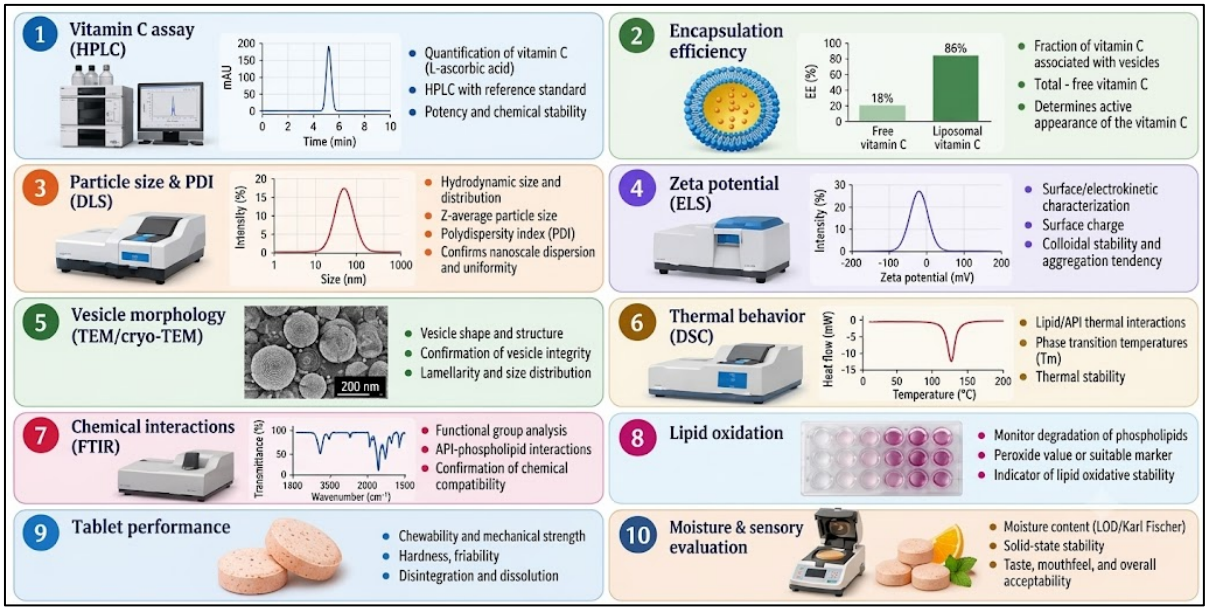


Figure 6: Integrated analytical characterization of liposomal vitamin C, including vitamin C assay, encapsulation efficiency, particle size and PDI, zeta potential, vesicle morphology, thermal behavior, chemical interactions, lipid oxidation, tablet performance, moisture, and sensory evaluation.

16 DEVELOPMENTAL FORMULATION CONCEPT

A practical development program can be built around a dry liposomal vitamin C intermediate rather than attempting to compress a liquid dispersion directly. The stages below are intended as a development framework: first establish a reproducible liposomal system, then optimize its size and stability, select a drying route, and finally integrate the dry carrier into a chewable matrix and evaluate the finished product. [26] In this context, WBCIL's Lipoedge™ Liposomal Vitamin C can serve as a commercial benchmark for the dry liposomal-intermediate approach, while its reported characteristics should be treated as product-specific rather than universal targets [15,17]. The proposed stepwise development workflow is summarized in Table 9.

Table 9: Stepwise development workflow for liposomal vitamin C chewable tablets, including key formulation activities and primary development responses.

Stage	Development activity	Primary response
1. Liposome screening	Screen phospholipid grade, lipid:cholesterol ratio, vitamin C concentration and hydration conditions	Size, PDI, EE%, zeta, assay
2. Size optimization	Microfluidization/extrusion/appropriate size-reduction process	Target size distribution and reproducibility
3. Stability screening	Evaluate pH, oxygen exposure, temperature and storage	Vitamin C retention + vesicle integrity
4. Drying study	Compare spray drying vs lyophilization/proliposome approach	Powder yield, moisture, rehydration, EE%, size/PDI
5. Chewable blend	Combine dry liposomal intermediate with mannitol/MCC, sweetener, flavour, disintegrant and lubricant	Flow, content uniformity, taste, compression
6. Compression study	Vary compression force and lubricant mixing	Hardness, friability, chewability, rehydrated liposome properties

7. Stability	Accelerated and long-term studies in final package	Assay, degradation, moisture, physical CQAs
8. Comparative study	Match vitamin C dose against non-liposomal chewable	AUC/C_{max}, release, sensory and stability comparison

17 PROPOSED HEAD-TO-HEAD STUDY: LIPOSOMAL VS NON-LIPOSOMAL CHEWABLE

The most informative product comparison would use two chewable tablets containing the same nominal amount of vitamin C: one conventional and one liposomal. As far as practical, tablet mass, flavour, sweetener system and the major excipient functions should be matched. This makes the liposomal carrier the main formulation difference and gives the comparison much more interpretive value [4,26]. The key endpoints for a matched head-to-head comparison are summarized in Table 10.

Table 10: Comparative endpoints for evaluating the performance, integrity, stability, and pharmacokinetic advantages of liposomal versus conventional vitamin C chewable tablets.

Endpoint	Why compare	Preferred interpretation
Assay	Ensure equal vitamin C dose	Comparable dose before pharmacokinetic comparison
Taste	Determine whether liposomalization changes sensory profile	Lower sourness/aftertaste only if statistically demonstrated
Dissolution	Compare release from tablet matrix	Identify whether liposomal system changes release profile
Rehydrated size/PDI	Confirm vesicle recovery after compression	Stable size distribution supports carrier integrity
EE% after compression	Detect leakage or rupture	Minimal loss indicates process compatibility
Stability	Compare potency retention	Higher retention only if demonstrated under matched conditions
AUC/C_{max}	Compare systemic exposure	Higher exposure supports pharmacokinetic advantage
24-h exposure	Assess duration of elevated vitamin C	Potential prolonged exposure if reproducible
Dental pH/contact study	Assess oral acid exposure	Lower exposure only if experimentally demonstrated

A matched-dose comparison is more informative than comparing unrelated commercial products because liposomal formulations can differ substantially in lipid composition, dose, drying process and excipient matrix. The 2025 scoping review highlighted exactly this problem of heterogeneity. A carefully controlled head-to-head study would therefore provide stronger evidence about whether liposomalization itself improves the performance of a chewable tablet [19].

18 LIMITATIONS AND RESEARCH GAPS

The most important evidence gap is the lack of well-powered clinical studies specifically evaluating compressed liposomal vitamin C chewable tablets. Most available human studies have examined liquid liposomes, powders or other liposomal preparations. Their findings support the broader delivery concept, but they cannot be assumed to predict the pharmacokinetics of every finished chewable [19,20].

Encapsulation efficiency is another point that deserves caution. A high EE% tells us that much of the vitamin is associated with the carrier at the time of measurement; it does not by itself predict systemic exposure. Likewise, a low free-vitamin fraction does not guarantee that vesicles will remain intact in the gastrointestinal tract. Membrane composition, particle size, rigidity, digestion, release and interactions with the intestinal environment all contribute to the final outcome.

The stability program is also more demanding than for a conventional chewable. In addition to vitamin C oxidation, the developer must consider lipid oxidation, leakage, rehydration behaviour and changes in the liposome population. These extra critical quality attributes increase both the analytical workload and the number of failure modes that need to be understood during development.

Sensory and dental claims should be treated with the same level of caution. A liposome may change how much free acid is presented to the mouth, but the actual effect depends on the tablet matrix, lipid composition, excipients and release behaviour. Direct sensory testing and controlled oral-exposure studies are therefore needed before claiming a meaningful reduction in sourness or dental acid exposure.

19 CONCLUSION

Liposomal vitamin C chewable tablets are an interesting attempt to combine the familiarity of a chewable supplement with the delivery capabilities of a phospholipid carrier. The strongest current human evidence is that some liposomal vitamin C formulations can produce greater systemic exposure than conventional vitamin C at the same nominal dose. Other potential benefits-such as protection during processing and storage, altered gastrointestinal handling and reduced sensory exposure-are scientifically plausible, but they remain dependent on the formulation and the final dosage form.

The central formulation challenge is to preserve the carrier while turning it into a robust, pleasant tablet. Drying, powder handling, excipient blending, compression and storage can each effect vesicle recovery, vitamin C potency and tablet performance. The finished product should therefore be evaluated as a formulation-process-package system, with rehydrated particle size, PDI, zeta potential, encapsulation efficiency and leakage measured alongside vitamin C assay and degradation products before and after tabletting.

WBCIL's Lipoedge™ Liposomal Vitamin C is a useful industry example of this translational pathway. The reported use of sunflower-derived phosphatidylcholine, nanoscale particles, high encapsulation efficiency and a dry, water-dispersible material suitable for tablet-oriented applications shows how a characterized liposomal intermediate can be positioned for solid oral development. [15,17]

For product development, the most informative next step is a matched-dose, head-to-head comparison with a conventional vitamin C chewable. Such a study can examine bioavailability, chemical stability, release, taste, oral exposure and other relevant performance attributes under controlled conditions. Until direct evidence is available for the finished chewable, claims should clearly distinguish established findings from formulation-specific expectations.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author's Contribution

All authors contributed equally in writing the draft, conceptualisation, review & editing, investigation and research. Mr Sunil Agarwal has also provided guidance and supervised the entire work.

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