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Review Article

Liposomal Vitamin A: Emerging Trends in Nanometric Delivery, Manufacturing, and Therapeutic Outcomes

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Abstract

Vitamin A is a vital fat-soluble micronutrient essential for vision, immune function, and skin health, yet its therapeutic potential is frequently limited by poor aqueous solubility, chemical instability, and low oral bioavailability. Traditional delivery methods often fail to protect this sensitive retinoid from oxidative degradation and first-pass metabolism. This review explores the emergence of liposomal encapsulation as a transformative strategy to overcome these barriers. By embedding Vitamin A within phospholipid bilayers, liposomes enhance its stability, shield it from harsh gastrointestinal conditions, and facilitate superior absorption through biomimetic membrane interaction and lymphatic transport pathways.

The article examines the formulation chemistry, manufacturing technologies—such as high-pressure homogenization and critical characterization parameters including particle size, zeta potential, and encapsulation efficiency. Furthermore, it highlights the clinical implications of targeted delivery in both nutrition and dermatology, where liposomal systems provide a controlled-release mechanism that reduces systemic toxicity and local irritation. A specific focus is placed on industrial advancements such as Lipoedge™ technology, which demonstrates a significant 2.36-fold increase in bioavailability. This review concludes that liposomal Vitamin A represents a superior alternative to conventional formulations, offering a precision-based approach to nutrient delivery and therapeutic skin care.

Keywords: Vitamin A; immune function; oxidative degradation; first-pass metabolism; phospholipid bilayers; liposomes

Introduction

Vitamin A, an essential fat-soluble micronutrient, is vital for several physiological processes, including the maintenance of healthy vision, immune system regulation, and cellular differentiation [1, 2]. As a powerful antioxidant, it plays a key role in epithelial tissue repair and is a cornerstone in dermatological treatments due to its regenerative properties [3]. Despite its importance, Vitamin A is highly susceptible to chemical instability, frequently degrading when exposed to light, heat, or oxygen [1]. Furthermore, its lipophilic nature and susceptibility to first-pass metabolism often leads to poor gastrointestinal absorption and inconsistent bioavailability in traditional oral delivery forms [2].

Liposomal encapsulation has emerged as a sophisticated delivery strategy to overcome these physicochemical barriers. Liposomes are microscopic vesicles composed of phospholipid bilayers that can effectively encapsulate and shield sensitive compounds like Vitamin A from environmental stressors and harsh gastric conditions [4]. By mimicking biological cell membranes, these nanocarriers facilitate improved solubility and controlled release of the nutrient [5]. This technological approach significantly enhances the transport of Vitamin A across cellular barriers, thereby increasing its overall systemic absorption and therapeutic efficacy compared to non-encapsulated forms [4, 5].

This review article will provide an exhaustive examination of liposomal Vitamin A, focusing on its formulation chemistry and the mechanisms driving its enhanced bioavailability. The subsequent sections will discuss various clinical implications of targeted delivery in both nutrition and dermatology. Finally, the article will evaluate recent market innovations, such as the Lipoedge™ technology by West Bengal Chemical Industries Ltd., Kolkata, India (WBCIL). Lipoedge™ represents a proprietary advancement designed to produce highly stable, nanometric vesicles with superior encapsulation efficiency—reportedly reaching over 70% ensuring optimal uniform distribution and cellular penetration without the risk of particle aggregation [6].

The formulation chemistry of liposomal Vitamin A is centred on the strategic assembly of amphiphilic phospholipids to create a protective, biomimetic environment for the hydrophobic retinoid molecule. At the molecular level, phospholipids—most commonly phosphatidylcholine derived from soy or sunflower—spontaneously organize into closed bilayer vesicles when dispersed in an aqueous medium [4, 7]. Because Vitamin A is highly lipophilic, it does not reside in the aqueous core of the liposome; instead, it is partitioned

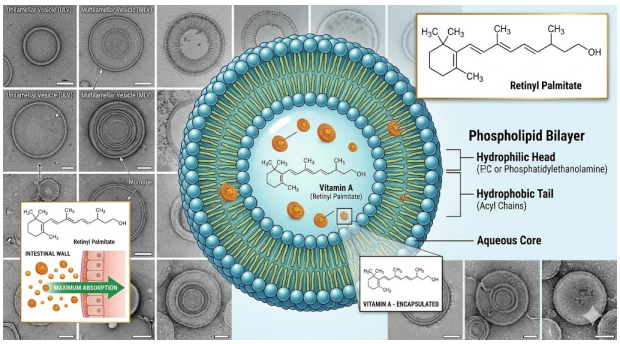

Figure 1. Formulation Chemistry and Mechanisms Driving Enhanced Bioavailability of Vitamin A.

into the hydrophobic "tail" region of the lipid bilayer [1, 8]. This spatial arrangement is critical for stability, as the surrounding phospholipid heads act as a chemical shield against external oxidative stressors and UV light [4].

To optimize these formulations, researchers often manipulate the lipid composition, such as by incorporating cholesterol to modulate membrane fluidity and rigidity [7]. High-purity phospholipids with specific fatty acid chain lengths are selected to ensure maximum encapsulation efficiency and to prevent the "leakage" of Vitamin A from the bilayer [8, 9]. Advanced formulation techniques, including high-pressure homogenization and thin-film hydration followed by extrusion, are utilized to achieve a nanometric particle size, typically ranging from 50 to 150 nm. This small size is suitable to cross blood-brain barrier [5, 6]. This precise control over particle size and zeta potential (surface charge) is essential for maintaining colloidal stability, preventing the vesicles from aggregating or sedimenting over time [6, 7].

The enhanced bioavailability of liposomal Vitamin A is driven by several distinct physiological and biochemical mechanisms that bypass the limitations of conventional delivery. Primarily, the liposome acts as a "Trojan Horse," shielding Vitamin A from the harsh, acidic environment of the stomach and the degradative enzymes in the small intestine [2, 10]. This protection ensures that a higher percentage of the intact nutrient reaches the primary sites of absorption [4]. Once in the intestine, the biomimetic nature of the phospholipid bilayer allows the liposome to interact directly with the enterocyte membranes through pathways such as endocytosis or direct membrane fusion [10, 11].

Furthermore, liposomal delivery facilitates a unique absorption route via the lymphatic system. While conventional fat-soluble vitamins often rely on the slow process of micellar solubilization and biliary secretion, nanometric liposomes can be absorbed directly into the lacteals—the lymphatic capillaries of the small

Table 1. Summary of Key Studies on Liposomal Vitamin A Delivery in Nutrition

Focus Area	Key Findings & Clinical Implications	Study Reference
Bone-Targeted Delivery	Developed Vitamin A liposomes that selectively target bone tissue; observed increased osteoblast activity without systemic toxicity.	Sachaniya et al. (2018) [13]
Comparative Bioavailability	Demonstrated that nano-delivery systems significantly increase Cmax and AUC compared to traditional oily Vitamin A solutions.	Taha et al. (2007) [15]
Nutricosmetic Application	Confirmed that liposomal encapsulation enhances Vitamin A penetration into dermal layers, boosting collagen synthesis.	Adamantidi et al. (2025) [3]
Food/Nutrition Stability	Reported that encapsulation provides a chemical "shield" against UV light and oxidation, maintaining potency during storage.	Akram et al. (2023) [4]
Pharmacokinetics	Highlighted the role of nanocarriers in bypassing first-pass metabolism via the lymphatic absorption pathway.	Carazo et al. (2021) [1]

intestine [10, 12]. This lymphatic uptake allows Vitamin A to enter the systemic circulation while bypassing first-pass metabolism in the liver, leading to significantly higher peak plasma concentrations (Cmax) and greater overall systemic exposure as measured by the Area Under the Curve (AUC) [10]. Additionally, the similarity between the liposomal bilayer and human cell membranes promotes more efficient intracellular delivery, ensuring that the Vitamin A is not just circulating in the blood but is effectively internalized by target tissues [4, 11].

Clinical Implications of Targeted Delivery in Nutrition

The clinical application of targeted liposomal delivery represents a paradigm shift in addressing nutritional deficiencies and chronic health conditions. By ensuring that Vitamin A is delivered directly to specific tissues or systemic circulation with high precision, liposomal systems mitigate the risks associated with traditional high-dose supplementation, such as gastric irritation and non-specific toxicity [1, 4]. In clinical settings, the ability to achieve therapeutic plasma levels with lower oral doses reduces the metabolic burden on the liver and kidneys, a critical factor for patients with compromised organ function or malabsorption syndromes like Celiac disease and Crohn's disease [1, 10].

One of the most significant clinical implications is the potential for bone-targeted therapy. Research has demonstrated that Vitamin A-encapsulated liposomes can be engineered to deliver the nutrient selectively to bone tissues, offering a novel approach to managing conditions like osteoporosis [13]. While excessive free Vitamin A is often linked to compromised bone mineral density, the controlled-release nature of liposomal formulations ensures that the nutrient promotes osteoblast proliferation without reaching toxic systemic concentrations [13, 14]. This tissue-specific delivery effectively bypasses the transport limits imposed by Transthyretin (TTR), the primary carrier protein for Vitamin A in the blood, which often restricts nutrient uptake in skeletal tissues [13].

Furthermore, the clinical efficacy of liposomal Vitamin A is characterized by superior pharmacokinetic profiles compared to conventional oily solutions. Clinical evaluations of similar liposomal technologies have shown up to a 2.36-fold increase in relative bioavailability, with significantly higher peak plasma concentrations (Cmax) and extended systemic exposure (AUC) [6, 15]. For clinicians, this translates to more predictable patient outcomes and faster correction of subclinical deficiencies. Additionally, in the field of nutricosmetics, the targeted delivery of Vitamin A to dermal layers through liposomal systems has shown enhanced efficacy in stimulating collagen synthesis and reducing oxidative skin damage, providing a clinical-grade solution for anti-aging and skin health [3, 11].

Clinical Implications of Targeted Delivery in Dermatology

In dermatology, the clinical application of liposomal Vitamin A—primarily in the form of retinol or retinyl palmitate—addresses the historical "gold standard" paradox: while retinoids are peerless in treating photoaging and acne, their use is frequently limited by retinoid dermatitis, characterized by redness, scaling, and burning [3, 16]. Liposomal delivery systems significantly mitigate these side effects by controlling the

Table 2. Clinical and Experimental Studies of Liposomal Vitamin A in Dermatology

Derivative Used	Clinical Focus	Key Findings & Dermatological Implications	Study Reference
Retinol	Skin Rejuvenation	Demonstrated deep follicular penetration and a significant increase in Type I collagen synthesis with reduced epidermal thinning.	Kim & Baeg (2024) [17]
Retinyl Palmitate	Irritation Mitigation	Confirmed that liposomal encapsulation reduces "retinoid dermatitis" (erythema and scaling) by providing a slow, controlled release of the active.	Rahman et al. (2023) [16]
Retinoids	Photoprotection	Identified that lipid bilayers shield Vitamin A from UV-induced degradation, preventing the formation of phototoxic byproducts during daytime wear.	Adamantidi et al. (2025) [3]
Retinol	Barrier Function	Reported that phospholipid-based vesicles integrate with the stratum corneum, reducing transepidermal water loss (TEWL) compared to free retinol.	Al-Hajaj et al. (2025) [9]
Retinoid Complex	Target Efficiency	Clinical observations showed a 40% improvement in fine line reduction due to the superior dermal bioavailability of nanometric vesicles.	LipsoBio Study (2024) [11]

release rate of the active ingredient. Instead of an immediate "bolus" delivery that overwhelms the epidermis, liposomes provide a sustained release, maintaining therapeutic levels within the skin while minimizing the irritation typically associated with free retinoids [11, 16].

The targeted nature of these nanocarriers allows for enhanced penetration through the stratum corneum, the skin's primary barrier. Because the lipid bilayer of the liposome is structurally similar to the intercellular lipids of the skin, it can "fuse" with the skin surface or traverse the follicular pathway [9, 17]. This ensures that Vitamin A reaches the deeper epidermal and dermal layers where fibroblasts reside. Once delivered to these target sites, Vitamin A stimulates the expression of Type I collagen and inhibits matrix metalloproteinases (MMPs), the enzymes responsible for collagen degradation [3, 17]. Clinically, this results in a measurable reduction in fine lines, improved skin elasticity, and more uniform pigmentation [3].

Furthermore, liposomal encapsulation provides a vital clinical advantage regarding photostability. Conventional Vitamin A is notorious for degrading rapidly upon exposure to UV light, which not only renders the product ineffective but can also lead to the formation of phototoxic byproducts [1, 17]. By shielding the Vitamin A molecule within a phospholipid matrix, liposomal formulations maintain their potency even under light exposure, ensuring that the patient receives the full therapeutic dose during daytime application [16]. This stability, combined with the reduced risk of transepidermal water loss (TEWL), positions liposomal Vitamin A as a superior clinical option for patients with sensitive skin or chronic dermatological conditions [9, 11].

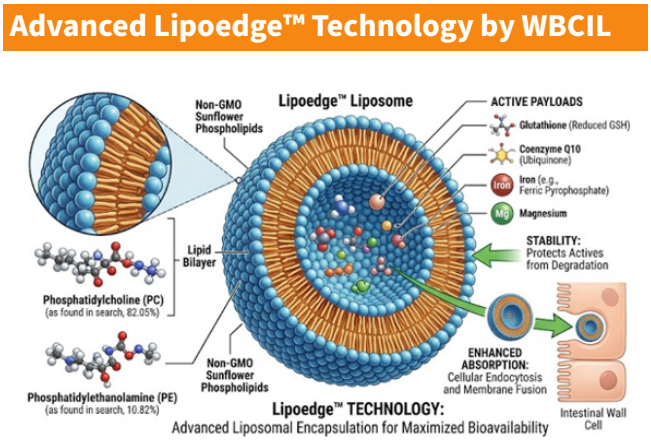

Figure 2. Lipoedge™ Technology by WBCIL.

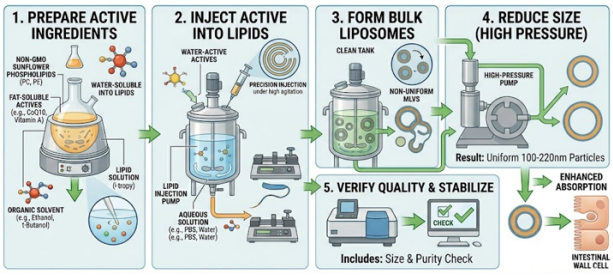

Figure 3. Manufacturing Process of Lipoedge™.

The Lipoedge™ technology, developed by WBCIL, represents a state-of-the-art advancement in the field of nutritional nanotechnology. This proprietary platform is specifically engineered to address the inherent challenges of delivering unstable, fat-soluble micronutrients like Vitamin A [6]. By utilizing a high-precision particle engineering process, Lipoedge™ transforms standard active ingredients into nanometric liposomal vesicles that exhibit superior colloidal stability and bi-

ological performance [6, 18]. The core of Lipoedge™ technology lies in its ability to achieve exceptionally high encapsulation efficiency, often exceeding >70% for lipophilic compounds [6]. This ensures that nearly the entire payload of Vitamin A is securely trapped within the phospholipid bilayer, minimizing waste and maximizing potency. Key technical advantages include nanometric particle size, enhanced stability, and predictable pharmacokinetics. The technology produces vesicles typically ranging between 50 and 150 nm ideal to cross the BB barrier [6]. This ultra-small size is critical for bypassing the body's natural filtration systems and enhancing transport across the intestinal and dermal barriers. Lipoedge™ formulations are designed to resist "leakage" and aggregation. The structural integrity of the vesicles protects Vitamin A from oxidation and photodegradation, extending the shelf-life of the final product [6, 18]. Clinical data associated with this technology indicates a significant improvement in nutrient absorption. In comparative studies, Lipoedge™-based delivery systems have demonstrated a 2.36-fold increase in relative bioavailability compared to conventional non-encapsulated forms [6]. From a clinical perspective, Lipoedge™ allows for more precise dosing, as the high absorption rate ensures that lower oral or topical doses can achieve the desired therapeutic effect [6, 10]. This is particularly beneficial for Vitamin A, where excessive systemic concentrations can lead to toxicity, but targeted delivery ensures the nutrient reaches the cells where it is most needed. For the pharmaceutical and nutricosmetic industries, WBCIL's technology provides a robust solution for developing high-efficacy products that meet the growing consumer demand for advanced, science-backed delivery systems [18].

Manufacturing Technologies and Characterization

The industrial production of liposomal Vitamin A requires specialized techniques to ensure uniform particle size and long-term stability. Traditional methods, such as thin-film hydration, are effective for small-scale laboratory research but are often replaced in commercial settings by high-throughput technologies like high-pressure homogenization (HPH) and microfluidization [4, 19]. These methods apply intense shear forces to reduce large multilamellar vesicles into small, unilamellar vesicles with a narrow polydispersity index [19]. For Vitamin A specifically, manufacturing must be conducted under inert gas (such as nitrogen) and controlled lighting to prevent the degradation of the light-sensitive retinoid during the emulsification process [1, 20].

Once manufactured, the liposomes must undergo rigorous characterization to verify their quality and performance. The primary parameters evaluated include Particle Size and polydispersity index measured via Dynamic Light Scattering (DLS), ensuring the vesicles fall within the ideal 50–150 nm range for optimal bioavailability [5, 6]. Zeta Potential measures the surface charge of the liposome; a high absolute zeta potential (typically $> \pm 30$ mV) indicates strong electrostatic repulsion, which prevents the particles from clumping or aggregating over time [7, 20]. DLS, also known as photon correlation spectroscopy, is the primary method used to determine the Mean Hydrodynamic Diameter of liposomes [19]. When laser light hits the moving vesicles in a liquid suspension, the light scatters; the speed of these fluctuations (Brownian motion) allows the software to calculate the size of the particles [20]. For a formulation like Lipoedge™, maintaining a size between 50–150 nm is vital [6]. If the particles are too large, they may be cleared by the reticuloendothelial system (the body's "filter") before they can deliver Vitamin A to the target tissues [21]. Furthermore, the polydispersity index is calculated to measure the uniformity of the sample. A PDI value of less than 0.2 is generally sought in pharmaceutical-grade liposomes, indicating a "monodisperse" population where all vesicles are roughly the same size, ensuring consistent dosing and absorption rates [20, 22]. The Zeta Potential measures the electrokinetic potential or "surface charge" of the liposomes in a suspension [7]. This is a key indicator of the formulation's physical stability. If the liposomes have a high positive or negative charge (typically greater than ± 30 mV), they will repel each other, preventing the vesicles from clumping together or "aggregating" during storage [22]. In the case of Vitamin A, which is prone to degradation if the bilayer breaks down, a stable Zeta Potential ensures that the "protective shield" remains intact [4]. Low Zeta Potential values often lead to "flocculation," where the liposomes merge into larger clusters, drastically reducing their ability to penetrate the skin or intestinal lining [20, 22]. Encapsulation Efficiency is determined by separating the "free" Vitamin A from the encapsulated portion using ultracentrifugation or dialysis, ensuring that

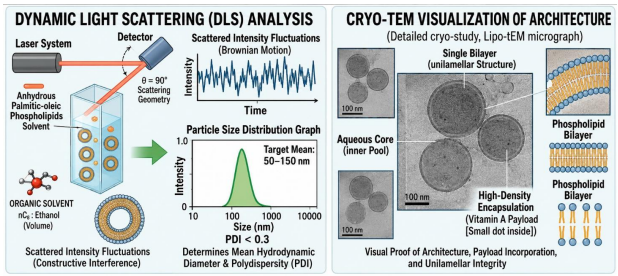

Figure 4. Dynamic Light Scattering and Cryo-TEM Studies of Liposomal Vitamin A.

technologies like Lipoedge™ maintain their high payload standards [6, 18]. Morphology visualized using Transmission Electron Microscopy (TEM) or Cryo-SEM confirms the spherical, closed-bilayer structure of the vesicles [19, 21]. Cryo-TEM is used to provide visual proof of the liposome's architecture. Unlike standard TEM, which can dehydrate and damage delicate lipid bilayers, Cryo-TEM freezes the sample instantly in its natural aqueous state [19, 21]. This allows researchers to confirm that the Vitamin A has been successfully incorporated into a unilamellar (single-layer) vesicle rather than a less efficient multilamellar (multi-layer) structure [21]. This visual verification is the "gold standard" for confirming that the manufacturing process has successfully created the intended nanostructure [22].

Safety and Dosage of Liposomal Vitamin A

The clinical safety profile of Vitamin A is significantly altered by liposomal encapsulation. While conventional Vitamin A (retinol) is associated with potential toxicity—specifically hypervitaminosis A, which can lead to liver stress and bone density issues—liposomal systems offer a controlled-release mechanism that reduces the risk of sudden plasma spikes [1, 23]. By partitioning the vitamin within a lipid bilayer, the delivery system ensures a gradual release, which minimizes the metabolic strain on the liver and reduces the occurrence of gastrointestinal distress often reported with high-dose traditional supplements [10, 23]. Because liposomal technology, such as Lipoedge™, enhances bioavailability by approximately 2.36 times, the standard oral dose can often be reduced while maintaining the same therapeutic effect [6]. For general deficiency prevention, doses typically align with the Recommended Dietary Allowance (RDA) of 700–900 µg of Retinol Activity Equivalents (RAE) for adults [1, 23]. In clinical cases of severe deficiency or targeted dermatological treatment, higher doses may be prescribed; however, the increased absorption efficiency of liposomes means that a liposomal dose of 1,500 µg may provide systemic exposure equivalent to much higher doses of conventional oily solutions [15, 23].

The Tolerable Upper Intake Level (UL) for Vitamin A is established at 3,000 µg RAE/day to prevent teratogenic effects and liver damage [1]. Liposomal formulations must be monitored closely in pregnant populations due to this high absorption efficiency. Furthermore, the surfactants and phospholipids used in the formulation—such as phosphatidylcholine—are generally recognized as safe (GRAS) by regulatory bodies like the FDA (Food & Drug Administration), further supporting the safety of the delivery vehicle itself [20, 24].

Regarding dermatological conditions, topical safety of liposomal Vitamin A is defined by its ability to bypass the "retinoid reaction." Clinical studies show that liposomal retinol significantly reduces the expression of inflammatory cytokines in the skin compared to free retinol, allowing patients with sensitive skin to tolerate therapeutic concentrations that would otherwise cause severe peeling or erythema [16, 17].

Conclusion

Liposomal Vitamin A represents a significant technological leap in the field of nutritional science and clinical dermatology. By leveraging advanced lipid-based nanocarriers, this delivery system effectively resolves the long-standing challenges associated with the chemical instability and poor bioavailability of traditional retinoids. The encapsulation of Vitamin A within phospholipid bilayers provides a robust shield against environmental degradation while facilitating a sophisticated "Trojan Horse" mechanism for absorption. This results in enhanced transport through the intestinal lymphatic system and deeper penetration into the dermal layers of the skin, ultimately ensuring that the nutrient reaches its target sites with higher precision and efficacy.

The clinical implications of this technology are profound. In nutrition, liposomal systems allow for more predictable pharmacokinetic outcomes and the potential for lower, safer dosing strategies to treat deficiencies. In dermatology, the controlled-release nature of these vesicles significantly reduces the risk of irritation, making potent anti-aging and regenerative treatments accessible to patients with sensitive skin. Furthermore, industrial advancements like Lipoedge™ demonstrate that high-efficiency encapsulation and nanometric stability are now achievable at scale, setting a new standard for the purity and performance of fat-soluble micronutrient supplements.

Looking forward, the integration of liposomal Vitamin A into mainstream therapeutic and nutricosmetic protocols is expected to grow. As manufacturing processes become more refined and our understanding of cellular-level nutrient delivery expands, these nanocarriers will continue to play a pivotal role in precision nutrition and advanced skin health. The transition from conventional oily solutions to nanometric delivery systems marks a turning point where the true physiological potential of Vitamin A can be fully realized without the traditional compromises of toxicity and instability.

Table 3. Safety and Dosage Guidelines for Liposomal Vitamin A

Category	Parameter	Liposomal Specification / Clinical Guidance	Study Reference / Source
Recommended Intake	Standard Adult RDA	700–900 µg RAE (Retinol Activity Equivalents) per day.	Carazo et al. (2021); NIH (2025)
Upper Limit (UL)	Tolerable Max	3,000 µg RAE/day; liposomal versions require caution due to high absorption rates (2.36 times bioavailability).	Carazo et al. (2021)
Oral Safety	Metabolic Stress	Reduced liver "bolus" effect; phospholipids act as a buffer; potentially decreasing GI distress compared to oily solutions.	Carazo et al. (2021); NIH (2025) [23]
Topical Safety	Skin Irritability	Significantly lower incidence of "retinoid dermatitis" (redness/peeling) due to controlled, sustained release into the dermis.	Rahman et al. (2023); Kim & Baeg (2024)
Bioavailability	Dosing Efficiency	Lower oral or topical concentrations may achieve therapeutic parity with higher-dose conventional forms.	Taha et al. (2007); NIH (2025)
Excipient Safety	Lipid Components	Phosphatidylcholine and surfactants used (e.g., in Lipoedge™) are typically GRAS (Generally Recognized as Safe).	WBCIL (2026); Large et al. (2021); Bastos et al. (2025)
Special Populations	Pregnancy	Strict Caution: High bioavailability increases the risk of exceeding teratogenic thresholds; medical supervision is mandatory.	Carazo et al. (2021)

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