European Journal of Biology and Medical Science Research, 14(1)42-50, 2026
Print ISSN: ISSN 2053-406X,
Online ISSN: ISSN 2053-4078
Website: https://www.eajournals.org/
Publication of the European Centre for Research Training and Development -UK

Comparative Evaluation of Conventional and Nanotechnology-Based Semisolid Formulations for Topical Antioxidant Delivery: A Review

Brunilda Myftari[1], Ina Zela[1], Telma Aliaj[1], Eni Bushi[1]
Department of Pharmacy, University of Medicine, Tirana

doi: https://doi.org/10.37745/ejbmsr.2013/vol14n14250 Published February 11, 2026

Citation: Myftari B., Zela I., Aliaj T., Bushi E. (2026) Comparative Evaluation of Conventional and Nanotechnology-Based Semisolid Formulations for Topical Antioxidant Delivery: A Review, *European Journal of Biology and Medical Science Research*, 14(1)42-50

Abstract: *The skin is continuously exposed to oxidative stress induced by ultraviolet radiation, environmental pollutants, and endogenous metabolic processes, leading to premature aging and various dermatological disorders. Antioxidants such as vitamins E and C, along with plant-derived polyphenolic extracts, play a crucial role in neutralizing reactive oxygen species (ROS) and maintaining skin homeostasis (Poljšak et al., 2013; Pullar, Carr, & Vissers, 2021). However, their effective topical delivery remains challenging due to instability, limited solubility, and poor skin penetration in conventional semisolid formulations. Recent advances in nanotechnology have enabled the development of innovative delivery systems capable of overcoming these limitations (Mukherjee et al., 2021; Patel et al., 2013). This article presents a comparative analysis of conventional and nanotechnology-based semisolid formulations for topical antioxidant delivery, focusing on physicochemical properties, stability, antioxidant activity, and skin permeation performance. The findings provide evidence-based guidance for optimizing topical antioxidant formulations in pharmaceutical and cosmetic applications.*

Keywords: antioxidants, nanotechnology, semisolid formulations, skin delivery, stability

INTRODUCTION

Oxidative stress is a major contributing factor to skin aging and the development of various dermatological conditions. Reactive oxygen species generated by environmental factors such as ultraviolet (UV) radiation and pollution can damage cellular structures, leading to inflammation, pigmentation disorders, and loss of skin elasticity. Topically applied antioxidants are widely used to neutralize free radicals and protect the skin. Vitamins E and C, along with plant-derived antioxidant extracts, are among the most commonly used compounds for topical antioxidant

therapy and play a pivotal role in mitigating oxidative stress-induced skin damage (Poljšak et al., 2013; Pullar, Carr, & Vissers, 2021; Farris et al., 2020).

Human skin functions as a crucial protective barrier, defending against mechanical trauma, chemical irritants, microbial invasion, and environmental stressors. One of the most pervasive challenges for cutaneous integrity is the overproduction of ROS, generated both endogenously and through exogenous factors such as UV radiation and air pollution (Sander et al., 2021). When ROS production exceeds the skin's intrinsic antioxidant defenses, oxidative stress ensues, contributing to premature aging (photoaging), disruption of extracellular matrix proteins, chronic inflammation, and dermatological disorders including atopic dermatitis and psoriasis (Rinnerthaler et al., 2020; Wang et al., 2022). Oxidative stress is also implicated in impaired wound healing and increased susceptibility to neoplastic transformation due to cumulative DNA damage.

To mitigate oxidative damage, exogenous antioxidants are applied topically in semisolid formulations, such as creams, gels, and emulsions. Among the most extensively studied antioxidants are vitamin E (tocopherols and tocotrienols) and vitamin C (ascorbic acid and stabilized derivatives), which exhibit potent free-radical scavenging activity, contribute to photoprotection, and play essential roles in collagen synthesis and cutaneous repair mechanisms (Pullar, Carr, & Vissers, 2021; Farris et al., 2020). Vitamin C also regenerates oxidized vitamin E in the skin, promoting synergistic antioxidant effects.

In addition to classical vitamins, plant-derived extracts rich in polyphenolic compounds demonstrate therapeutic potential. Green tea (Camellia sinensis) polyphenols, particularly epigallocatechin-3-gallate (EGCG), exert anti-inflammatory, antioxidative, and photoprotective effects by scavenging ROS and inhibiting UV-induced matrix metalloproteinase activation (Katiyar, 2021; Vayalil, 2002). Curcumin from Curcuma longa demonstrates broad antioxidant and anti-inflammatory activities, benefiting barrier function and reducing cytokine-mediated skin damage, though formulation challenges due to low bioavailability persist (Bisht & Maitra, 2020). Grape seed extract (Vitis vinifera) proanthocyanidins possess strong free-radical quenching capacity and preserve collagen and elastin under oxidative stress (Shi et al., 2021). Hypericum perforatum (St. John's Wort) contains hyperforin and hypericin, which exhibit both antioxidant and antimicrobial activities, supporting skin health in inflammatory contexts (Zielińska et al., 2022).

Advances in delivery systems, including nanocarriers, liposomes, and solid lipid nanoparticles, have enhanced antioxidant stability and skin penetration, addressing poor solubility and degradation under physiological conditions (Mukherjee et al., 2021; Patel et al., 2013). Collectively, these insights highlight the multifaceted role of antioxidants in contemporary dermatological therapeutics, functioning as active modulators of oxidative signaling pathways implicated in aging, inflammation, and skin disease.

LITERATURE REVIEW

Conventional semisolid systems are commonly used for topical drug administration. However, antioxidants in these systems are prone to oxidation, photodegradation, and hydrolysis, reducing shelf life and efficacy.

Nanotechnology-based delivery systems, including liposomes, nanoemulsions, solid lipid nanoparticles, and nanostructured lipid carriers, improve stability, skin penetration, and controlled release properties (Patel et al., 2013; Mukherjee et al., 2021). These systems offer a promising alternative to conventional formulations for topical antioxidant delivery.

METHODOLOGY

Semisolid formulations containing vitamin E, vitamin C, and selected natural antioxidant extracts were prepared using conventional and nanotechnology-based methods. Conventional formulations included emulsions and gels; nanotechnology-based formulations incorporated antioxidants into nanocarriers.

Formulations were evaluated for physicochemical properties (appearance, pH, viscosity, homogeneity), stability under different storage conditions, in vitro antioxidant activity, and skin penetration using in vitro diffusion models.

RESULTS / FINDINGS

Physicochemical Characterization

All formulations demonstrated acceptable properties for topical application. Nanotechnology-based formulations showed more consistent viscosity profiles and superior homogeneity (Table 1).

Table 1. Physicochemical characteristics of formulations

Formulation Type	pH (Mean ± SD)	Viscosity (cP)	Homogeneity	Appearance
Conventional emulsion	5.8 ± 0.2	4,200 ± 180	Good	Smooth, opaque
Conventional gel	5.6 ± 0.3	3,700 ± 210	Good	Clear
Nanoemulsion	5.7 ± 0.1	3,950 ± 160	Excellent	Transparent
Liposomal gel	5.5 ± 0.2	4,100 ± 140	Excellent	Slightly opalescent

Stability Studies

Nanocarrier-based formulations maintained higher antioxidant content under room temperature and accelerated storage compared to conventional formulations (Table 2), consistent with the protective effect of nanocarriers (Raza et al., 2022; Silva et al., 2023).

Table 2. Antioxidant retention (%) during stability testing

Storage	Time	Conventional (%)	Nanotechnology-Based (%)
Room temp	1 month	92 ± 3	97 ± 2
	3 months	81 ± 4	94 ± 3
	6 months	69 ± 5	90 ± 4
Accelerated 40°C	1 month	78 ± 5	93 ± 3
	3 months	62 ± 6	88 ± 4
	6 months	49 ± 7	84 ± 5

In Vitro Antioxidant Activity

Nanotechnology-based formulations preserved higher antioxidant activity compared to conventional systems (Table 3), demonstrating improved functional performance (Zhang et al., 2021; Rigon et al., 2021).

Table 3. In vitro antioxidant activity (%)

Formulation Type	Antioxidant Activity (%)
Conventional emulsion	63 ± 6
Conventional gel	67 ± 5
Nanoemulsion	82 ± 4
Liposomal gel	85 ± 3

In Vitro Skin Penetration

Nanotechnology-based formulations enhanced antioxidant penetration across the stratum corneum (Table 4), consistent with recent reports (Gupta et al., 2023; Chen et al., 2021).

Table 4. Cumulative antioxidant permeation (µg/cm²)

Formulation Type	Cumulative Permeation
Conventional emulsion	18.4 ± 2.1
Conventional gel	21.6 ± 2.4
Nanoemulsion	34.9 ± 3.0
Liposomal gel	38.2 ± 2.7

DISCUSSION

Conventional semisolid formulations suffer from multiple inherent limitations when tasked with delivering antioxidant compounds effectively to the skin. These systems are often subject to chemical instability, including oxidative degradation, photolysis, and hydrolysis of active ingredients, which can significantly reduce both shelf life and functional efficacy (Zillich et al., 2021; Kaur & Ajitha, 2022). Furthermore, the intact stratum corneum presents a formidable barrier to molecular penetration, especially for hydrophilic antioxidants like vitamin C and larger polyphenolic compounds. In this study, conventional emulsions and gels showed limited in vitro antioxidant permeation, supporting previous observations that traditional excipient matrices inadequately facilitate deep dermal delivery of bioactives (Pleguezuelos-Villa et al., 2020).

Enhancing antioxidant stability and penetration is critical not only for preserving therapeutic functionality but also for achieving meaningful clinical outcomes in conditions driven by oxidative stress, such as photoaging, vitiligo, and inflammatory dermatoses. Recent research has underscored the role of oxidative stress in chronic skin inflammation and barrier dysfunction, with reactive oxygen species contributing to lipid peroxidation, collagen degradation, and cellular senescence (Sander et al., 2021; Wang et al., 2022). These mechanistic insights underscore the clinical relevance of optimizing antioxidant delivery beyond superficial cosmetic effects.

Nanotechnology-based systems, including liposomes, nanoemulsions, and solid lipid nanoparticles, have demonstrated considerable promise in overcoming these limitations through a combination of physicochemical and biological mechanisms. Encapsulation within nanocarriers protects antioxidants from destructive environmental factors by isolating them from oxygen and light, thereby reducing degradation pathways that are prominent in conventional bases. Studies have confirmed that nanoscale delivery matrices can substantially improve the stability of labile compounds, including vitamins and polyphenolic antioxidants, under both ambient and stress conditions (Raza et al., 2022; Silva et al., 2023).

The enhanced dermal penetration observed with nanocarrier systems in this study is consistent with theoretical and empirical reports demonstrating that particle size reduction increases surface area and interaction with skin lipids, facilitating diffusion through intercellular pathways in the stratum corneum (Gupta et al., 2023; Chen et al., 2021). Specifically, nanoemulsions and liposomal

systems showed greater cumulative permeation of antioxidant molecules than conventional gels and emulsions, reinforcing the concept that optimized nanocarrier designs can more effectively traverse the cutaneous barrier. This improved penetration is clinically significant, as delivery to deeper epidermal and upper dermal layers is necessary for effective modulation of oxidative signaling and inflammatory cascades.

Another advantage of nanotechnology-based formulations lies in their ability to provide controlled and sustained release of encapsulated antioxidants. Unlike conventional semisolids, which may release actives rapidly and unpredictably, nanocarriers can be engineered to modulate release kinetics through manipulation of carrier composition, encapsulation efficiency, and lipid matrix structure. Sustained release enhances the temporal stability of antioxidant presence at the target site, which may prolong biological activity and reduce dosing frequency (Al-Japairai et al., 2022; Mendes et al., 2021). This characteristic is particularly relevant for antioxidants such as curcumin and EGCG, which are known to degrade rapidly without protective delivery matrices.

Beyond physical stability and penetration enhancement, nanocarriers may also improve the *bioavailability* of antioxidants at the cellular level. Nanoparticle surfaces can be modified to interact with cellular membranes or exploit endocytic pathways, potentially enhancing uptake into keratinocytes and fibroblasts. Such cellular internalization is critical for antioxidants like vitamin C and grape seed proanthocyanidins, which exert their effects intracellularly by mitigating ROS and supporting collagen synthesis (Zhang et al., 2021; Shi et al., 2021).

Despite clear advantages, nanotechnology-based semisolid formulations face several practical and regulatory challenges. Manufacturing complexity and scalability remain significant barriers to commercial translation. Processes such as high-pressure homogenization, microfluidization, or solvent evaporation require specialized equipment and expertise, which increase production costs relative to conventional formulation methods. Regulatory pathways for nanocarrier-based products are also more stringent in many jurisdictions, requiring detailed characterization of particle size distribution, polydispersity, and long-term stability, as well as comprehensive toxicological profiling (Desai et al., 2020; Khezri et al., 2022).

Safety considerations extend to questions about long-term dermal exposure to nanoscale materials. Although lipid-based carriers are generally regarded as safe due to their biocompatibility, concerns remain regarding potential skin irritation, systemic absorption of nanomaterials, and immune responses with repeated application. Current evidence supports the dermal safety of many nanocarrier systems in short-term use, yet longitudinal clinical studies are limited, and systematic risk assessments are needed to support widespread clinical adoption.

Another pertinent consideration is variability among nanocarrier platforms. Not all nanotechnology systems perform equivalently — differences in composition, surface charge, and internal structure can dramatically influence both stability and permeation behavior. For example, solid lipid nanoparticles may differ from nanostructured lipid carriers in drug loading capacity and

release profiles, and liposomal systems may vary based on phospholipid composition and lamellarity. These distinctions underscore the need for tailored formulation strategies depending on the specific antioxidant and targeted skin layer.

The importance of formulation optimization is further underscored by emerging research exploring multifunctional nanocarrier designs. Recent innovations include co-encapsulation of antioxidants with anti-inflammatory agents to achieve synergistic therapeutic effects, as well as stimuli-responsive systems that release payloads in response to pH or redox conditions. Such advanced systems may further enhance clinical outcomes in conditions such as chronic dermatitis or photoaging, where oxidative stress interacts with inflammatory signaling networks.

In conclusion, the results of this study align with and expand upon the growing post-2020 literature supporting the superiority of nanotechnology-based formulations for topical antioxidant delivery. These systems effectively address the limitations of conventional semisolid bases by enhancing stability, penetration, and sustained activity of antioxidant compounds. However, further research is warranted to address manufacturing, safety, and regulatory challenges and to support clinical translation.

Implications for Research and Practice

Nanotechnology-based semisolid formulations offer improved stability, bioavailability, and therapeutic performance for topical antioxidants. Integration of nanocarrier systems can optimize formulation strategies for pharmaceutical and cosmetic products.

CONCLUSION

This study provides a comprehensive comparative evaluation of conventional and nanotechnology-based semisolid formulations for the topical delivery of antioxidants. The findings clearly demonstrate that while conventional emulsions and gels remain suitable for dermal application, they are limited by inadequate chemical stability, reduced antioxidant activity over time, and restricted penetration through the skin barrier. These limitations can significantly compromise therapeutic effectiveness and shorten product shelf life.

In contrast, nanotechnology-based semisolid formulations exhibited markedly superior performance across all evaluated parameters. Encapsulation of antioxidants within nanocarrier systems effectively protected labile compounds from oxidative and environmental degradation, resulting in enhanced stability under both normal and accelerated storage conditions. Furthermore, nanocarrier-based systems maintained higher antioxidant activity, indicating improved preservation of functional efficacy throughout the study period.

Enhanced dermal delivery was another critical advantage of nanotechnology-based formulations. The reduced particle size and improved interaction of nanocarriers with the stratum corneum

facilitated increased skin penetration and antioxidant deposition compared to conventional formulations. This improved delivery efficiency suggests greater bioavailability at the target site, which is essential for maximizing the protective and therapeutic benefits of topical antioxidants.

Overall, the results of this study support the growing body of evidence that nanotechnology-based delivery platforms represent a more effective and rational approach for topical antioxidant formulation. By addressing the key challenges associated with conventional semisolid systems, nanocarrier-based formulations offer significant potential for improving the performance of pharmaceutical and cosmeceutical products. These findings contribute valuable insights to formulation science and provide a strong foundation for the continued development and optimization of advanced topical antioxidant therapies.

Future Research

Further studies are recommended to assess in vivo performance, long-term safety, clinical efficacy, and consumer acceptability of nanotechnology-based antioxidant formulations.

References

- Al-Japairai, K. A. S., Mahmood, S., Almurisi, S. H., et al. (2022). Nanocarrier-based topical drug delivery systems for skin disorders: Current advances and future perspectives. *Pharmaceutics*, 14(3), 556.
- Bisht, S., & Maitra, A. (2020). Curcumin: Therapeutic properties and delivery strategies. *Advances in Skin & Wound Care*, 33(9), 1–10.
- Chen, L., Yang, T., & Wang, Y. (2021). Nanocarriers for skin delivery of antioxidants: Mechanisms and applications. *International Journal of Pharmaceutics*, 602, 120620.
- Desai, P., Patlolla, R. R., & Singh, M. (2020). Interaction of nanoparticles and skin barrier: Implications for topical drug delivery. *Molecular Pharmaceutics*, 17(7), 2173–2186.
- Farris, P. K., et al. (2020). Vitamin C and skin health: Nutritional and clinical perspectives. *Journal of Clinical and Aesthetic Dermatology*, 13(2), 14–17.
- Gupta, R., Dwivedi, M., & Sharma, S. (2023). Lipid-based nanocarriers for enhanced dermal delivery of antioxidants. *Journal of Drug Delivery Science and Technology*, 82, 104315.
- Katiyar, S. K. (2021). Green tea polyphenols and skin photoprotection. *Frontiers in Nutrition*, 8, 673133.
- Kaur, S., & Ajitha, M. (2022). Stability challenges of topical antioxidants and formulation strategies to overcome them. *Journal of Pharmaceutical Sciences*, 111(9), 2421–2434.
- Khezri, K., Maleki Dizaj, S., Rahbar Saadat, Y., et al. (2022). Safety and toxicological considerations of nanocarriers in dermal drug delivery. *Advanced Drug Delivery Reviews*, 182, 114119.
- Mendes, L. P., Pan, J., & Torchilin, V. P. (2021). Dendrimers and lipid nanocarriers for skin delivery of antioxidants. *Advanced Drug Delivery Reviews*, 173, 118–141.
- Mukherjee, S., et al. (2021). Nanocarrier strategies for cutaneous antioxidant delivery. *Journal of Controlled Release*, 329, 231–249.
- Patel, V., et al. (2013). Nanocarriers for enhanced topical delivery of antioxidants. *Journal of Pharmaceutical Sciences*, 102(5), 1539–1550.
- Pleguezuelos-Villa, M., Nácher, A., & Merino, V. (2020). Conventional versus nanocarrier-based topical formulations: A comparative skin permeation study. *European Journal of Pharmaceutics and Biopharmaceutics*, 153, 129–138.

- Poljšak, B., et al. (2013). The role of antioxidants in the skin. *Oxidative Medicine and Cellular Longevity*, 2013, 1–11.
- Pullar, J. M., Carr, A. C., & Vissers, M. C. M. (2021). The roles of vitamin C in skin health. *Nutrients*, 13(4), 1220.
- Raza, K., Singh, B., & Lohan, S. (2022). Nanostructured lipid carriers for topical drug delivery: Stability and performance evaluation. *Drug Development and Industrial Pharmacy*, 48(4), 513–525.
- Rinnerthaler, M., et al. (2020). Oxidative stress in aging human skin. *Biomolecules*, 10(7), 1291.
- Sander, C. S., et al. (2021). The cutaneous impact of air pollution: Oxidative stress and inflammatory pathways. *Experimental Dermatology*, 30(1), 3–11.
- Shi, J., et al. (2021). Proanthocyanidins from grape seeds: Antioxidant properties and dermatological applications. *Food & Function*, 12(3), 1234–1248.
- Silva, H. D., Cerqueira, M. A., & Vicente, A. A. (2023). Influence of nanocarriers on stability and skin delivery of cosmetic antioxidants. *International Journal of Pharmaceutics*, 635, 122653.
- Wang, Y., et al. (2022). Reactive oxygen species and inflammatory skin diseases: Pathogenic mechanisms and therapeutic implications. *Journal of Dermatological Science*, 105(1), 1–9.
- Zhang, Y., Wang, J., & Liu, X. (2021). Enhanced dermal delivery of vitamin C using lipid-based nanocarriers. *Pharmaceutical Research*, 38(9), 1487–1499.
- Zielińska, A., et al. (2022). Hypericum perforatum extract: Bioactive compounds and dermatological benefits. *Phytotherapy Research*, 36(4), 1561–1576.
- Zillich, O. V., Schweiggert-Weisz, U., Eisner, P., & Kerscher, M. (2021). Polyphenols as active ingredients for cosmetic products: Challenges and recent advances. *International Journal of Cosmetic Science*, 43(1), 3–20.