




# Nanoparticles as a Promising Approach for Improving Skin Anti-Aging Activity

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**Abstract:** The aging of skin is a multifaceted process influenced by internal factors and external influences. These factors contribute to the breakdown of skin structure, diminished skin resilience, and observable indications of aging. Conventional topical formulations often fail to deliver active chemicals adequately due to the skin's inherent barriers and the solubility and instability of numerous substances. Emerging nanotechnology-based technologies offer a viable solution to these restrictions. This paper analyzes the role of diverse organic and inorganic nanoparticle-based formulations as delivery systems in improving the distribution and efficacy of anti-aging agents. As part of its novelty, this article integrates findings on both synthetic and natural anti-aging compounds, providing a comprehensive comparison of their nano-enabled enhancements findings from in vitro and in vivo models, along with clinical studies. Comparative studies consistently demonstrate that nano-formulations surpass conventional approaches in enhancing antioxidant defense, stimulating collagen synthesis, and suppressing enzymes associated with skin aging.

**Keywords:** topical system delivery, antioxidant, nanoparticles, anti-aging activity

## Introduction

The integumentary system, recognized as the largest organ of the human body, is continuously exposed to the external environment, serving as the primary protective barrier.<sup>1-3</sup> In addition to its protective function, the skin significantly affects an individual's visual attractiveness.<sup>4</sup> However, persistent exposure to both intrinsic and extrinsic factors renders the skin susceptible to many disorders that can negatively impact overall quality of life.<sup>5</sup> Common dermatological issues, especially in the facial area, include acne, dry skin, irritation, hyperpigmentation, and manifestations of aging.<sup>6,7</sup>

Within dermatology, skin aging continues to be a primary focus.<sup>8</sup> The skin is among the organs whose biological aging process begins at birth.<sup>9</sup> Annually, the rate of collagen and elastin production within the dermis may diminish by approximately 1%, with a substantial increase of up to 30% occurring within the initial five years post-menopause, followed by a gradual decline of 1-2% in the following years. This occurrence has substantial implications for the disruption of connective tissue integrity and significantly contributes to the development of wrinkles.<sup>10,11</sup>

The clinical signs of skin aging, usually first noticeable in adults during their mid-20s to early 30s, are primarily characterized by the appearance of fine lines and wrinkles, dryness, sagging skin, and hyperpigmentation.<sup>12,13</sup> Consequently, it is essential to implement strategies that prevent and mitigate skin aging. In addition to collaborating with dermatological professionals who employ a range of methods, including laser rejuvenation and invasive interventions, an anti-aging regimen is also pursued through the utilization of facial care products or topical therapeutic agents.<sup>10,14</sup>

Most cosmetic formulations are designed for topical application. Unfortunately, conventional delivery methods, including gels, creams, lotions, and emulsions, frequently exhibit poor efficacy due to the skin's inherent barrier, which impedes the diffusion of active chemicals into the deeper layers.<sup>15,16</sup> The effectiveness of these active substances

can be substantially affected by their molecular properties.<sup>17</sup> Peptides demonstrate significant potential as efficacious anti-aging agents, yet they encounter substantial obstacles when administered topically. At physiological pH levels, their ionic characteristics make them vulnerable to degradation by proteolytic enzymes present in the skin. The comparatively high molecular weight of peptides constitutes a considerable obstacle to their transdermal absorption.<sup>18</sup> Like many topical treatments, citrus peel extracts have several drawbacks that reduce their potency. These problems encompass insufficient penetration into the stratum corneum, vulnerability to enzymatic degradation, and general chemical instability.<sup>19</sup> The physicochemical properties of these compounds can pose significant obstacles that reduce their anti-aging efficacy when incorporated into topical formulations.

Nevertheless, research suggests that nanotechnology holds great promise for enhancing the formulation and delivery of cosmetic products through multiple mechanisms.<sup>20</sup> Lipid fluidization and disruption of the stratum corneum by ethanol in ethosomes, high deformability of transfersomes that enables passage through intercellular lipid pathways, and improved skin hydration provided by nanostructured lipid carriers, which facilitates deeper penetration of anti-aging agent.<sup>21–23</sup> By meticulously choosing a suitable carrier system, one can effectively tackle the physicochemical obstacles encountered by active chemicals. This thoughtful selection is crucial for enhancing their ability to penetrate the skin and attain optimal localized therapeutic outcomes.<sup>15</sup> Currently, some relevant commercially available nanocosmetic formulations exhibiting anti-aging properties are available in various dosage forms, such as anti-aging serum (C-Vit Liposomal Serum<sup>®</sup>, Longevity-C Serum<sup>®</sup>), and anti-aging cream (Antiage Response Cream<sup>®</sup>, Dragon's Blood Hyaluronic Night Cream<sup>®</sup>, Filler Intense Cream<sup>®</sup>).<sup>24</sup>

This review presents information about the development of various nanoparticle formulations, including inorganic nanoparticles, lipid-based nanoparticles, lipid vesicular systems, polymeric nanoparticles, and nanoemulsions, as advanced delivery systems designed to enhance the anti-aging efficacy of active compounds in both *in vitro* and *in vivo* studies. It also incorporates a comparative discussion of synthetic and natural anti-aging agents, offering a novel perspective on the advantages and innovative potential of nanotechnology-based delivery approaches over conventional methods.

## Methods

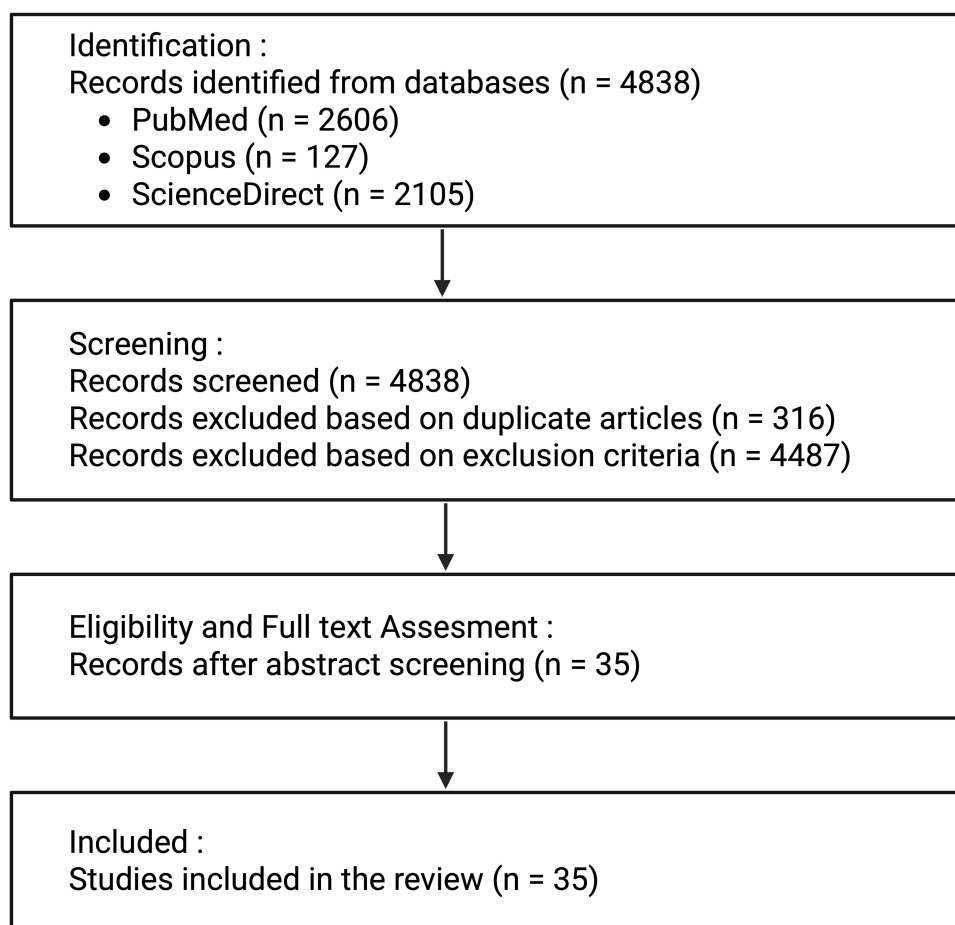
The articles used in this review were published in the past decade. In this review, articles in PubMed, ScienceDirect, and Scopus are reviewed with a primary focus on cosmetic and topical applications of nanoparticle-based formulations. Duplicate records were manually removed, followed by a stepwise screening of titles, abstracts, and full texts to assess their relevance to the study's objectives. Articles were selected based on their investigation of nanoparticle-based formulations designed to improve anti-aging performance.

The inclusion criteria comprised original research articles reporting on the application of nanotechnology to enhance anti-aging efficacy using both natural and synthetic materials. The exclusion criteria included articles that discussed general nanotechnology unrelated to topical dosage form, did not focus on nanoparticle-based approaches for skin anti-aging, and did not compare the anti-aging efficacy of nanoparticle-based formulations with conventional formulations. Review articles and publications written in languages other than Indonesian and English were excluded.

Duplicate articles, titles, abstracts, and full-text screenings were manually sorted. A total of 35 articles, as shown in [Figure 1](#), were selected from the final screening based on the enhancement of the skin anti-aging activity of nanoparticles. Relevant articles were identified by screening titles and abstracts to confirm their eligibility. The full text of the selected articles was then reviewed. Mendeley reference manager was used to compile the articles chosen for this review. The data extracted for this review includes the author's name, year of publication, type of nanoparticles, active compounds (phytochemical or synthetic), anti-aging activity enhancement parameter, and relevant citations, presented in tabular format.

## Nanoparticles as a Promising Delivery System for Improving Anti-Aging Activity

The integumentary system is the body's most extensive organ system, playing an essential role in protection and regulation. The skin, a fundamental component of this system, consists of three main layers: the epidermis, dermis, and hypodermis.<sup>3</sup> The epidermis is the outermost layer and serves as the principal barrier. Located under the epidermis, the dermis is abundant in connective tissue and contains collagen and elastin fibers that confer strength and suppleness to



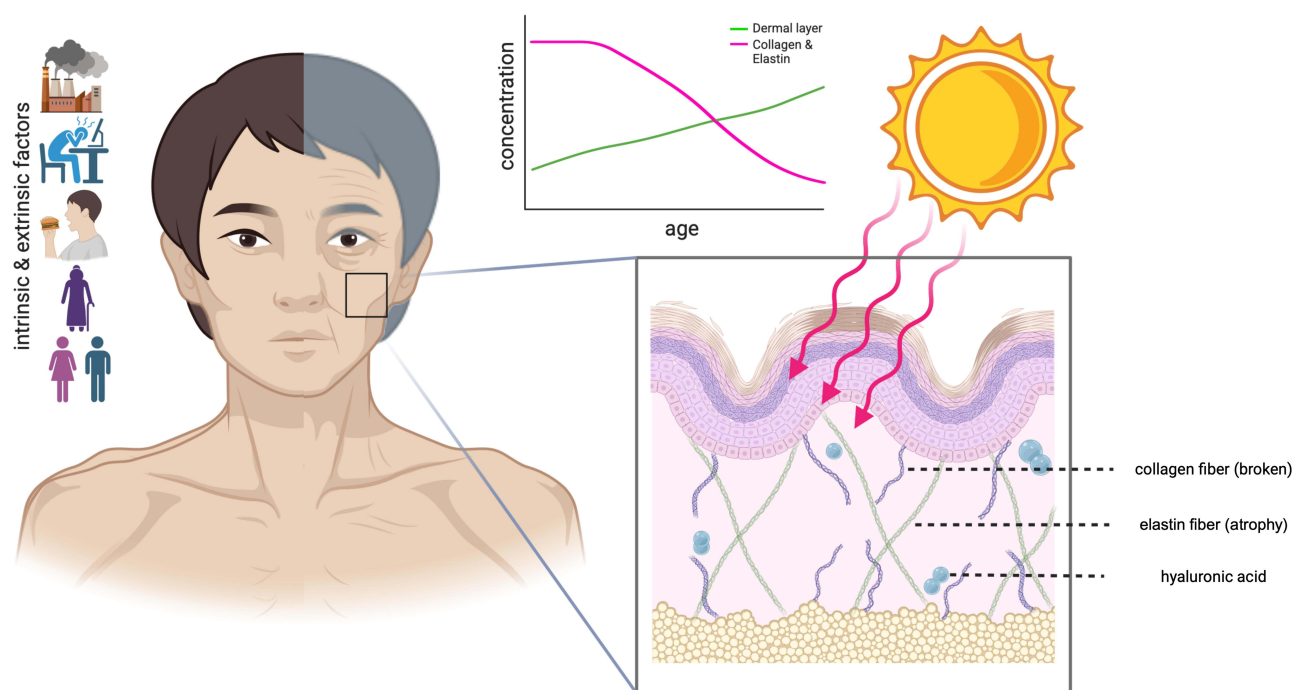
**Figure 1** A flow diagram of the search strategy.

the skin. This layer is also home to fibroblasts, blood vessels, and nerve endings, rendering it essential for the skin's overall functionality and health. The deepest layer, the hypodermis, consists mainly of adipose and connective tissues that provide cushioning for the body and function as an energy storage reservoir.<sup>25-27</sup>

Skin aging is the result of a complex interaction between biological and environmental factors (Figure 2).<sup>28</sup> This occurrence has implications for aesthetic factors and significantly affects the skin's defensive functions.<sup>27,29,30</sup> Intrinsic aging is genetically determined and represents an inevitable physiological process.<sup>30,31</sup> Age is a primary factor in the skin aging process.<sup>32</sup> On the other hand, women often experience a faster decline in skin elasticity. This condition is closely correlated with differences in skin structure and hormones.<sup>11</sup> Genetic differences among ethnicities can also influence the skin's resilience to aging.<sup>33</sup> For instance, Caucasians are more prone to early wrinkles and sagging skin compared to other ethnic groups.<sup>34,35</sup>

A variety of external factors frequently interact with the intrinsic aging process, thereby enhancing the rate of skin aging.<sup>36</sup> As shown in Figure 3, repeated UV exposure can trigger the formation of ROS and initiate inflammatory and oxidative processes, leading to physical changes in the regeneration of the extracellular matrix (ECM). ROS are known to induce the expression of proteolytic enzymes such as matrix metalloproteinases (MMPs), including collagenase, elastase, and hyaluronidase. These enzymes are responsible for the skin aging process as they increase the degradation of collagen, elastin, and hyaluronic acid, resulting in the loss of skin elasticity and the formation of wrinkles.<sup>36-39</sup> The formation of ROS is also influenced by exposure to air pollution and poor nutritional levels.<sup>40,41</sup>

Topical treatments aim to minimize systemic exposure by controlling the penetration of active substances into the stratum corneum (SC). Figure 4 illustrates that the transport of active substances through the SC occurs via three main pathways.<sup>42</sup> The intercellular route is regarded as the primary pathway.<sup>43</sup> In this mechanism, small molecules permeate



**Figure 2** The skin-aging process and its influencing factors.

through the lipid matrix located between corneocytes.<sup>44</sup> The route allows small hydrophobic molecules to penetrate the tight lipid junctions between cells through a winding path, although the permeability of highly lipophilic compounds remains limited.<sup>45</sup> In addition, there are transcellular and transfollicular pathways. The transcellular pathway is represented by diffusion across corneocytes. In contrast, the transfollicular pathway occurs through skin appendages (hair follicles, sebaceous glands, and sweat ducts) and can offer an alternative route for compounds to cross the SC.<sup>46,47</sup> These appendages open onto the skin surface, providing a shortcut in the form of a trans-follicular route that facilitates penetration. The physical structure of hair follicles also acts as a mechanical accumulation space and a temporary storage site for substances.<sup>45,47</sup>

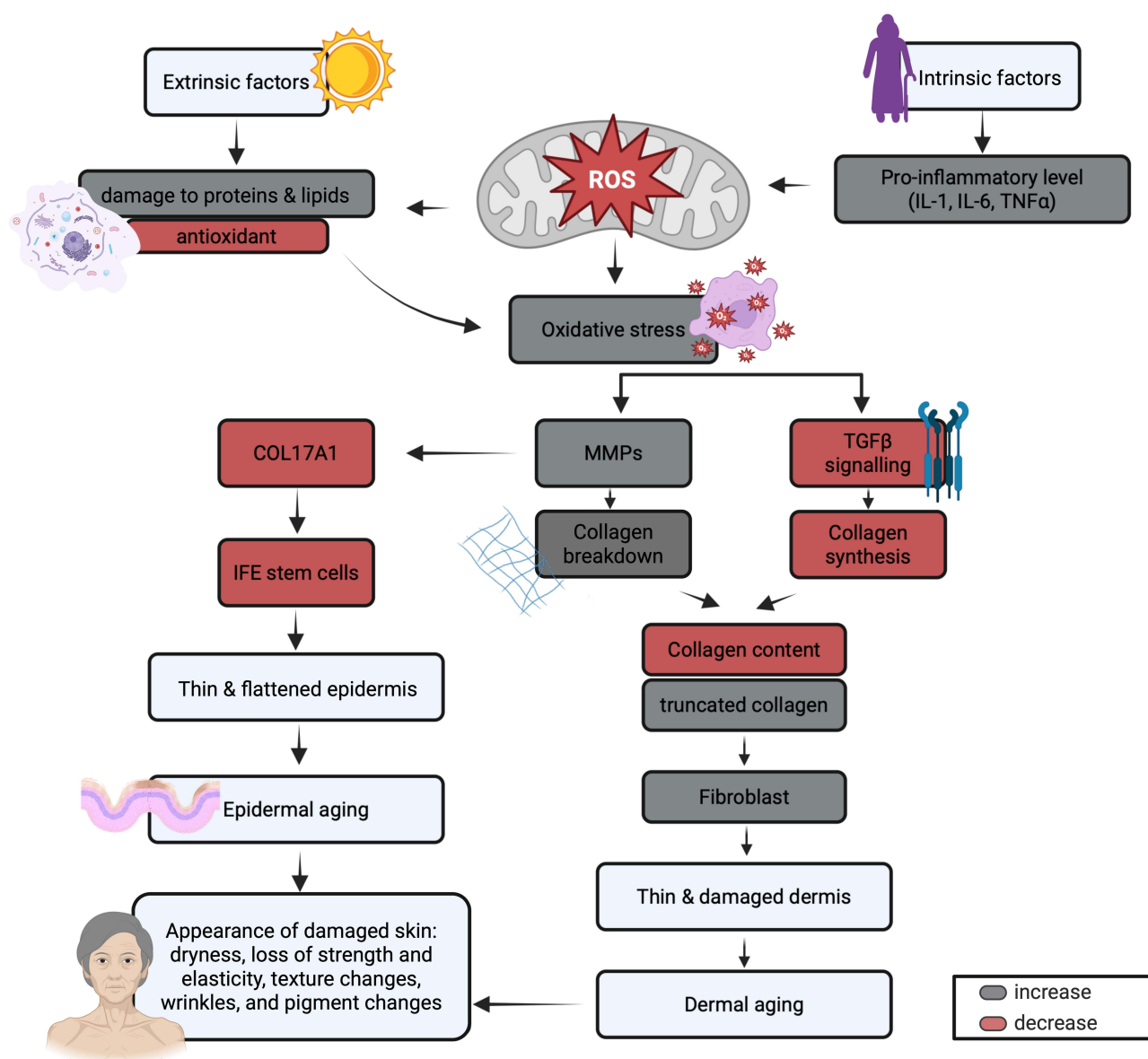
However, the main challenge in developing these products is attaining maximum penetration of active compounds through the outermost layer of the skin.<sup>31</sup> The membrane's extremely selective permeability renders it especially difficult for hydrophilic and large molecules to penetrate. Only compounds possessing particular physicochemical features can traverse this barrier. To address these challenges, novel delivery systems, including nanoparticles, are being explored to improve the penetration of active compounds through topical applications and to augment their pharmacological efficacy.<sup>17</sup>

One of the most recent methodologies in the field of anti-aging involves the application of nanotechnology-based delivery systems, referred to as nanocosmeceuticals (Figure 5).<sup>8</sup> Nanocosmeceuticals are cosmetic products developed by integrating a nanoparticle-based delivery system with active molecules that provide pharmacological benefits.<sup>48</sup> This system works through passive therapeutic targeting, where the active compound is released either naturally or via controlled mechanisms at the designated site using biomarkers that external stimuli can trigger.<sup>49</sup> In this way, the management of various manifestations of skin aging can be carried out more optimally.<sup>8</sup>

Over the past decade, nanoparticles have become a key focus in anti-aging treatment innovations because of their advantages in stabilizing active compounds and improving their delivery into the skin. Several studies on the application of nanoparticles in anti-aging formulations are summarized in Table 1.

## Inorganic Nanoparticles

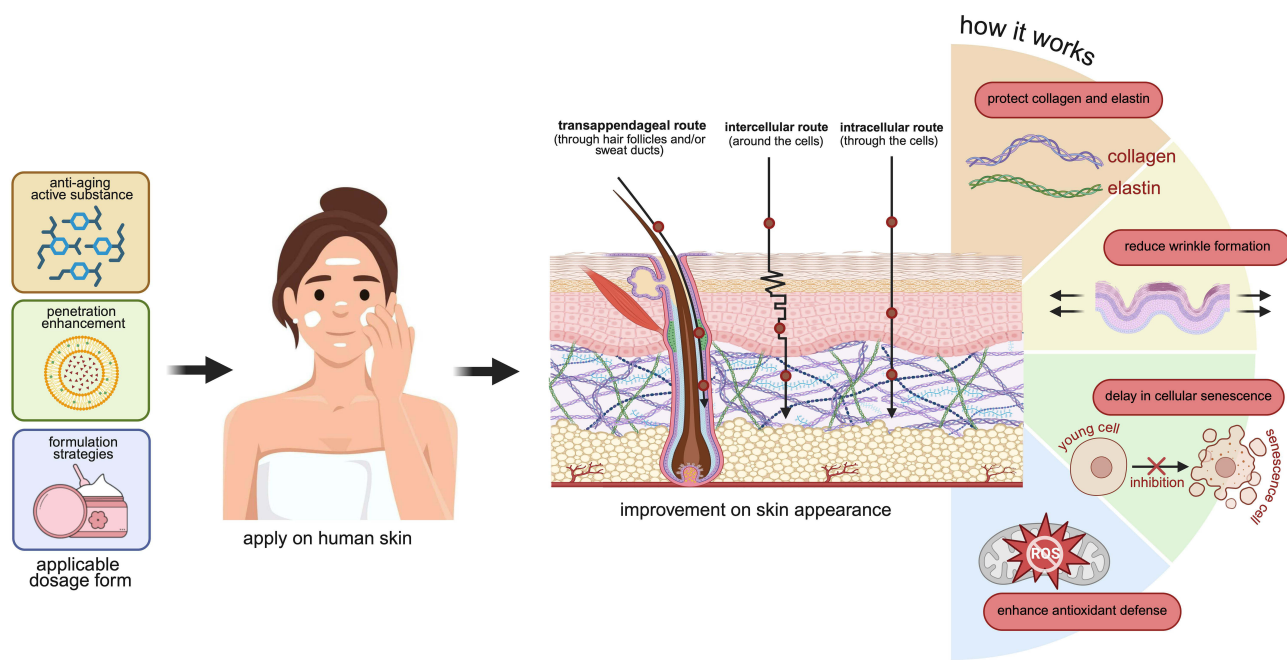
Metal nanoparticles, including silver, gold, and magnesium, possess distinctive chemical and physical properties, especially a substantial surface area to volume ratio.<sup>81</sup> The development of gallic acid-coated gold nanoparticles was



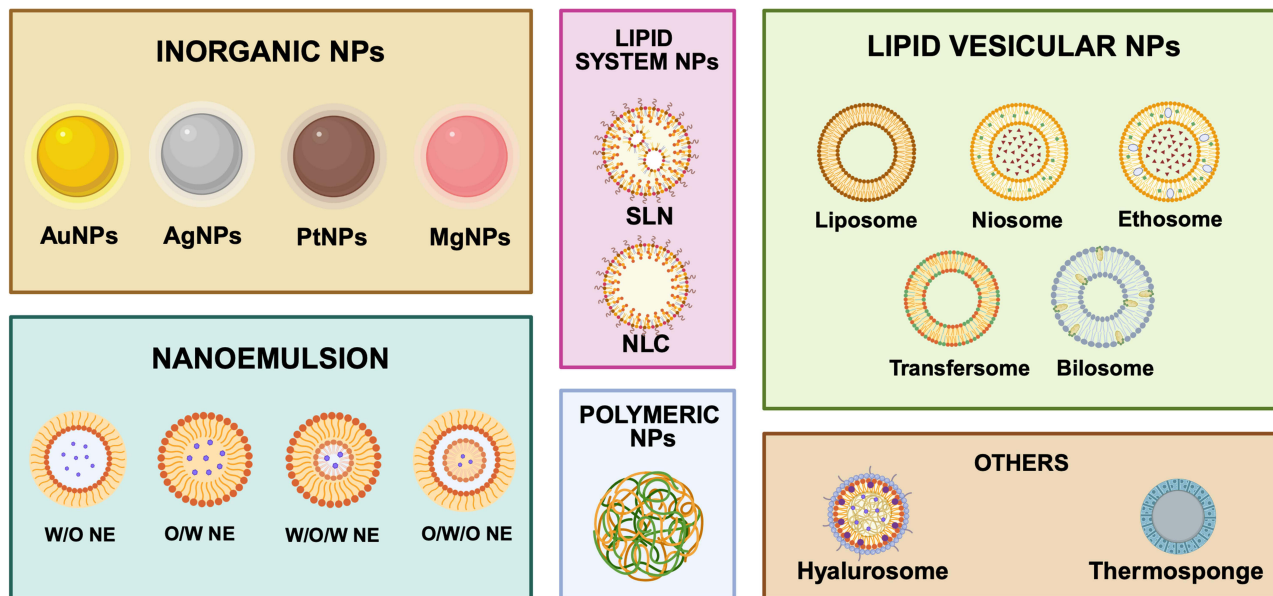
**Figure 3** The changes in epidermal and dermal components during the during the aging process.

carried out by Wu et al, producing AuNP particles measuring <200 nm and able to penetrate the stratum corneum through intercellular, transcellular, and hair follicle pathways. Since GA-AuNPs were found to suppress MMP-1 expression more effectively than pure gallic acid, they may be used as a carrier to increase the anti-aging properties of gallic acid. The phenolic group in gallic acid exhibits the ability to adsorb onto metallic surfaces. This study evaluated the anti-aging potential of GA-AuNPs on human dermal fibroblast cells and MMP-1 expression exposed to high concentrations of glucose. The findings indicated that GA-AuNPs at a concentration of 10 $\mu$ g/mL can reduce MMP-1 expression by obstructing the ROS-mediated ASK 1 pathway.<sup>52</sup>

Numerous herbal medicines have been documented to exhibit pharmacological properties, including anti-aging effects. Although often considered as waste, related research on *Eucalyptus camaldulensis* Dehnh from the Myrtaceae family has proven that the bark contains polyphenol compounds as a wrinkle prevention agent contained in AgNPs with a capacity of 28  $\mu$ g/mL. Polyphenol compounds contain hydroxyl groups that can interact with carboxylate groups in the active area of elastase, so that they can interfere with enzyme activity and play a role in maintaining skin elasticity and preventing wrinkles. Inhibition is also carried out on the collagenase enzyme through bonds between the hydroxyl group



**Figure 4** The main penetration pathways and skin anti-aging mechanisms. Anti-aging active substances formulated in appropriate dosage forms are applied to the skin, where nanoparticle-based strategies enhance penetration. The arrows represent the penetration pathways, including the transappendageal, intercellular, and intracellular routes, enabling deeper skin delivery. This mechanism contributes to improved skin appearance by protecting collagen and elastin, reducing wrinkle formation, delaying cellular senescence, decreasing reactive oxygen species (ROS), and enhancing antioxidant defence.



**Figure 5** Common nano-sized structure used for topical drug delivery.

or benzene ring structure with the active part of the enzyme, causing changes in the conformational structure and reducing collagenase enzyme activity.<sup>53</sup> Leaf extract *Symphytum officinale* loaded in AgNPs has been shown to significantly suppress IL-6 secretion in a dose-dependent manner, which is a cytokine that helps accelerate aging by increasing MMP production.<sup>54</sup>

Platinum-based active compounds are crucial in regulating oxidative stress. Zhang et al showed that platinum nanoparticles (PtNPs) exhibited effective antioxidant activity. The intrinsic antioxidant properties of PtNPs facilitate

**Table 1** Nanoparticles with Enhanced Anti-Aging Activity

No.	Types of Nanoparticles	Active Compounds/Plants/Synthesis	Anti-Aging Activity Enhancement Parameters	Ref
<b>4.1. Inorganic Nanoparticles</b>				
1.	MgO-NPs	Heptacosane & Nonacosane ( <i>Rosa floribunda charisma</i> petal extract)	RcNps showed excellent anti-aging activity enhancement compared to EGCG, through inhibition of collagenase, elastase, hyaluronidase, and tyrosinase enzymes with IC <sub>50</sub> of 8.7 ± 1.66; 82.5 ± 2.93; 191.4 ± 5.68; and 158.6 ± 5.20 µg/mL, respectively.	[50]
2.	PtNPs	Flavonoids ( <i>Nymphaea tetragona</i> flower extract)	Significantly suppress tyrosinase activity and melanin biosynthesis induced by UVB radiation in A375 cells. PtNPs enhance collagen I biosynthesis in HFF-1 cells via the stimulation of the TGF-β/Smad pathway.	[51]
3.	AuNPs	Gallic acid	GA-AuNPs 10 µg/mL was shown to decrease the activation of NFκB and AP-1 which contributed to decreased MMP-1 expression thereby increasing the inhibition of type I collagen degradation.	[52]
4.	AgNPs	Rutin ( <i>Eucalyptus camaldensis</i> Bark Waste Extract)	EBE and EBE-AgNPs showed IC <sub>50</sub> of 0.156 mg/mL ± 0.05 and 2.315 ± 0.07 µg/mL, respectively, and showed significant differences in the percentage of cells in the G2/M phase, the number of apoptotic cells, p53 and p21 expression, and a significant increase in telomerase levels. EBE-AgNPs also showed increased activity in inhibition of elastase, collagenase, and tyrosinase enzymes compared to EBE.	[53]
5.	AgNPs	<i>Symphytum officinale</i>	S-AgNPs significantly inhibited the production of MMP-1 by 47.8% (concentration 10 µg mL <sup>-1</sup> ) and 53.3% (concentration 100 µg mL <sup>-1</sup> ) and IL-6 by 17.8% (concentration 10 µg mL <sup>-1</sup> ) and 54.4% (concentration 100 µg mL <sup>-1</sup> ), as well as increased the expression of type I procollagen.	[54]
<b>4.2. Lipid System Nanoparticles</b>				
1.	SLN	Flavonol Glycoside ( <i>Prunus persica</i> L. var. Florida Prince leaves extract)	PPEE-SLNs exhibited collagenase inhibitory activity (% inhibition 87.03% ± 1.31 and IC <sub>50</sub> 283.92 ± 4.33), tyrosinase inhibitory activity (% inhibition 78.12% ± 1.50 and IC <sub>50</sub> 303.03 ± 4.15), and elastase inhibitory activity (% inhibition 89.02% ± 2.31 and IC <sub>50</sub> 54.01 ± 2.16), which were significantly stronger than those of the extract preparation. Basically in vivo such as mice, this formulation showed significant protective activity against UV exposure and was able to effectively improve wrinkle conditions.	[14]
2.	SLN	Terpenes (Frankincense essential oil from <i>Boswellia papyrifera</i> (Del.)	FO-SLNs enhanced anti-photoaging activity in UVB-exposed mice beyond the effects shown by Vit-A-Palmitate by stimulating Procollagen I synthesis and suppressing the expression of collagen-degrading enzymes MMP1 and MMP9. FO-SLNs show normal histological structure of epidermis and dermis and are able to provide protection against epidermal thickening and collagen damage in the dermis layer.	[55]
3.	SLN	Vitamin A	Vit-A-SLN-gel showed significant improvement in penetration into the skin layers compared to Vit A suspension gel.	[56]
4.	SLN	Epigallocatechin Gallate, Resveratrol dan Myricetin (Vine cane Extract)	SLNs are able to provide protection of active compounds, increase bioavailability, and increase adequate antioxidant activity. Against oxidative stress at a natural compound concentration of 0.81 µg/mL	[57]
5.	NLC	Phenolic compound ( <i>Mangifera indica</i> L. Extract)	The results of the permeation test were proven to be higher compared to M-Ext, resulting in in vivo test results conducted on the human cheek area increasing improvements in the level of volunteer skin erythema, decreasing the TEWL index, decreasing wrinkles by up to 50%, increasing moisture levels and elasticity.	[58]
6.	NLC	Phenolic diteroens, triterpenoids, monoterpenoid ( <i>Rosemary officinalis</i> L.)	In vivo test results showed better activity of RM-LNC than RHE in providing protection against UV rays, restoring antioxidant biochemical status, improving epidermal and dermal histological conditions, and significantly reducing levels of inflammation and wrinkle markers.	[39]

(Continued)

**Table I** (Continued).

No.	Types of Nanoparticles	Active Compounds/Plants/Synthesis	Anti-Aging Activity Enhancement Parameters	Ref
7.	NLC	Phenolic compound ( <i>Citrus sinensis</i> L. peel extract)	The results of the analysis of the use of O-NLC-E for 3 months significantly provided anti-aging benefits through reduced skin erythema, TEWL, melanin, and increased skin elasticity and hydration compared to O-Ext and B-NLC-E.	[19]
8.	NLC and SLN	Hesperidin ( <i>Citrus sinensis</i> L. peel extract)	Based on the analysis software, the NLC system showed superior results compared to SLN in CSPE delivery by assessing the physicochemical test results. Visual display of symptoms photoaging in mice showed significant improvement after topical application of CSPE-NLC cream for 5 weeks. Collagen and SOD levels increased significantly in the CSPE-NLC group, while PGE2, COX2, JNK, MDA, and elastin levels decreased.	[59]
<b>4.3. Lipid Vesicular System Nanoparticles</b>				
1.	Niosome	Gallic acid	Gallic-acid loaded in niosome showed excellent skin anti-aging activity compared to the control group. The test results showed a decrease in melanin ( $55.92 \pm 4.92\%$ compared to control), inhibition of tyrosinase ( $53.18 \pm 3.67\%$ of control), tyrosinase-2 protein ( $24.61 \pm 7.92\%$ of control), and inhibition of matrix metalloproteinase-2 ( $38.46 \pm 1.53\%$ of control) and antioxidant activity ( $87.03 \pm 0.99\%$ cell viability) with superior stability of active compounds.	[60]
2.	Lipniosome	<i>Trigonella foenum-graecum</i> L. extract	The extract exhibited an in vitro collagenation inhibitory effect 2.6 times more potent than vitamin C. Ex vivo skin penetration test showed higher amount of LNF rutin accumulated in the skin compared to standard rutin and extract. LNF was also shown to increase the induction of collagen production in human dermal fibroblast cells compared to the extract, which was 30% (on day 7) and 50% (on day 14)	[61]
3.	Liposome	Polyphenols (Propolis)	CRPP increases cell viability, cell proliferation and energy metabolism of dermal fibroblasts thereby increasing the protective ability of skin tissue against UVB and reducing the expression of MMP-3 and MMP-9.	[62]
4.	Liposome	Morin	Encapsulation of morin in liposomes significantly increased its water solubility compared to morin in free form. LM has been shown to increase inhibition of ROS production, protecting keratinocytes from oxidative stress through decreasing MMP-1 expression by suppressing MAPK pathway activation (p-ERK and p-p38)	[63]
5.	Liposome	Royalactin (Royal Jelly)	The physicochemical characteristics of RJDS and the phytochemical content contained therein were shown to be stable compared to pure royal jelly. RJDS showed significant increases in NHDF cell viability and metabolism as well as collagen expression.	[64]
6.	Liposome, Ethosome, Transethosome	Cycloastragenol	Transetosomes show the best ability to deliver active compounds.	[65]
7.	Ethosome	Polyphenolic compounds (Rosehips extract from <i>dog rose</i> L.)	Significant antioxidant activity in encapsulated formulation compared to unencapsulated extract formulation. Ethosomal has been shown to enhance TPC retention thereby enhancing anti-aging effectiveness.	[66]
8.	Ethosome	Gammaoryzanol	Both in vitro and in vivo studies showed enhanced antioxidant and anti-aging effects relative to the control group. Histopathological analysis of mouse skin revealed enhanced penetration of active compounds, leading to a skin structure nearly indistinguishable from normal following UVA irradiation, in contrast to the state observed with the unloaded ethosomal formulation and GO suspension.	[67]

(Continued)

Table I (Continued).

No.	Types of Nanoparticles	Active Compounds/Plants/Synthesis	Anti-Aging Activity Enhancement Parameters	Ref
9.	Ethosome	Rutin ( <i>Sambucus nigra</i> L.)	Ethosomes loaded with extract showed increased in vitro collagenase inhibitory activity ( $99.67 \pm 0.09\%$ ) and skin compatibility compared to free extract and positive control ( $93.57 \pm 0.61\%$ and $84.36 \pm 0.91\%$ ).	[68]
10.	Ethosome	Epigallocatechin-3-gallate	The inhibition value of collagenase enzyme increased after application of EGCG-loaded ethosome ( $71.9 \pm 1.23\%$ ) and also increased the inhibition value of elastase enzyme ( $75.2\%$ ) compared to EGCG solution ( $68.0 \pm 1.54\%$ and $67.2 \pm 1.60\%$ , respectively).	[69]
11.	Transfersome & Nanoemulsion combined in a gel formulation	<i>Centella asiatica</i> and Bergamot essential oil	Effectively protects and repairs skin histology due to UVB exposure by assessing the decrease in epidermal thickness due to UVB exposure ( $57.3 \mu\text{m}$ ), increase in collagen fiber density ( $55.9\%$ ), increase in SOD expression ( $58.29\%$ ) and decrease in MDA expression ( $48.78\%$ ), as well as increase in type I collagen expression ( $54.07\%$ ) which is better than CA-Non-TF and BEO-NE ( $76.3 \mu\text{m}$ ; $46.4\%$ ; $51.90\%$ ; $54.51\%$ and $48.18\%$ respectively).	[70]
12.	Bilosome	<i>Arthrospira plantensis</i> extract	In vivo testing shows that SPR-BS provides a protective effect against UVB rays and improves anti-aging effectiveness compared to conventional SPR formulations. SPR-BS also produces a lower irritation index.	[71]
<b>4.4. Polymeric Nanoparticles</b>				
1.	Polymeric NPs	Flavonoid & Phenolic compounds (Propolis)	The results of in vitro tests showed that polymeric nanoparticles provided better anti-aging activity compared to the control by increasing collagen production by $19.81\text{--}24.59\%$ and significantly reducing intracellular collagenase activity by $7.46\text{--}31.52\%$ .	[72]
2.	Polymeric NPs	Glycitein, Quercetin, Kaempferol, Ellagic acid ( <i>Toona sinensis</i> leaves extract)	The use of chitosan-alginate showed optimal elastase enzyme inhibition ability with an $\text{IC}_{50}$ of $87.50\%$ .	[73]
3.	Polymeric NPs	Glycyrrhizic acid	GA-PLGA NPs have been shown to increase anti-aging activity compared to GA in conventional preparations by improving the physicochemical profile (large molecular weight and low bioavailability) thereby increasing GA penetration into the skin, thereby increasing GA inhibition of MMP-1.	[74]
4.	Polymeric NPs	Coenzyme-Q10	COQ-NPs have been shown to reduce ROS close to basal values in cells that have been irradiated with UVB, which is due to the ability of nanoparticles (chitosan-rosmarinic acid) to optimally ward off free radicals compared to COQ in free form.	[75]
<b>4.5. Nanoemulsion</b>				
1.	Nanoemulsion	Bakuchiol ( <i>Psoralea corylifolia</i> seeds extract)	Improvement in wrinkle depth comparable to retinol nanoemulsion and discoloration in the skin of 30-year-old respondents was better than retinol nanoemulsion. The results of the toxicity test showed that the bakuchiol nanoemulsion was more biocompatible to normal cells than the nanoemulsion with retinol.	[76]
2.	Nanoemulsion	Gallic acid ( <i>Passiflora quadrangularis</i> Fruit Extract)	Skin evaluation in human volunteers after 60 days of use showed an increase in hydration of up to $19.58\%$ and a significant decrease in wrinkles of $8.56\%$ after 30 days of use.	[77]
3.	Nanoemulsion	Oleic acid, Palmitic acid, Palmitoleic acid, Linoleic acid, Tocopherol dan Tocotrienol (Macadamia Nuts Oil)	Macadamia nut oil nanocream showed better skin anti-aging activity compared to conventional cream after 4 weeks of testing with parameters of increased skin moisture ( $45.83\%$ vs $36.84\%$ ), decreased skin pore size ( $30.16\%$ vs $23.26\%$ ), decreased melanin secretion ( $24.24\%$ vs $23.02\%$ ) and wrinkle improvement ( $28.57\%$ vs $27.18\%$ ).	[78]

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**Table I** (Continued).

No.	Types of Nanoparticles	Active Compounds/Plants/Synthesis	Anti-Aging Activity Enhancement Parameters	Ref
4.	Nanoemulsion	Levan ( <i>Bacillus subtilis natto</i> KBI)	Non-invasive tests showed that nanocream was superior to conventional cream in improving skin moisture (14.9% vs 6.6%), increasing elasticity (1.1% better), skin smoothness (1.7% better), wrinkle volume (2.3% vs 2.1%) and wrinkle area (3.2% vs 2.8%)	[79]
<b>4.6. Others</b>				
1.	Hyalurosomes	Artemin, Hsp40 and Gp4G ( <i>Artemia franciscana</i> extract)	In vivo studies showed an increase in the dermis layer of the skin in male mice and the best increase in collagen production of all formulations was shown by Gp4G formulated in hyalurosomes. This formulation also showed good stability, efficiency and penetration into deeper skin layers.	[80]
2.	Thermosponge nanoparticle	Peptide	RG-TNP is proven to increase skin permeability 40 times greater than RG in free form. Clinical trial results show increased anti-aging effectiveness through anti-wrinkle evaluation, skin roughness, elasticity, skin suppleness, and depigmentation.	[18]

the neutralization of harmful free radicals, protect the skin from oxidative harm, and preserve cellular redox equilibrium, thus aiding in the retardation of the skin-aging process. Moreover, the elevated biocompatibility of PtNPs reduces the risk of allergic reactions or dermal irritation. PtNPs can replicate the actions of natural antioxidant enzymes, including catalase, peroxidase, superoxide dismutase, and glutathione peroxidase, which are implicated in the aging process.<sup>82</sup> PtNPs at a concentration of 1 µg/mL showed increased collagen I production in HFF-1 cells. This investigation reported a size reduction of PtNPs as the concentration of the extract increased. Smaller nanoparticles possess an augmented surface area, thereby increasing the efficiency of nanoparticles in stimulating collagen biosynthesis.

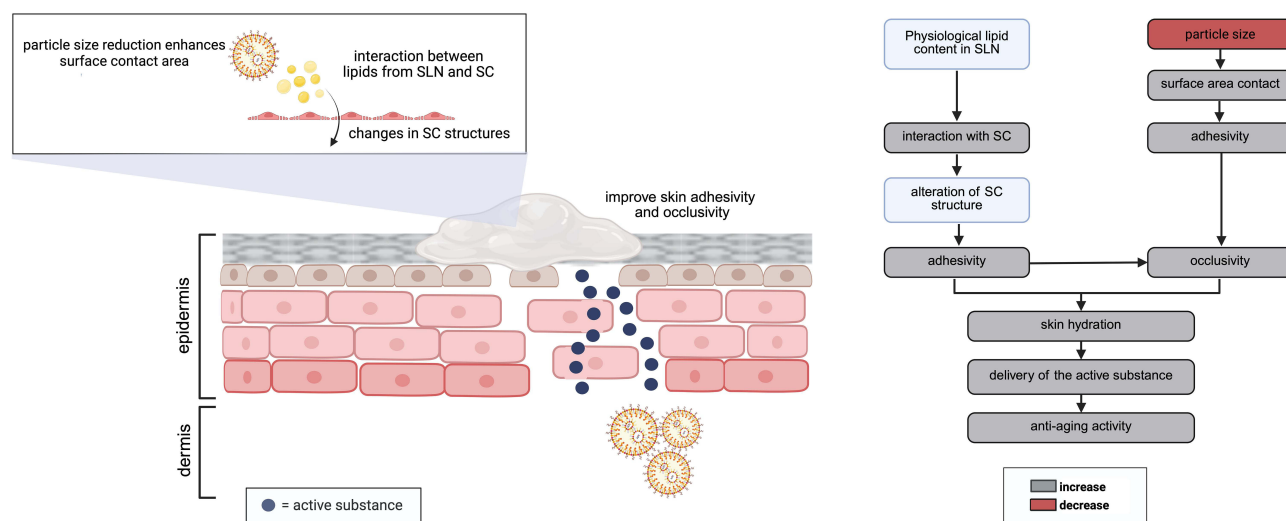
## Lipid System Nanoparticles

### Solid Lipid Nanoparticle (SLN)

There are two sub-pathways involved in the transepidermal route of active drug delivery: the intercellular and transcellular pathways. In general, the mechanism of action of vesicles in modulating skin permeability involves the following: the penetration of intact vesicles into the skin layer, the release of lipid structures by vesicles, direct drug transfer into the skin through lipid contact, and delivery through hair follicles and perspiration glands.<sup>83,84</sup> The mechanisms involved are highly dependent on the formulation, especially the composition and size of the particles.<sup>15</sup>

Solid lipid nanoparticles (SLN) are nano-sized solid delivery systems that can carry both hydrophobic and hydrophilic compounds. SLN has high encapsulation efficiency, good solubility, stability, and allows controlled release at the target site, thereby increasing bioavailability and pharmacological activity.<sup>85,86</sup> Olibanum, derived from *Boswellia*, contains essential oils. The SLN formulation enhances the solubility of frankincense oil (FO), facilitating skin permeation and bioavailability in anti-aging treatments. The outcomes of anti-collagenase and anti-elastase assays demonstrated greater anti-photoaging effects by suppressing wrinkle formation and improving skin structure. The study revealed better anti-photoaging activity of FO-SLN compared to both FO and Vitamin A. The optimal formulation was attained by optimizing particle size, zeta potential, and entrapment efficiency by nanotechnology initiatives.<sup>55</sup>

The enhancement of anti-aging activity is attributed to the penetration ability of SLN, which is explained as a result of three main mechanisms: adhesion, occlusivity, and skin hydration. As shown in [Figure 6](#), the adhesion mechanism is related to the physiological lipid content in SLN, which allows interaction with the stratum corneum layer, triggering changes in the lipid structure of the stratum corneum layer and supporting increased penetration of active compounds.<sup>87</sup> The small size of nanoparticles greatly enhances adherence and increases the contact area with the skin surface.<sup>88</sup> Occlusivity depends on lipid concentration, sample volume and particle size. The combination of these properties plays a role in preventing water loss through transepidermal and opening gaps between corneocytes, thus supporting the penetration of anti-aging agents into deeper skin layers and optimal anti-aging activity is obtained.<sup>83</sup>



**Figure 6** The possible mechanism of enhanced skin absorption and increased anti-aging activity by Solid Lipid Nanoparticles.

A comparative study was conducted between the formulation of SLN gel containing Vitamin A and conventional Vitamin A gel suspension. The results of in vitro assessments indicated that the Vit-A-SLN gel exhibited superior skin penetration ability than the Vitamin A suspension gel. The Franz diffusion assay showed a substantial enhancement in penetration into the skin layers, indicating a more optimal localized effect, thereby enhancing the potential for anti-aging activity.<sup>56</sup>

### Nanostructured Lipid Carrier

Nanostructured Lipid Carrier (NLC) represents the subsequent evolution of solid lipid nanoparticles (SLN), consisting of a lipid matrix stabilized by surfactants, with its production process influenced by the type and ratio of lipid and surfactant used.<sup>89</sup> Because it is lipophilic, NLC can penetrate the epidermis without additional modification.<sup>90</sup> NLC can address the limitations of SLN, including inadequate loading capacity resulting from the crystallization process and stability issues during storage.<sup>91</sup> NLC is also an alternative carrier system for liposomes and emulsions.<sup>92</sup>

In the study by Salem et al, Corriander Essential Oil formulated in the NLC system (CEO-NLC) was more optimal than SLN. The lipid phase used in SLN consisted only of *cocoa butter*. In contrast, the NLC lipid phase consists of a combination of *cocoa butter* and olive oil, yielded a physicochemical profile with a measure of the lipid system, PDI (*polydispersity index*), and better zeta potential compared to SLN. The lower particle size ( $175.24 \pm 24.25$  nm) and PDI value ( $0.245 \pm 0.011$ ) of CEO-NLC indicate a homogeneous size distribution, while the higher zeta potential value ( $-27.47 \pm 3.78$ ) in CEO-NLC.<sup>93</sup>

The zeta potential value defines the charge on the particle surface and is essential for the stability of the nanoparticle system. A high absolute zeta potential value signifies a robust repulsive force among particles, thereby reducing the risk of aggregation.<sup>93</sup> A negative zeta potential value indicates that the active compound is not only adsorbed on the surface but also stored in the lipid core. The negatively charged particle surface is biocompatible and low in toxicity, allowing interaction with the skin and effective release of the content.<sup>57</sup>

Extract from skin and seeds of *Mangifera indica* L. (M-ext) has potent antioxidant and anti-aging effects. Still, its effectiveness is not optimal due to the limitations of the skin in absorbing the compound. Ex vivo studies through mouse skin and in vivo studies on the cheeks of human volunteers for three months were conducted with a vehicle as a comparator, showing that the NLC can increase the effectiveness of antioxidants and has a good safety profile.<sup>58</sup>

The same test method was also carried out in the study by Khan et al to evaluate the ability of *Citrus sinensis* L. peel extract against oxidative stress and skin aging. The NLC formulation enhances the penetration of active compounds, mitigates the adverse effects of high doses, and significantly improves anti-aging activity.<sup>19</sup> The same study also demonstrated that the *Citrus sinensis* L. peel extract in the NLC formulation, when applied topically for 5 weeks,

showed significant improvements *in vivo*. Anti-aging activity was assessed through significantly increased collagen and SOD levels, while PGE2, COX2, MDA, and elastin levels decreased.<sup>59</sup>

### Lipid Nanocapsules

A class of core-shell nanoparticles, referred to as LNCs, has been developed specifically for drug encapsulation. In these structures, lipid-derived surfactants form the outer shell while the inner core is composed of oil-based substances. Their hydrophilic outer surface can be engineered to enhance targeted drug delivery. The incorporation of polyethylene glycol (PEG) into the lipid layer of the nanoparticles can produce a lipid-based system in which the oily core is effectively enclosed within a protective barrier.<sup>94,95</sup>

In the study by Ibrahim et al, rosemary hexane extract was successfully incorporated into LNCs and further formulated into a mucoadhesive topical gel. The *in vivo* evaluation using a UVB-irradiated rat model demonstrated that incorporating rosemary extract into LNCs (RM-LNC) substantially enhanced their protective and restorative activities against photoaging. Treatment with RM-LNC gel (4% and 10%) markedly restored cutaneous antioxidant status and effectively reduced inflammatory biomarkers. Markers of extracellular matrix degradation, such as MMP-1, GM-CSF, elastase, and neprilysin, were also significantly lowered following RM-LNC gel treatment, indicating a protective effect on dermal collagen and elastin integrity. Histopathological examination further supported these biochemical findings. Rats treated with the 10% RM-LNC gel exhibited more normalized epidermal characteristics, minimal inflammation, and improved collagen organization, characteristics closely resembling those of healthy and non-irradiated skin.<sup>39</sup>

### Lipid Vesicular System

#### Niosome

Niosomes are small, stable, and effective vesicles, either unilamellar or multilamellar, that can deliver drugs to specific targets because they can encapsulate both hydrophilic and hydrophobic compounds.<sup>96</sup> With high stability, niosomes have the potential as drug carriers, increasing the stability and penetration of active substances through the skin, making them suitable for use in semisolid formulations.<sup>97,98</sup>

In another study, gallic acid was formulated into a niosome system. The results showed optimal skin anti-aging activity, including melanin suppression effects through tyrosinase inhibition, antioxidant activity, and MMP-2 inhibition.<sup>60</sup> A comparative study of niosome emulgel was also conducted against emulgel containing free active compounds. Based on the evaluation of physicochemical data, it can be concluded that the emulgel formulation enriched with GSH-loaded niosomes can be considered as a new nanocosmeceutical candidate with the potential to improve user comfort. In addition, the niosome-based delivery system also has the potential to increase *in vivo* effectiveness.<sup>48</sup>

Vesicular components are abundant on the surface of the stratum corneum. Still, their number decreases in the inner skin, indicating the possibility that niosomes have fused and mixed with natural stratum corneum lipids. Penetration of niosomes into the skin may increase due to changes in thermodynamic activity or the influence of released particles on the protective function of the stratum corneum.<sup>99</sup>

#### Liposome

Liposomes are spherical vesicles formed by a phospholipid bilayer that can encapsulate one or more liquid compartments. Liposomes have advantages due to their good biocompatibility and safety profile. In addition, liposomes can form a lipid layer that moisturizes the skin, increases the concentration of active compounds in the epidermis and dermis, and restricts transdermal absorption, thereby minimizing skin irritation.<sup>49,63</sup>

Liposome is an alternative carrier type that has been studied for the encapsulation of propolis. Spanidi et al developed a liposomal system encapsulating propolis, demonstrating excellent efficacy as a topical anti-aging treatment. Propolis is hydrophobic, complicating its formulation for topical application. Propolis contains flavonoids and phenolic acids as its primary polyphenolic constituents. The results of this study demonstrated elevated polyphenol encapsulation efficiency, commendable physicochemical stability, and a regulated release rate.<sup>62</sup>

Apart from propolis, another bee product that has been widely used is royal jelly, which is a thick, slightly acidic, glandular secretion produced by the bee species, *Apis mellifera* L. Polyphenol and 10-HDA components in royal jelly

have been shown to have anti-aging activity through inhibition of metalloproteinase synthesis and increased collagen synthesis. Royal jelly is unstable to temperature and light. High temperatures can cause discoloration and degradation of components due to Maillard, enzymatic, and lipid-protein reactions, while light will cause oxidation.<sup>64</sup>

The study by Spanidi et al utilized the ability of cyclodextrin to encapsulate polyphenols and increase skin penetration, as well as the ability of liposomes to encapsulate components for local delivery and controlled release. The test results proved that cyclodextrin-liposome encapsulation was able to improve stability, physicochemical characteristics, retention of polyphenols, and 10-HDA. These vesicles are able to deliver active compounds that penetrate into the deep epidermis, regulate collagen production and deposition, and improve fibroblast function.<sup>64</sup> The use of cyclodextrin is able to convert hydrophobic molecules into more hydrophilic cyclodextrin complexes, thus allowing the use of a more expansive aqueous core space of liposomes compared to lipid bilayers. In addition, the use of cyclodextrin can also affect the stability and size of liposomes.<sup>100</sup>

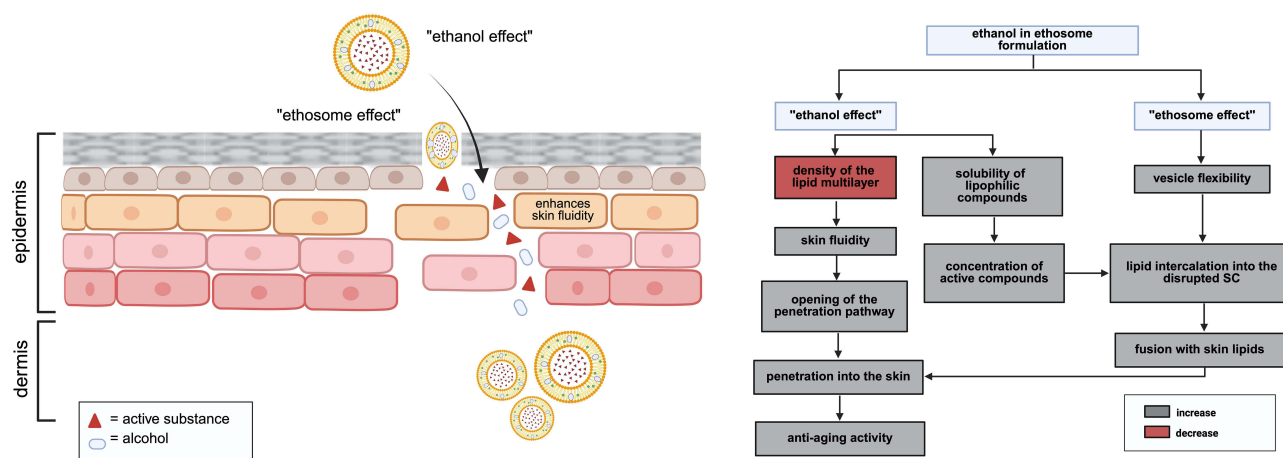
Morin, a polyphenol compound, exhibits a variety of biological activities that can be used to treat various dermatological issues, including anti-aging. Morin has poor solubility in water, which hampers its bioavailability and absorption profile. The liposomal formulation enhances the penetration of morin over the stratum corneum and facilitates its deposition. In the Tra et al study, explained that liposomal flavonoids not only offer a better safety profile but also stabilize the compound and prolong its effectiveness.<sup>63</sup>

Morin formulated in liposomes enhances its solubility by almost 500-fold and successfully penetrates the barrier, while the free form of morin cannot pass through the stratum corneum. Significantly reduces the expression of MAPK proteins, such as p-ERK and p-p38, which then leads to the suppression of MMP-1 expression. MMPs secreted by keratinocytes are responsible for the breakdown and fragmentation of collagen fibers. The penetration of morin is also significantly increased when the outer layer of the lipid vesicle is rendered more pliable, facilitating its ability to permeate the stratum corneum and hair follicles effectively. Liposomal vesicles are deposited in the epidermis and dermis without entering the receptor fluid, thus suppressing the safety profile of liposomes that do not attain the systemic circulation.<sup>63</sup>

## Ethosome

Ethosome is a third-generation vesicle, characterized by its softness and flexibility, composed of phospholipids, ethanol, and water, which is capable of sustained drug release at the target site.<sup>101,102</sup> The study by Mota et al compared the collagenase inhibitory activity of the active compound naringenin extract. *Sambucus nigra* L. in vitro. The collagenase inhibition activity values of free extract, positive control, and ethosome containing extract were  $93.57 \pm 0.61\%$ ,  $84.36 \pm 0.91\%$ , and  $99.67 \pm 0.09\%$ , respectively.<sup>68</sup> Gamma-oryzanol-loaded ethosome incorporated into hydrogel also showed higher in vitro antioxidant activity on rat skin compared to the conventional formulation.<sup>67</sup>

The enhancement of anti-aging activity through ethosome application is linked to its efficacy as a penetration enhancer, attributed to ethanol's role in imparting flexibility to the vesicles, loosening skin phospholipids, and facilitating the fusion of vesicles with skin lipids (Figure 7). This process promotes targeted penetration through the stratum corneum



**Figure 7** The possible mechanism of enhanced skin absorption and increased anti-aging activity by Ethosome.

to deeper layers, in contrast to liposomes. The inclusion of phospholipids in the ethosome is a supporting factor by providing higher hydration to the skin, hence facilitating the penetration of active substances.<sup>66,69,103</sup>

Ethosome has been reported to be able to retain active substances within the skin for an extended duration and facilitate their penetration into deeper skin layers, hence optimizing pharmacological efficacy. A study by Yucel et al examined the effectiveness of EGCG, which successfully penetrated cells, in inhibiting collagenase and elastase enzymes. The inhibitory efficacy of both enzymes by the nanoformulation exceeded that of the solution form. EGCG is a major component in green tea that plays an effective role in anti-wrinkle care through the MMP inhibition mechanism.<sup>69</sup>

## Polymeric Nanoparticles

Polymer-based nanoparticles are considered to have higher efficiency in delivering active compounds. In general, polymer nanoparticles are divided into two main types, namely nanospheres, where the active substance is evenly distributed and nanocapsules that encapsulate the active compound in a hollow core coated by a polymer membrane. The advantages of this system include high solubility in water, tiny particle size, good physical stability, long shelf life, and non-toxic properties.<sup>49</sup>

Natural polymer nanoparticles provide the potential to serve as a delivery mechanism, enhancing pharmacological activity and stability within the cosmetic domain. Lestari et al conducted a development technique for chitosan-alginate and chitosan-pectin nanoparticles utilizing the ionic gelation method. This study evaluated the *in vitro* anti-aging effects of the elastase enzyme and showed a significant level of inhibition. Natural polymers, like chitosan, alginate, and pectin, serve an essential role as carriers. The primary advantage resides in its hydrophilic characteristics, facilitating optimal water interaction and enabling the gradual and regulated release of active compounds. Chitosan can increase solubility and bioavailability, while alginate and pectin can control the release rate.<sup>73,104</sup>

In line with these advances in polymeric nanoparticles, An et al further developed a nanosphere system using poloxamer (PN&) as a polymer for propolis to overcome its poor solubility and enhance its dermal activity compared with its non-nano formulation (PN1). This was evident in the *in vitro* assays, where PN1 did not produce a significant increase in intracellular collagen levels and achieved only a modest 7.25% reduction in MMP-1 activity at a concentration 0.0063%. In contrast with PN7, which elevates intracellular collagen production by 19.81–24.59% at concentrations of 0.016–0.063% and reduces MMP-1 activity by 7.46–31.52%. By clinical results, propolis nanospheres produced the most significant improvement, including a 28% increase in skin moisture, as well as more pronounced reductions in wrinkles and enhancements in elasticity, firmness, and density by improving the solubility profile, release pattern, release pattern, and distribution of active compounds.<sup>72</sup>

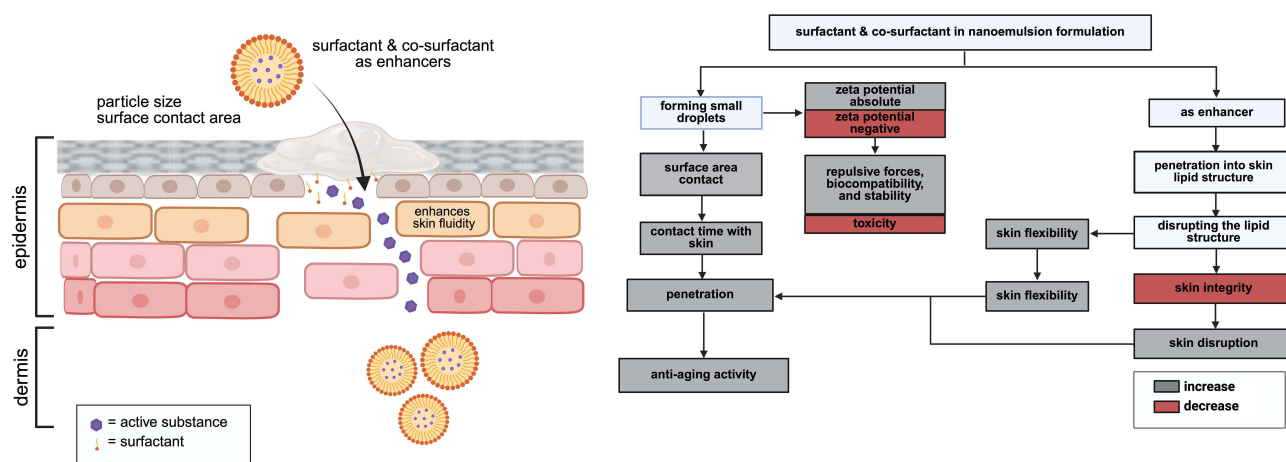
## Nanoemulsion

Nanoemulsion is a stable dispersion in nano size involving two immiscible phases, with the role of surfactants to maintain its stability. Nanoemulsion has promising potential as an effective cosmeceutical because of its ability to dissolve hydrophobic substances, reduce side effects, and its flexibility in the modification process.<sup>105–107</sup>

Lewinska et al successfully developed an oil-in-water nanoemulsion for the topical delivery of bakuchiol that has good skin biocompatibility, increased skin permeability, and low toxicity levels. The fluorescence of the active compound increased at a depth of 80  $\mu\text{m}$  and then expanded to 140  $\mu\text{m}$  after 7 hours with a decrease in intensity. This indicates that the carrier gradually spreads deeper and remains stable, allowing the transport of bakuchiol in its intact form. The results of *in vivo* studies showed better anti-aging effects compared to conventional retinol preparations, such as wrinkle reduction and improvement of skin condition.<sup>76</sup>

Nanoemulsion consists of oil, surfactant, and cosurfactant. Each component has a responsibility to achieve optimal formulation (Figure 8). Oil functions as the core of the droplets and antioxidant compounds will be trapped in the core. Surfactant regulates the size of the droplets and plays a role in increasing skin penetration in topical formulations because it can dissolve lipids in the stratum corneum, which is the main barrier on the skin. At the same time, cosurfactant helps surfactant to stabilize the droplets.<sup>108</sup>

Some essential oils are known to have low water solubility and high volatility, so their anti-aging activity tends to decrease when formulated in commercial products (Samanci et al, 2023). A study by Hanum et al revealed that a topical



**Figure 8** The possible mechanism of enhanced skin absorption and increased anti-aging activity by Nanoemulsion.

nanoemulsion of macadamia nut oil had superior anti-aging activity, especially in terms of moisture, pore size, melanin content, and skin wrinkles when compared to regular emulsion formulation.<sup>78</sup>

The use of active compounds from bacteria in anti-aging treatments has been reported. Levan is a fructose polymer synthesized by *Bacillus subtilis*, which has a high molecular weight, so it is formulated in a nano system. In this study, a non-invasive evaluation was performed, showing that the cream with nanoemulsion increases anti-aging activity. The nanoemulsion preparation was superior when compared to the conventional cream. Nanoemulsion increased skin moisture (6.6% higher), elasticity (1.1% higher), and better skin smoothing effect (1.7% superior), reduced the volume and area of wrinkles more effectively (2.3% and 3.2%, respectively), and decreased the depth of wrinkles (decreased by 5.2%).<sup>79</sup>

## Others

Some essential oils are known to have low water solubility and high volatility, so their anti-aging activity tends to decrease when formulated in commercial products.<sup>108</sup> To increase the effectiveness of anti-aging, formulations such as a combination of transfersome and nanoemulsion in the form of a gel preparation as a drug delivery system that combines several active compounds from Bergamot essential oil and extracts have been developed. *Gotu Kola*. Study results in vivo showed that the combination gel preparation was able to significantly prevent erythema, wrinkles, and inhibit histological damage such as epidermal hyperplasia, degradation of collagen and elastin fibers. This combination was also able to reduce oxidative stress by increasing SOD activity, reducing MDA, inhibiting inflammatory cytokines, and increasing type I collagen expression.<sup>70</sup>

Zewail et al conducted a study on the development of a bilosome formulation containing biologically active ingredients. Spirulina, a microalgae from the group *cyanobacteria*, has a high phytochemical content as an antioxidant. The spirulina-loaded bilosomal formulation (SPR-BS) is designed by combining lecithin and *bile salt* to overcome skin penetration barriers. The results of biochemical analysis and histopathological examination showed that the anti-aging effect of SPR-BS was superior to that of conventional spirulina.<sup>71</sup> *Bile salt* has an excellent ability to dissolve lipophilic compounds by forming interactions with cell membranes, thereby increasing the absorption process of encapsulated drugs. *Bile salt* can increase the bioavailability and therapeutic effectiveness of active compounds in bilosomes when combined with lipid membranes. *Bile salt* also plays a vital role in improving the stability of bisomes through the formation of bilayer structures with phospholipids.<sup>109</sup>

Hyalurosomes, which contain active components from *Artemia franciscana*, have been successfully developed as an anti-aging delivery. Study in vivo using coloring H&E and Masson's trichrome showed an increase in the dermis layer and collagen production in the skin of male mice compared to the control group. In the test, hyaluronic acid in the hyalurosomes formulation can activate the TGF- $\beta$ /Smad signaling pathway in fibroblast cells, which promotes the

production of type I collagen and elastic fibers in the skin. The relationship between collagen and fibroblast cell proliferation is determined by the primary function of the cells in producing collagen protein.<sup>80,110</sup>

Peptides still face some limitations when applied topically. Peptides are easily degraded and the molecular mass of peptides is relatively large. To overcome these limitations, Lee et al's research developed peptides through the use of solvent-free thermosponge nanoparticles. Evaluation of skin penetration ability was carried out by in vitro using fluorescence microscopy, which showed that the membrane applied with a thermosponge displayed higher signal intensity compared to the free peptide. In addition, free peptide was only found in the stratum corneum, while Peptide-TNP penetrated deeper into the epidermis. In clinical trials, Peptide-TNP was shown to provide significant anti-aging effects on wrinkles around the eyes, accompanied by increased skin elasticity, reduced pigmentation, and skin tightening.<sup>18</sup>

## Conclusion

Nanotechnology-based delivery systems offer notable advantages in enhancing the stability, skin penetration, and biological activity of anti-aging agents from both natural and synthetic sources. Across available studies, nano-formulations consistently demonstrate superior outcomes to conventional preparations, including more potent antioxidant effects, improved collagen synthesis, and reduced activity of aging-related enzymes. Although no single nanoparticle system can be deemed universally optimal, given the strong influence of each substance's characteristics, specific trends are evident. Lipid-based nanocarriers, particularly nanoemulsions, liposomes, and nanostructured lipid carriers, show the most consistent improvements over non-nano forms and exhibit favorable properties in terms of biocompatibility, formulation flexibility, and manufacturing practicality.

Nonetheless, regulatory challenges, long-term safety requirements, and the need for reliable industrial scale-up remain key barriers to the broader adoption of nanoparticle-based technologies. Addressing these issues will be essential to advancing their integration into effective and market-ready anti-aging skincare products.

## Acknowledgments

We would like to thank the Indonesia Endowment Fund for Education (LPDP) under the Ministry of Finance, Republic of Indonesia, for its scholarship funding support and the APC was funded by Padjadjaran University.

## Disclosure

The authors report no conflicts of interest in this work.

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