

Enhancing the Bioavailability of Noni Fruit (*Morinda citrifolia* L.) Through Nanotechnology as a Topical Anti-Aging Formulation

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ABSTRACT

Premature aging reduces collagen production and activates MAPK and MMPs pathways. Continuous use of retinol may cause adverse effects; therefore, natural ingredients are recommended as alternative therapies. Noni fruit (*Morinda citrifolia* L.) has potential anti-aging properties; however, its polyphenolic compounds are sensitive and exhibit limited skin absorption. The application of nanotechnology may address these bioavailability challenges. This review aimed to identify, analyze, and provide evidence regarding the enhancement of bioavailability of Indonesian herbal plants through nanotechnology-based topical formulations for managing skin aging. A systematic literature review was conducted by searching accredited national and international journals indexed in Google Scholar using the keywords "Aging," "Morinda citrifolia L.," and "Nano" from 2014 to 2024. From 2,950 identified articles, 80 met the inclusion criteria. The findings indicate that noni fruit contains diverse bioactive compounds with significant anti-aging potential. It is rich in vitamin C, flavonoids, and phenolic compounds. Nanoparticle formulations of noni fruit enhance its anti-aging efficacy through multiple mechanisms and improve the permeation of active compounds into the skin. In conclusion, noni fruit demonstrates strong potential as a topical anti-aging agent, and its limitations can be overcome through nanoparticle-based technology, thereby increasing its therapeutic, functional, and economic value.

Keywords: aging; *Morinda citrifolia* L.; nanotechnology

INTRODUCTION

Premature skin aging is a complex biological process influenced by a combination of intrinsic (age-related) and extrinsic factors (UV exposure, air pollution, alcohol consumption, and poor nutrition). Approximately 80% of facial skin aging is attributed to UV radiation exposure. Structural and functional skin alterations occur due to collagen degradation, the primary component of the skin extracellular matrix, which accompanies photoaging [1–4]. Collagen reduction leads to significant changes in dermal connective tissue, resulting in wrinkles, roughness, and skin laxity [5]. Intracellular reactive oxygen species (ROS) contribute to premature skin aging by activating the mitogen-activated protein kinase (MAPK) pathway, which induces the transcription factor activator protein-1 (AP-1) and subsequently regulates matrix metalloproteinases (MMPs), particularly MMP-1 (collagenase type-1), MMP-3 (stromelysin-1), and MMP-9 (gelatinase-B). These enzymes degrade collagen types I, III, and IV. Inhibition of MMP activity is therefore a key strategy in preventing photoaging [6–8]. Retinol is one of the compounds known to prevent skin aging; however, prolonged use may cause adverse effects such as erythema, pruritus, burning sensations, and skin peeling [9]. Consequently, natural ingredients are strongly recommended as alternative therapeutic options.

Indonesia is rich in medicinal plants with potential anti-aging properties, including noni fruit (*Morinda citrifolia* L.). This plant contains bioactive compounds such as ascorbic acid, terpenoids, alkaloids, beta-sitosterol, scopoletin, carotene, and polyphenols (flavonoids, flavone glycosides, and rutin), which exhibit antioxidant, anti-aging, antibacterial, antiviral, antifungal, antitumor, analgesic, hypotensive, anti-inflammatory, and immune-boosting activities [10–14]. These compounds are found in the fruit, roots, stems, and leaves [15]. However, most natural products contain polyphenols that are highly sensitive to processing, distribution, storage conditions, alkaline pH, and are poorly water-soluble, leading to limited absorption. Nanoparticle technology may offer a solution to these bioavailability challenges. Nanoparticles possess a large surface area, enhancing their effectiveness and facilitating penetration through the skin lipid bilayer [16]. Nanocosmetics derived from Indonesian herbal plants are expected to help address premature skin aging, particularly in the context of increasing environmental pollutants and free radicals that damage skin structure.

The protective mechanisms of noni fruit compounds against premature skin aging generally involve reducing ROS reactivity, inhibiting oxidative processes, suppressing MMP activity, and increasing collagen synthesis. These effects are attributed to phenolic, flavonoid, and triterpenoid compounds. Both phenolics and flavonoids contain phenolic rings with hydroxyl substituents that inhibit ROS, reduce metal ions, and modulate protein phosphorylation associated with enzyme inhibition and lipid peroxidation [5].

Nanotechnology and nanodelivery systems represent highly innovative advancements utilizing particles at the nanoscale (1–100 nm) [17]. The integration of nanotechnology into pharmaceutical sciences, particularly in cosmetics, has progressed rapidly. The United States FDA defines cosmetics as formulations intended for cleansing, beautifying, promoting attractiveness, or altering appearance without affecting the body's structure or function [18, 19]. The modification of cosmetic particles using nanotechnology has significant potential, leading to the development of nanocosmetics. Advantages of nanotechnology-based cosmetics include prolonged action, enhanced bioavailability, and improved aesthetic appeal. The small particle size and high surface-to-volume ratio make nanoparticles effective excipients in cosmetic formulations. Furthermore, the incorporation of nanoparticles does not alter the fundamental properties of cosmetics but enhances their appearance, coverage, and adhesion to the skin. Nanocosmetics are widely formulated as anti-aging products and are claimed to stimulate cell growth, protect skin structure, and improve hydration, thereby increasing their cosmetic effectiveness. However, limitations remain regarding stability, toxicity, and production costs. The small size of nanocosmetics increases surface area, and the positive surface charge of nanoparticles enhances biological interactions within the microenvironment, as bioavailability is more strongly influenced by dose than by the physicochemical properties of the active compound [20]. To date, no systematic review has specifically examined the enhancement of bioavailability of noni fruit compounds through nanotechnology in topical formulations for managing premature skin aging.

This review aims to identify, analyze, and provide comprehensive information regarding the enhancement of bioavailability of noni fruit compounds (*Morinda citrifolia* L.) through nanotechnology-based topical anti-aging formulations.

METHODS

This study employed a systematic review design to comprehensively identify, analyze, and interpret findings from previously published research articles [21], related to the enhancement of anti-aging potential of *Morinda citrifolia* L. through nanotechnology. The literature search was conducted using the Google Scholar database as the primary search engine. The keywords applied were "Aging," "Morinda citrifolia L.," and

"Nano," either individually or in combination, to ensure broad yet relevant coverage of the topic. The inclusion period was limited to publications from 2014 to 2024 (the most recent ten years) to ensure that the evidence reflected current scientific developments in nanotechnology and topical anti-aging formulations. The initial search identified a total of 2,950 manuscripts.

A structured screening and selection process was then conducted based on predetermined inclusion and exclusion criteria. The inclusion criteria were: (1) original research articles, (2) published between 2014 and 2024, (3) indexed in reputable international journals or accredited national journals, (4) available in full-text format, and (5) directly relevant to the keywords and research objectives. The exclusion criteria were: (1) review articles, (2) publications prior to 2014, (3) non-accredited national journals, (4) articles not directly related to aging, *Morinda citrifolia* L., or nanotechnology, and (5) articles without full-text access.

After applying these criteria and removing duplicates and irrelevant studies, a total of 80 articles met the eligibility requirements and were included in the final analysis. The selected articles were derived from accredited national journals and reputable international journals to enhance the validity, reliability, and scientific rigor of the synthesized data.

RESULTS

Antioxidants are compounds capable of scavenging reactive oxygen species (ROS), thereby preventing oxidative stress and reducing the risk of premature skin aging. Noni fruit (*Morinda citrifolia* L.) possesses unique characteristics due to its diverse bioactive constituents with strong antioxidant potential. A comprehensive literature search regarding the organoleptic characteristics and physicochemical composition of noni fruit is summarized in Table 1 [12, 22, 24–38].

The reported organoleptic changes indicate that noni fruit undergoes progressive color transformation during maturation, from dark green in the first month to translucent gray by the fifth month [22]. The pH values vary considerably across studies (3.4–7.4) [22, 24–27], reflecting differences in maturity stage, geographical origin, and analytical methods. Acidity levels, solubility profiles in various solvents (aqueous and organic), extract polarity, viscosity, moisture content, ash content, bulk density, volatility, fixed carbon, and calorific value have also been documented [22, 24, 26–30].

In terms of phytochemical composition, noni fruit contains significant levels of scopoletin [12, 31–33], catechins [34, 35], total phenolics [12, 24, 26, 27, 30, 36–38], flavonoids [12, 24, 26, 31, 36, 38], carotenoids [24], and vitamin C [26, 27, 30, 37, 38]. Additional components include dehydroascorbic acid [27], cellulose, lignin, elemental carbon, hydrogen, oxygen, nitrogen [28], sugars such as glucose and fructose [27], proteins, and carbohydrates [30]. The high phenolic and flavonoid content strongly supports the antioxidant and anti-aging potential of noni fruit.

Skin aging

Skin aging is a natural biological process that progresses with increasing age. The skin is the most visibly affected organ, showing clinical signs such as wrinkles, pigmentation, reduced elasticity, and dryness. These manifestations result from a combination of endogenous factors (genetics, metabolism, and hormonal changes) and exogenous factors (chronic UV exposure, pollution, radiation, chemicals, and toxins).

Anti-aging potential

Anti-aging formulations generally consist of two primary groups of agents: antioxidants and cell regulators. Noni fruit demonstrates potential in both categories. Its bioactive compounds neutralize excessive free radicals through hydrogen atom donation, stabilizing radical species and interrupting oxidative chain reactions. Additionally, these compounds contribute to cellular protection and repair against oxidative damage.

The mechanisms underlying the anti-aging potential of noni fruit compounds are summarized in Table 2 [3, 12, 15, 26, 37, 53, 55–63].

Table 1. Organoleptic characteristics and physicochemical composition of *Morinda citrifolia* L. (noni fruit)

Parameter	Results
Organoleptic (fruit color by month)	Month 1 = dark green [22] Month 2 = yellowish green [22] Month 3 = pale yellow [22] Month 4 = pale yellow [22] Month 5 = translucent gray [22]
pH	3.90–3.9 [24] 3.54–4.00 [22] 7.1–7.4 [25] 3.90–6.16 [26] 3.4±0 [27]
Total acidity	0.17–0.18% [24] 3.20–6.82 g/100 g [22] 0.35–0.44 g/100 g [26] 1.76 ± 0.01 g citric acid/100 g fresh weight (fw) [27]
Solubility	1.33±0.06 °Brix [24] 9.00–9.20 °Brix [22] 5.8 ± 0.0 °Brix [27] Distilled water 60–64% [28] Chloroform 10–56% [28] DMSO 17–92% [28] Dimethylformamide 56–74% [28] Methanol 52–74% [28]
Extract polarity	0.40–0.81 [29]
Moisture content	91% [22]
Viscosity	16.27±0.23 mPas [24]
Ash content	0.66–1.34% [22] 0.60–5.73% [26] 7.180±0.044% [28] 0.87–1.34 g/100 g fw [30]
Bulk density	0.312±0.001 g/cm ³ [28]
Volatility	78.799±0.592% [28]
Fixed carbon	14.02±0.553% [28]
Higher heating value	17.185±0.103 MJ/kg [28]
Scopoletin content	1.43±0.72 mg/g [31] 24.26–65 ppm (µg/g fw) [32] 2.45±0.2 mg/g [12] 0.67 mg/g (summer harvest) & 0.321 mg/g (winter harvest) [33]
Catechin content	1,111.2 mg/100 g [34, 35]
Total phenolic content	2.93±0.07 mg RE/100 mL [24] 9.15% [36] 748.40±8.85 µg GAE/g FW [37] 0.95 g/100 mL [38] 7,486.38 µg GAE/g [26] 47.6 ± 2.0 mg GAE/100 g [27] 4.84 ± 0.72 mg GAE/g [31] 39.4±0.005 mg GAE/g extract [12] 3,022.8–3,647.0 µg/g fw [30]
Total flavonoid content	1.01±0.19 mg RE/100 mL [24] 9.14% [36] 0.017 g/100 mL [38] 1.61 ± 0.63 mg GAE/g [31] 385.57 µg OE/g [26] 5.9±0.008 mg OE/g extract [12]
Carotenoid content	0.02±0.00 mg βCE/100 mL [24]
Vitamin c content	76.24±1.13 mg/100 g [37] 71.1±1.4 mg/100 g [27] 50.989 mg/100 g [38] 336.62 mg/100 g [26] 97.1 ± 2.3 mg/100 g [27] 115.85–182.42 mg/100 g fw [30]
Dehydroascorbic acid	26.0 ± 0.8 mg/100 g [27]
Extractive value	4.497±0.346% [28]
Cellulose	33.114±0.261% [28]
Lignin	9.569±0.399% [28]
Carbon	44.468±0.077% [28]
Hydrogen	5.626±0.003% [28]
Oxygen	41.559±0.091% [28]
Nitrogen	2.518±0.161% [28]
Glucose	2.07±0.01 g/100 g fw [27]
Fructose	2.44±0.02 g/100 g fw [27]
Dry weight	7.37±0.06% fw [27]
Protein	8.73–15.63 g/100 g fw [30]
Carbohydrate	6.60–9.60 g/100 g fw [30]

Table 2. Bioactive compounds of noni (*Morinda citrifolia* L.) and their biological activities

Compound	Method	Results	Mechanism of Action
Flavonoids	Melanogenesis assay	Reduced melanin synthesis by up to 25%	Inhibits melanin production without affecting cell proliferation [15]
	DPPH	IC50 0.596 mg/mL	Triggers lipid peroxidation into hydrogen and lipid peroxide [37]
Polyphenols	DPPH	Scavenged 92±0.08%, higher than L-ascorbic acid 82.0±1.3% at 100 µg/mL	Extracts at 50 and 100 µg/mL reduced IL-6 and TNF-α in LPS-induced RAW 264.7 cells and inhibited NO, iNOS mRNA expression, MMP-1 (25%), elastase (7%), while increasing type-1 procollagen by 20.0% [3]
	ABTS	Scavenged 89±1.1%, higher than L-ascorbic acid 79±1.2% at 100 µg/mL	—
	Collagen type-II gene expression assay	Stimulated type-II collagen: expression of COL2A1 gene in raw noni fruit with seeds reached 32.12%. No cellular or DNA toxicity observed.	Stimulates collagen production, reduces collagen degradation, and inhibits melanogenesis [53, 56]
Phenols, flavonoids, scopoletin	ABTS	IC50 24.92±0.9 µg/mL	Phenolics act as reducing agents and hydrogen atom donors to free radicals [12]
Flavonoids and vitamin C	FRAP	5,535.31±37.48 to 312,014.2±2,397.19 mmol TE/100 g (Trolox equivalent); 129,785.3±2,397.19 to 467,970.4±5,085.25 mmol AA/100 g (ascorbic acid equivalent)	Phenolics function as reducing agents, hydrogen donors, free radical scavengers, and terminate lipid peroxidation chain reactions [26]
Triterpenoids	DPPH	Inhibited free radicals by 78.19%; highest compound identified by GC was squalene (13.32%).	Glutathione peroxidase (GPx) reduces H ₂ O ₂ to H ₂ O and GSSG; peroxiredoxin activates GSH S-transferase Pi and phospholipid-hydroperoxide GPx, leading to lipid peroxide reduction into lipid alcohol [21,55]
Phenolics	DPPH	IC50 of DNG 150.9 µg/mL; noni juice 155.7 µg/mL	Scavenges free radicals [57]
Scopoletin	In-silico study	According to the UniProt database, scopoletin functions as an inhibitor of CA1.	Carbonic Anhydrase 1 (CA1) converts CO ₂ into bicarbonate and protons, accompanied by ROS production that damages proteins and causes gene mutations [58]
Iridoids	Melanin, erythema, and UV-A-induced wrinkle assay	After 12 days of 3% noni fruit extract cream application in adult women: wrinkles reduced; brighter skin (30%), smaller pores (39%), melanin decreased 11%, erythema decreased 13%, and skin moisture increased 24%.	Significantly inhibits melanogenesis in B16 cells and enhances type-I collagen and fibroblast synthesis. Reduction of erythema is notable as noni juice and leaf extract may cause skin irritation [3, 59]
Polysaccharides	Antioxidant enzyme activity, cytokine levels, and gene expression assay	Improved antioxidant status and immune function in Kashmiri goats; body weight gain with non-significant feed intake increase under NFP supplementation.	NFP supplementation increased NO, IL-6, TNF-α, catalase, GPx, TrxR, and total T-SOD activity; decreased malondialdehyde and ROS levels [60]
Alkyl disaccharide and phenyl ethanediol	NO, NF-κB, and QR1 inhibition assay	NO inhibition 3.7±0.1–13.3±0.01%; NF-κB 28.0±2.0–56.0±2.1%; QR1 0.8–1.8	Isolated compounds potentially inhibit NO, TNF-α, NF-κB, and QR1 production [61]
Scopoletin	ABTS	IC50 24.92±0.9 µg/mL	Ethanol hydroxyl groups interact with phenolic compounds, increasing phenolic solubility in ethanol [12]
Stigmasterol	α-amylase inhibition assay	IC50 stigmasterol 10.29±0.76 µg/mL; noni extract 14.16±5.72 µg/mL	Enhances intestinal glucose absorption, reduces gluconeogenesis, activates α-cells, and stimulates insulin release [62]
Quercetin, 4-ethyl catechol, 4-vinyl catechol, 4-methyl catechol	Collagen level assay	Collagen levels formed in rabbit dorsal skin ranged from 42.49–72.22%.	Activates Nrf-2, suppresses ROS, inhibits COX-1, COX-2, 12-LOX, 12-HTT, TXB2, and 12-HETE pathways, thereby increasing TGF-β1 in collagen synthesis [63]

Flavonoids exhibit melanogenesis inhibition (reducing melanin synthesis by up to 25%) without affecting cell proliferation [15], along with antioxidant activity demonstrated by DPPH assays (IC50 0.596 mg/mL) [37]. Polyphenols show strong radical scavenging activity in DPPH and ABTS assays, surpassing L-ascorbic acid at 100 µg/mL [3]. They reduce IL-6 and TNF-α levels in LPS-induced RAW 264.7 cells and inhibit nitric oxide (NO), iNOS mRNA expression, MMP-1 (↓25%), elastase (↓7%), while increasing type-I procollagen (↑20%) [3].

Phenolic compounds, flavonoids, and scopoletin demonstrate ABTS radical scavenging activity (IC50 24.92±0.9 µg/mL) [12]. Triterpenoids inhibit free radicals (78.19%), with squalene (13.32%) identified as a major component [55]. Iridoids significantly inhibit melanogenesis in B16 cells and increase collagen type-I synthesis and fibroblast activity, leading to reduced wrinkles, melanin levels, and erythema after topical application for 12 days [3, 59]. Quercetin and catechol derivatives enhance collagen synthesis (42.49–72.22%) via activation of the Nrf-2 pathway and suppression of ROS-mediated inflammatory pathways [63].

Collectively, these findings confirm that noni fruit acts through multiple mechanisms, including ROS scavenging, MMP inhibition, collagen stimulation, anti-inflammatory modulation, and melanogenesis suppression.

Application of nanocosmetics

Although herbal bioactive compounds offer substantial therapeutic benefits, many are chemically unstable and have limited skin permeability. Therefore, topical nanoparticle systems have emerged as promising alternative delivery strategies. Over the past decade, topical nanoparticle development in cosmetics has expanded rapidly. Each nanoparticle system presents distinct characteristics, advantages, and limitations, as summarized in Table 3 [9, 70, 73–78].

Table 3. Comparison of lipid- and surfactant-based nanocarrier drug delivery systems including niosomes, nanoemulsions, solid lipid nanoparticles (SLN), and nanostructured lipid carriers (NLC)

No	System	Definition	Advantages	Disadvantages
1	Niosome [9, 73, 74]	Nanoparticles similar to liposomes but composed of non-ionic surfactants.	<ul style="list-style-type: none"> • Reduced toxicity • Increased bioavailability, skin penetration ability, and stability • Protects sensitive active compounds 	<ul style="list-style-type: none"> • Susceptible to microbial contamination • Polymorphic changes may occur • Particle size enlargement • Expensive
2	Nanoemulsion [75, 76]	A colloidal dispersion of oil, water, surfactant, and co-surfactant.	<ul style="list-style-type: none"> • Increased absorption and bioavailability • Reduced biotoxicity 	<ul style="list-style-type: none"> • Surfactant selection must be carefully considered • Decreased solubility • High partition coefficient and molecular weight
3	SLN [70, 74, 77]	Solid Lipid Nanoparticles (SLN) are lipid matrix particles formulated by replacing liquid lipids with solid lipids.	<ul style="list-style-type: none"> • Reduced drug leakage • Organic solvents can be avoided • Biocompatible and biodegradable • Increased skin hydration • Easy production • Minimal side effects • Targeted delivery • Stable 	<ul style="list-style-type: none"> • Limited active compound entrapment • Less controlled drug release • Low drug loading capacity
4	NLC [74, 77, 78]	Second-generation lipid nanoparticles containing a mixture of solid and liquid lipids.	<ul style="list-style-type: none"> • Increased loading capacity • Organic solvents can be avoided • Minimal leakage • Suitable for both hydrophilic and hydrophobic active compounds 	<ul style="list-style-type: none"> • Reduced melting point • Less structured matrix

Niosomes are vesicular nanoparticles composed of non-ionic surfactants, offering reduced toxicity and enhanced bioavailability but with limitations such as microbial susceptibility and high cost [9, 73, 74]. Nanoemulsions improve absorption and reduce biotoxicity but require careful surfactant selection [75, 76]. Solid lipid nanoparticles (SLN) provide improved stability and hydration while minimizing leakage [70, 74, 77]. Nanostructured lipid carriers (NLC), considered second-generation lipid nanoparticles, increase drug-loading capacity and reduce leakage, although they may exhibit lower melting points and structural irregularities [74, 77, 78].

Nanoparticle-based Indonesian herbal preparations as anti-aging agents

Most natural antioxidants are plant-derived, particularly polyphenols, which possess photoprotective, anti-photoaging, anti-inflammatory, anti-melanogenesis, and antioxidant properties. However, these compounds are sensitive to alkaline pH, enzymatic degradation, and environmental conditions. Nanoparticle technology enhances their stability, permeability, and bioavailability. The findings of previous studies on nanoparticle-based Indonesian herbal anti-aging formulations are summarized in Table 4 [16, 75, 76, 78, 81, 86–88].

Table 4. Particle size and anti-aging mechanisms of various nanoformulations

No	Formulation	Size (nm)	Anti-aging mechanism
1	Noni fruit nanoencapsulation [16]	534	Donates hydrogen atoms and prevents chain reactions of lipid and protein peroxidation.
2	Noni fruit nanoemulsion [86]	50–75	Suppresses production of pro-inflammatory cytokines, reduces bacterial translocation, promotes tissue repair, and provides systemic anti-inflammatory effects.
3	Niosome Ellagic acid [87]	204–536.7	Prevents collagen degradation (MMP3 expression ↓, Col1A1 ↑, and Timp3 ↑), inhibits ECM protein degradation in fibroblast cells, and increases TERT expression to avoid telomere shortening.
4	Nanoemulsion Bakuchiol achieved [75]	200–243	Inhibits DNA polymerase 1.
5	SLN <i>Elaeis guineensis</i> [81]	609.70–640.11	Hydrates the epidermis, inhibits oxidation, and suppresses melanogenesis.
6	NLC Peppermint oil [88]	188.25–197.80	Prevents collagen and elastin breakdown and reduces wrinkle formation.
7	NLC <i>Citrus sinensis</i> L. [78]	237.8–476.9	Decreases PGE2, COX2, JNK, MDA, and elastin levels.
8	Nanoemulsion D-limonene [76]	84.30–384.7	Donates hydrogen atoms.

Nano-encapsulation of noni fruit (534 nm) enhances hydrogen atom donation and prevents lipid and protein peroxidation chain reactions [16]. Noni nanoemulsions (50–75 nm) suppress pro-inflammatory cytokines and promote tissue repair [86]. Niosomal ellagic acid (204–536.7 nm) inhibits collagen degradation (↓MMP3, ↑Col1A1, ↑Timp3) and enhances telomerase activity [87]. SLN and NLC systems containing herbal bioactives such as *Elaeis guineensis*, peppermint oil, and *Citrus sinensis* L. demonstrate anti-oxidative and anti-melanogenic effects [78, 81, 88]. Overall, nanoparticle-based formulations significantly enhance the anti-aging efficacy of Indonesian herbal bioactive compounds by improving stability, targeted delivery, and skin penetration while preserving their multifunctional biological activities.

DISCUSSION

Endogenous antioxidants are naturally produced in the body and include enzymes such as glutathione peroxidase, catalase, and superoxide dismutase. These enzymes require micronutrients including selenium, iron, copper, zinc, and manganese as cofactors for their formation and optimal catalytic activity, enabling effective antioxidant defense. Noni fruit contains all of these minerals, which may help enhance endogenous antioxidant defense mechanisms. In addition, noni contains glutathione, ascorbic acid, alpha-tocopherol, beta-carotene, bilirubin, selenium, dihydrolipoic acid, melatonin, flavonoids, anthraquinones, and other compounds that contribute to protecting the body against free radical damage [22, 23].

The literature summarized indicates that the harvesting stage of noni fruit can be visually determined by its shape and color; as the fruit ripens, it becomes paler and softer. The pH value of noni fruit extract varies widely, ranging from 3.4 to 7.4, indicating a relatively acidic nature due to the presence of ascorbic acid, caproic acid, capric acid, hexanoic acid, octanoic acid, and butanoic acid [39–43]. Caproic acid, caprylic acid, hexanoic acid, octanoate, and butanoic acid contribute to the unpleasant odor of noni fruit, resembling rancid cheese [44]. Noni fruit extract is highly polar and therefore readily soluble in polar solvents such as water, methanol, and ethanol, but relatively poorly soluble in semi-polar and non-polar solvents [28, 45, 46]. The phytochemical composition of noni fruit is highly complex. Among its constituents, catechins, phenolics, flavonoids, carotenoids, and vitamin C have strong potential as anti-aging agents; however, these compounds are sensitive during pharmaceutical formulation processes [30, 34, 35, 47–52]. Catechins are also found in noni leaves, with total catechin content of 141.88±5.04 mg/g [48]. Therefore, further processing is necessary to protect the active compounds of noni fruit and improve its anti-aging therapeutic quality.

Skin aging

Skin aging is a natural process that occurs with increasing age. The skin is the most visibly affected organ and is influenced by both endogenous factors (genetics, metabolism, and hormones) and exogenous factors (chronic light exposure, pollution, radiation, chemicals, and toxins). Prematurely aged skin is characterized by thickened epidermis, hyperpigmented spots, deep wrinkles, sagging, dullness, and roughness [3,53]. Loss of fibrillin structure and reduced type VII collagen contribute to wrinkle formation by weakening the dermal–epidermal junction. Increased collagen degradation mediated by matrix metalloproteinases, serine proteases, and other proteolytic enzymes also accelerates premature skin aging. The three major structural components of the dermis—collagen, elastin, and glycosaminoglycans (GAGs)—are key targets in aesthetic anti-aging strategies [5, 54].

Anti-aging

Two major groups of agents are commonly incorporated into anti-aging formulations: antioxidants and cell regulators. Antioxidants, including vitamins, polyphenols, and flavonoids, reduce collagen degradation by lowering free radical (FR) concentrations in tissues. Cell regulators such as retinol, peptides, and growth factors (GF) directly influence collagen metabolism and stimulate collagen production [7, 20].

Vitamins C, B, and E are among the most important antioxidants due to their relatively small molecular weights, allowing skin penetration. Vitamin C at concentrations of 5–15% has demonstrated anti-aging effects by inducing Col-1 and Col-3 production, supporting collagen synthesis enzymes, and inhibiting MMP-1. Niacinamide regulates cellular metabolism and regeneration and is used at 5% concentration as an anti-aging agent. Vitamin E, used at concentrations of 2–20%, exhibits anti-inflammatory and antiproliferative effects, smooths the skin, enhances stratum corneum moisture retention, accelerates epithelialization, and contributes to protection against photoaging [54].

Phenolic compounds, widely found in fruits and vegetables, act as free radical scavengers and inhibit oxidases and other enzymes. Plant antioxidants play an essential role in therapy. Oxidative stress contributes to the development of various pathophysiological conditions including cancer, inflammation, aging, and cognitive dysfunction. Consequently, herbal products from traditional medicine have gained global popularity due to their long-standing use, efficacy, and relatively low toxicity. Herbal preparations are increasingly described as complementary and alternative treatments for neurodegenerative disorders [64].

Noni fruit is a promising herbal anti-aging agent with multiple mechanisms of action. In addition to its anti-aging potential, noni fruit also exhibits anti-hyperpigmentation effects through ROS scavenging, inhibition of melanogenesis, stimulation of collagen synthesis, and enhancement of fiber formation [65,66]. Collagen plays a crucial role in maintaining skin elasticity and firmness; declining collagen levels lead to shortened fibrous cells, epidermal irregularities, and wrinkle formation [3, 39, 59, 67]. Excessive ROS scavenging also helps prevent melanogenesis. Continuous UV exposure induces excessive melanogenesis, resulting in dark spots due to increased levels of NO, TNF- α , NF- κ B, and QR [3, 15, 49, 68–71].

Nanocosmetic applications

The subcutaneous layer prevents excessive water loss and xenobiotic penetration through dermal layers. Corneocytes and intercellular lipids, enclosed within highly cross-linked protein envelopes, maintain optimal hydration gradients. Cosmetic lipids such as phosphatidylcholine improve skin moisture and emollient properties. Surfactants and polar lipids in lipid-based nanoparticle cosmetics are also essential for maintaining skin function and preventing disease [72].

Although these herbal compounds are highly beneficial in preventing premature skin aging, they are sensitive and often have difficulty reaching therapeutic targets, making topical nanoparticles a promising alternative delivery system. Over the past decade, topical nanoparticles in nanocosmetics have developed rapidly. This systematic review indicates four types of topical nanoparticle systems derived from Indonesian herbal plants: particulate carriers (niosome), vesicular carriers (SLN and NLC), and emulsion-based carriers (nanoemulsion). Each system has distinct characteristics.

Niosomes

Niosomes are amphiphilic vesicular systems that entrap active compounds within a bilayer structure. They exhibit physicochemical properties similar to liposomes, but their bilayers are formed from non-ionic surfactants [79]. Nanoemulsions appear transparent and consist of oil droplets stabilized by surfactants and co-surfactants. Due to their small droplet size (<200 nm), nanoemulsions enhance skin permeation and facilitate penetration [20].

Nanoemulsions

Nanoemulsions are colloidal dispersions composed of oil, water, surfactant, and co-surfactant. Although thermodynamically unstable, they are kinetically stable systems. Droplet sizes for topical drug delivery range from 50 to 200 nm. Nanoemulsions may be classified as oil-in-water, water-in-oil, or bicontinuous systems, and as neutral, positively charged, or negatively charged based on droplet surface charge. Nanoemulsions offer advantages over conventional emulsions, including high stability, increased interfacial area, enhanced solubility, and improved bioavailability. They facilitate lipid extraction from the stratum corneum, overcoming its barrier function and enhancing penetration, and may also induce keratin denaturation [80].

Solid lipid nanoparticles

Solid lipid nanoparticles (SLN) are topical drug carriers composed of fatty acids, waxes, glycerides, and triglycerides, and may be combined with polymeric nanoparticles, lipid emulsions, or liposomes. With sizes ranging from 50–1000 nm, SLNs remain solid at room temperature, are easy to produce, and exhibit low toxicity. SLNs enable controlled drug delivery and selective targeting due to their biocompatibility and biodegradability, minimal skin irritation, and ability to protect active components [81]. Flavonoids incorporated into SLNs demonstrate improved stability and reduced irritation [20]. However, due to solid lipid content, SLNs may undergo crystallization and recrystallization [72].

Nanostructured Lipid Carriers

Nanostructured lipid carriers (NLC) consist of a mixture of solid and liquid lipids. Typically around 200 nm in size, NLCs efficiently form hydrophobic monolayers on the skin, preventing water loss and enhancing hydration. Their occlusive and moisturizing properties make them highly suitable for cosmetic applications. Next-generation lipid nanoparticles such as SLN and NLC demonstrate significant potential [20].

Indonesian Herbal Nanoparticles as Anti-Aging Agents

Most natural antioxidants are plant-derived. Polyphenols exhibit photoprotective, anti-photoaging, anti-inflammatory, anti-melanogenic, and antioxidant properties. Retinol enhances collagen metabolism, while polypeptides and oligopeptides mimic collagen or elastin sequences, stimulating dermal collagen synthesis. HO-1, NQO-1, and SOD genes are regulated by Nrf2 [7,49,51,83–85]. Flavonoids activate Nrf2 via modification of Keap1 cysteine residues. UVA exposure stimulates Nrf2 and its target proteins (HO-1, NQO-1, GST), whereas UVA and UVB may downregulate Nrf2 signaling in keratinocytes, fibroblasts, and melanocytes. UV exposure increases ROS production, which upregulates MMP-1/3/9, leading to collagen degradation and inflammation [7].

Because polyphenol-rich Indonesian herbal compounds are sensitive to alkaline pH, enzymes, and nutrients, nanoparticle technology is employed to maximize their bioactivity. Literature summarized indicates strong potential of Indonesian herbal nanoparticles as topical anti-aging and antibacterial agents. Active compounds are encapsulated within polymeric or lipid shells stabilized by surfactants and co-surfactants. Optimal nanoparticle size for topical delivery ranges from 10–600 nm, with approximately 200 nm considered ideal for drug delivery systems [89–91]. Nanoparticles within this size range can passively traverse skin barriers and potentially reach systemic circulation [89]. The stratum corneum is largely impermeable to larger particles [91].

The anti-aging mechanisms of these nanoparticles vary, but generally involve two main strategies: (1) preventing and repairing structural damage through ROS scavenging to protect collagen expression, and (2) improving pigmentation by inhibiting melanogenesis. ROS scavenging via hydrogen atom donation [76,93] reduces collagen degradation, decreases MMP3 expression, increases CollA1 and Timp3 levels, inhibits ECM protein degradation in fibroblasts, and enhances TERT expression to prevent telomere shortening [87].

Melanogenesis is a complex enzymatic process within melanosomes producing eumelanin and pheomelanin [8]. Eumelanin is an insoluble dark brown–black polymer, while pheomelanin is a soluble yellow–red sulfur-containing polymer. Both are formed through cysteine or glutathione conjugation [69]. Continuous UV exposure initiates melanogenesis via oxidation of L-tyrosine to DQ catalyzed by tyrosinase (TYR), the rate-limiting enzyme. Subsequent intramolecular reactions lead to melanin formation, resulting in dark spots [69].

Despite promising findings, current evidence regarding noni as an anti-aging agent has limitations. Most available studies are in vitro or animal-based, with limited clinical data in humans. Variability in extraction methods affects bioactive composition and complicates standardization. No established dosage or consistent formulation has been validated for anti-aging effects, and long-term safety data remain limited. Therefore, further well-controlled clinical trials in humans are necessary to confirm efficacy and safety.

CONCLUSION

Based on the systematic review conducted, *Morinda citrifolia* L. (noni fruit) demonstrates significant potential as a topical anti-aging agent for the skin. The identified limitations of noni fruit, including issues related to stability, bioavailability, and penetration, can be effectively addressed through the application of topical nanotechnology-based delivery systems. Such nanotechnological approaches may enhance its therapeutic efficacy, improve physicochemical stability, increase skin permeation, and ultimately augment its functional, economic, and clinical value in anti-aging formulations.

Ethical consideration, competing interest and source of funding

-As this study was based exclusively on the analysis of previously published literature and did not involve human participants, animals, clinical data, or confidential personal information, ethical approval was not required. Systematic reviews that utilize secondary data from publicly accessible sources do not necessitate ethical clearance, as no direct intervention or interaction with research subjects is conducted.

-There is no conflict of interest related to this publication.

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