



ORAL COLLAGEN AND GLUTATHIONE SUPPLEMENTATION FOR SKIN HEALTH: A SYSTEMATIC REVIEW

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ABSTRACT

Oral collagen and glutathione supplements are increasingly used to support skin health, but clinical evidence varies by ingredient, formulation, dose, duration, and outcome. To systematically evaluate the clinical effectiveness, safety, and quality of evidence for oral collagen and glutathione supplementation in relation to skin health. A systematic literature review following PRISMA 2020 searched six primary electronic sources (PubMed/MEDLINE, Web of Science, ScienceDirect, SpringerLink, Wiley Online Library, and Taylor & Francis), with Google Scholar used as an additional source, for primary studies published from 2021 to 2026. Thirty-three articles met the inclusion criteria. Methodological quality was assessed using the JBI Critical Appraisal Checklist, and thematic mapping was performed with VOSviewer. Evidence was dominated by collagen supplementation: 25 studies assessed hydration or skin barrier function, 24 elasticity, and 21 wrinkles. Glutathione studies more often assessed pigmentation, melanin index, and skin brightness. Short-term safety was generally favourable, with mostly mild and transient adverse events. Most included studies had good methodological quality, although allocation concealment and blinding were not always fully reported. VOSviewer identified skin hydration, collagen peptides, skin elasticity, and skin aging as the most prominent themes.

Keywords: glutathione; oral collagen; skin aging; skin health; skin pigmentation

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INTRODUCTION

Skin health reflects moisture, elasticity, barrier function, pigmentation, and tissue structure. Age-related changes include dryness, reduced elasticity, roughness, fine lines, and wrinkles. Skin aging is associated with reduced extracellular-matrix formation by fibroblasts and increased collagen degradation, which has contributed to growing use of nutricosmetics intended to support skin condition from within (Seong et al., 2024). Collagen is a major dermal component and is widely used in hydrolyzed or peptide forms. Randomized trials have reported improvements in hydration, elasticity, wrinkles, and pigmentation after 8–12 weeks, although magnitude of benefit varies by dose, source, participant characteristics, formulation, and study quality (Lee et al., 2023; Seong et al., 2024). Meta-analyses generally support benefits for hydration and elasticity but also show substantial heterogeneity and sensitivity to methodological quality and industry funding (Pu et al., 2023; Myung & Park, 2025; Moltó-Balado & Simeó-Monzó, 2026).

Glutathione is more closely associated with antioxidant activity and melanogenesis. Clinical outcomes therefore often include melanin index, brightness, hyperpigmentation, and skin tone. Studies of oral or combined glutathione formulations have reported favourable pigmentation changes, but the smaller evidence base and frequent use of multi-ingredient or combined oral-topical interventions make the independent effect of oral glutathione difficult to isolate (Sitohang et al., 2021; Wahab et al., 2021; Duperray et al., 2022; Sarkar et al., 2025). Products combining

collagen, glutathione, and other active ingredients are increasingly studied. A randomized trial of hydrolyzed collagen, glutathione, and vitamin E reported improvements in elasticity and wrinkle measures, but the contribution of each component could not be separated (Wisutthathum et al., 2026). Safety evidence is mainly short term, with most trials lasting 8–12 weeks and generally reporting no serious product-related events. This review therefore evaluated clinical effectiveness, safety, and evidence quality for oral collagen and glutathione supplementation while considering formulation, study design, outcomes, and methodological limitations.

METHOD

Study Design and PICO Framework

This systematic literature review followed PRISMA 2020 and focused on primary clinical studies published from 2021 to 2026. The research question was structured using PICO to define the population, intervention, comparator, and skin-related outcomes.

Table 1.
PICO Framework

Component	Criteria
Population	Adults aged ≥ 18 years with healthy skin, skin aging, dry skin, photoaging, wrinkles, or pigmentation changes.
Intervention	Oral hydrolyzed collagen, collagen peptides/tripeptides, bioactive collagen peptides, glutathione/reduced glutathione, or oral formulations containing collagen and/or glutathione.
Comparison	Placebo, no supplementation, or active comparator.
Outcome	Hydration, moisture, elasticity, wrinkles, roughness, texture, TEWL/barrier function, dermal structure/density, pigmentation, melanin index, dark spots, brightness, and safety/adverse events.

Literature Search and Study Selection

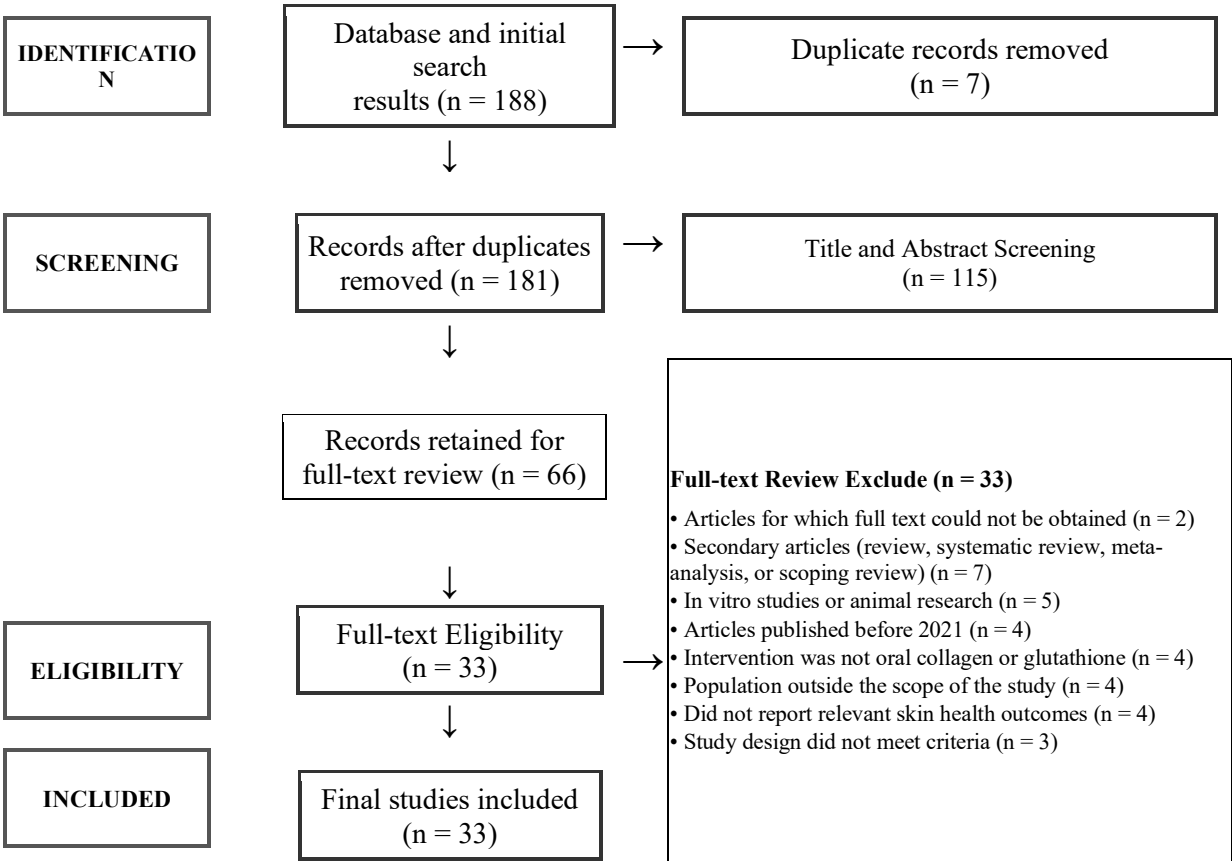


Figure 1. PRISMA 2020 Flow Diagram of Article Selection

Six primary electronic sources were searched: PubMed/MEDLINE, Web of Science, ScienceDirect, SpringerLink, Wiley Online Library, and Taylor & Francis. Google Scholar was used as an

additional source. Searches covered English-language articles published from 1 January 2021 to 28 September 2026, and reference lists were checked for additional eligible studies. The search combined terms for oral collagen or glutathione with skin-health outcomes and clinical-study terms. Search syntax was adapted to each source. Eligible studies included adults aged ≥ 18 years, oral collagen and/or glutathione interventions, relevant skin-health or safety outcomes, and randomized, controlled, or relevant prospective clinical designs. Reviews, meta-analyses, editorials, protocols, case reports, animal/in-vitro studies, topical/injectable-only interventions, studies without relevant outcomes, unavailable full texts, and publications before 2021 were excluded. Screening proceeded from title/abstract to full text.

Quality Appraisal, Data Extraction, and Analysis

Methodological quality was assessed with the JBI Critical Appraisal Checklist appropriate to study design, covering randomization, comparability, blinding, outcome measurement, completeness of data, and analysis. Data extracted from the 33 studies included country, sample, intervention, dose, duration, comparator, outcomes, findings, safety, and adverse events. Findings were synthesized narratively by hydration/barrier function, elasticity/dermal structure, wrinkles/texture, pigmentation, and safety. VOSviewer was used for co-occurrence mapping of author keywords and important title/abstract terms, with a minimum occurrence threshold of two and a thesaurus to merge synonymous terms.

RESULT

The 33 included studies were published between 2021 and 2026. Ten (30.3%) were published in 2021, eight (24.2%) in 2024, six (18.2%) in 2025, four (12.1%) in 2026, three (9.1%) in 2022, and two (6.1%) in 2023. Twenty studies (60.6%) were conducted in South Korea, Thailand, Taiwan, Japan, or China. Collagen was the main intervention in 22 studies (66.7%), seven (21.2%) used collagen with additional active ingredients, three (9.1%) focused on glutathione, and one (3.0%) combined collagen and glutathione. Most interventions lasted 9–12 weeks (54.5%).

Hydration/barrier function was assessed in 25 studies (75.8%), elasticity/firmness in 24 (72.7%), wrinkles/surface changes in 21 (63.6%), dermal structure in 11 (33.3%), and pigmentation-related outcomes in nine (27.3%). The JBI appraisal found that 30 studies met 10–13 criteria (operationally classified as good) and three—Chang et al. (2021), Bianchi et al. (2022), and González-Rodríguez et al. (2026)—met nine criteria (fair). Allocation concealment and blinding were the most frequently unclear domains.

Table 2.
Characteristics and Key Findings of the 33 Included Studies

Source	Country / Sample	Intervention/ Duration	Main Outcomes	Key Findings
Carrillo-Norte et al. (2024)	Spain; 80 healthy women aged ≥ 30 years	2.5 g low-molecular-weight collagen peptides for 6 weeks	Wrinkles, hydration, elasticity	Wrinkle volume decreased by 46%, area by 44%, and depth by 9%; the increase in hydration was 34% greater than with placebo ($p < 0.001$). Elasticity changed only slightly. Supplementation was mainly effective for wrinkles and hydration.
Chang et al. (2021)	Taiwan; 50 healthy adults	50 mL/day collagen drink for 28 days	Hydration, elasticity, radiance, spots, wrinkles, texture	By day 28, hydration increased by 27.54%, elasticity by 11.14%, and radiance by 26.14% compared with placebo; wrinkles decreased by 19.92% and spots by 12.42% ($p < 0.001$). The combination formula improved several skin parameters at the same time.
Demir-Dora et al. (2024)	Turkey; 112 women	10 g hydrolyzed collagen peptide for 8 weeks	Elasticity, hydration, roughness, sagging	Elasticity improved ($p = 0.009$), hydration $p = 0.003$ to < 0.001 , and roughness $p = 0.002$ to < 0.001 . At week 8, hydration was 65.8 vs 53.1 g/m ³ ($p < 0.001$). The product was considered effective and well tolerated.
Duperray et al. (2022)	Thailand; 124 Asian women	250 mg glutathione $\pm$ 500 mg L-cystine for 12 weeks	Brightness and dark spots	The combination increased L* by approximately 1.8% and ITA ^o by 8.7% ($p < 0.05$); dark-spot size had already decreased

Source	Country / Sample	Intervention/ Duration	Main Outcomes	Key Findings
				by 16.2% at week 6 ($p<0.01$). The combination produced a stronger effect than either ingredient alone and placebo.
Evans et al. (2021)	Canada; 50 women aged 45–60 years	Marine hydrolyzed collagen for 12 weeks	Wrinkles, elasticity, perceived skin quality	Wrinkle scores decreased by 35% from baseline ($p=0.035$), and the reduction in wrinkles on the right side of the face was 24% greater than with placebo. Cheek elasticity in participants aged 45–54 years improved by 20% at week 6 ($p=0.016$). Collagen was considered safe and beneficial for aging skin.
Bianchi et al. (2022)	Italy; 52 participants	Hydrolyzed collagen for 56 days	Hydration, elasticity, wrinkles	The hydration index increased from 50.0 ± 8.7 to 56.8 ± 8.2 , elasticity from 0.604 ± 0.1 to 0.651 ± 0.1 , and wrinkle depth decreased from 0.096 ± 0.01 to 0.089 ± 0.02 by day 56 (all $p<0.01$).
González-Rodríguez et al. (2026)	Spain; 62 participants with signs of aging	8 g hydrolyzed collagen or 300 mg MKARE® for 57 days	Firmness, elasticity, TEWL, hydration	MKARE® produced greater improvements in firmness and elasticity than hydrolyzed collagen and placebo at day 57 ($p<0.05$). Collagen did not show an advantage over MKARE® for the main mechanical parameters, although some changes in barrier function were also observed.
Himeno et al. (2022)	Japan; 44 healthy adults	5 g collagen or fermented collagen peptide for 3 months	Pigmentation, redness	Collagen reduced pigmented patches from the first month and redness by the third month, while fermented collagen reduced pigmented macules and patches ($p<0.05$ – 0.01). No adverse events were reported.
Hyun et al. (2025)	South Korea; 100 adults aged 35–60 years	1,500 mg GABALAGEN® for 12 weeks	Hydration, wrinkles, density, elasticity	Hydration increased by approximately 20% and wrinkle depth decreased by approximately 15% at week 12. Density and elasticity parameters also improved, with several comparisons reaching $p<0.05$. No intervention-related adverse effects were reported.
Jung et al. (2021)	South Korea; 50 participants, 44 completed the study	1,000 mg APCP for 12 weeks	Hydration, roughness, ceramide, NMF	Hydration increased by 7.33% ($p=0.031$) and roughness decreased by 4.09% ($p=0.036$) compared with placebo. NMF amino-acid derivatives increased ($p=0.006$), and total ceramide was higher ($p=0.014$).
Koizumi et al. (2023)	Japan; 31 participants aged 47–87 years	5 g fish collagen peptides for 12 weeks	Skin AGEs, HOMA-R	The change in AGEs was approximately $-4.73\pm 2.39\%$ in the collagen group versus $+4.85\pm 3.79\%$ with placebo; the difference was significant ($p<0.05$). Changes in AGEs correlated with HOMA-R ($r=0.5420$; $p=0.0246$).
Lee et al. (2025)	South Korea; 70 healthy adults	1,650 mg/day for 8 weeks + 2-week discontinuation period	Wrinkles, elasticity, hydration, density, pores	Wrinkle depth and scores, R2/R5/R7, surface and deep hydration, dermal density, and pore parameters improved from baseline and compared with placebo ($p<0.05$). Several effects were maintained two weeks after supplementation was stopped.
Lee et al. (2024)	South Korea; 85 randomized, 78 completed the study	1,000 mg Tripep20 for 12 weeks	Hydration, roughness, wrinkles, elasticity	Hydration increased from week 6 ($p<0.001$). Crow's-feet scores and Ra, Rq, and Rmax improved compared with placebo at week 12 ($p<0.05$); R2/R5/R7 also increased ($p<0.001$ from baseline).
Lee et al. (2023)	South Korea; 100 women aged 30–60 years	1,650 mg CPNS for 12 weeks	Hydration, desquamation, elasticity, wrinkles	Facial hydration was higher than with placebo at weeks 4, 8, and 12 (each reported as $p=0.000$ in the article). Elasticity improved from week 8, and wrinkles decreased by week 12.
Lin et al. (2021)	Taiwan; 50 participants	Fish-collagen formula for 8 weeks	Hydration, brightness, texture, crow's feet, collagen	After 8 weeks, hydration increased by 17.8%, brightness by 5.4%, crow's feet improved by 14.9%, texture by 9.9%, wrinkles by 29.3%, and collagen content by 22.3%. More than 68% of participants showed improvement in skin parameters.
Lin et al. (2026)	Taiwan; 75 healthy adults	Liposomal/non-liposomal CTP	Collagen density,	Both formulations improved dermal collagen density, hydration, and elasticity compared with

Source	Country / Sample	Intervention/ Duration	Main Outcomes	Key Findings
		formulation for 8 weeks	hydration, elasticity, wrinkles, brightness	placebo ($p<0.05$). The liposomal formulation produced greater elasticity at week 8 and was the only formulation to significantly reduce wrinkle area compared with placebo ($p<0.05$).
Maia Campos et al. (2021)	Brazil; 46 women aged 45–59 years	Hydrolyzed fish cartilage for 90 days	Wrinkles, dermal density and structure	Dermal echogenicity increased significantly compared with placebo ($p<0.05$). Nasolabial wrinkles decreased by approximately 31%, and periorbital wrinkles also improved ($p<0.05$). The findings indicated changes extending to dermal structure.
Miyanaga et al. (2021)	Japan; 99 women aged 35–50 years	1 g or 5 g collagen peptides for 12 weeks	Water content, TEWL, NMF, elasticity	Stratum-corneum water content increased in both the 1 g and 5 g groups ($p<0.05$ to $p<0.001$). Cheek TEWL improved with the 5 g dose at week 12 ($p<0.05$), and NMF components increased; elasticity and thickness did not show consistent changes.
Morakul et al. (2024)	Thailand; 72 women aged 40–60 years	5 g tuna collagen peptides for 8 weeks + 2-week discontinuation period	Hydration, TEWL, elasticity, density	At week 8, hydration, elasticity, and density increased and some TEWL measures decreased; most differences from placebo reached $p<0.05$. Most benefits persisted after two weeks without supplementation.
Perin et al. (2025)	Thailand; 198 women	5.5 or 11 g/day for 12 weeks	Hydration, thickness, wrinkles, texture, redness	In mature women, the 11 g dose increased hydration by 4.9% ($p<0.01$) and performed better than placebo ($p<0.05$); temporal skin thickness increased by 9.6% ($p<0.000001$). In younger women, texture and redness improved, and MED increased by 13.8–15.4% ($p<0.001$).
Proksch et al. (2025)	Germany; 66 women aged 35–55 years	2.5 g SCP for 8 weeks	Wrinkles, elasticity, hydration	Eye-wrinkle volume decreased and elasticity and hydration improved from week 4 ($p<0.05$), with more pronounced benefits by week 8. Cellular findings also indicated stimulation of dermal-matrix components ($p<0.05$).
Reilly et al. (2024)	United Kingdom; 138 participants randomized	8 g hydrolyzed collagen + vitamin C for 12 weeks	Dermal collagen, hydration, elasticity, wrinkles	Collagen fragmentation decreased by 44.6% compared with placebo ($p<0.01$). Hydration increased by 13.8%, R2 elasticity by 22.7%, and the Rz wrinkle index decreased by 19.6% (all $p<0.01$).
Sangsuwan & Asawanonda (2021)	Thailand; 36 postmenopausal women	5 g hydrolyzed collagen for 4 weeks + 4-week discontinuation period	Elasticity	Elasticity of the right and left cheeks was better than with placebo at week 4 ($p=0.03$ and $p=0.006$), and the difference was still evident four weeks after supplementation was stopped ($p=0.004$ and $p=0.01$).
Seong et al. (2024)	South Korea; 100 healthy adults	Low-molecular-weight collagen peptides for 12 weeks	Wrinkles, elasticity, hydration, melanin	Wrinkle roughness and volume parameters improved compared with placebo at week 12 ($p<0.0001$). R2, R5, and R7 also improved, together with increased hydration and changes in pigmentation indices.
Sitohang et al. (2021)	Indonesia; randomized, completed the study	90 83 Glutathione + vitamin C + ALA + zinc for 12 weeks	UV spots, polarized spots, skin colour	Improvements tended to be greater in the glutathione group, but the main differences from placebo did not reach statistical significance ($p>0.05$). Reported adverse effects were mild and transient.
Tak et al. (2021)	South Korea; 84 randomized, 74 completed the study	1,000 mg collagen tripeptide for 12 weeks	TEWL, hydration, wrinkles, elasticity	TEWL decreased more in the CTP group ($p<0.05$). The difference remained significant after adjustment for humidity/temperature ($p=0.024$), UVA ($p=0.032$), and combined weather factors ($p=0.031$).
Vleminckx et al. (2024)	East Asian population; 85 participants	5 g collagen peptides for 84 days	Dermal density, hydration, elasticity, wrinkles	Dermal density increased by 6.3% compared with placebo ($p<0.05$). The increase in hydration at day 84 was 8.4% greater ($p=0.023$), and improvements in elasticity appeared earlier in the collagen group.
Wahab et al. (2021)	Indonesia; women	46 600 mg oral glutathione and topical intervention for 8 weeks	Melanin index, L*	The combination produced changes in melanin index and L* that were significantly different from placebo ($p<0.05$). The combination tended to produce a greater brightening effect than monotherapy.

Source	Country / Sample	Intervention/ Duration	Main Outcomes	Key Findings
Wang et al. (2025)	China; 77 healthy women	5 g BCP for 12 weeks + 4-week washout	Hydration, TEWL, dermal density and thickness	Dermal density, hydration, and TEWL improved compared with placebo after 12 weeks ($p<0.05$). Improvements remained evident during the four-week washout, and dermal thickness also increased.
Wisutthathum et al. (2026)	Thailand; 140 randomized, 135 completed the study	5 g collagen + 250 mg glutathione + vitamin E for 12 weeks	Hydration, elasticity, wrinkles, safety	Hydration increased in both groups ($p<0.001$) without a significant between-group difference. R2, R5, and R7 were better than with placebo ($p<0.05$), and crow's-feet roughness decreased more. No product-related adverse events were reported.
Zague et al. (2025)	Brazil; 85 women aged 45–60 years	2.5 g Col-OP for 84 days	Hydration, firmness, elasticity	Firmness and elasticity improved compared with placebo ($p<0.05$), while the change in hydration was not significant. In vitro, procollagen, decorin, and biglycan expression increased ($p<0.001$).
Zhang et al. (2026)	China; 70 healthy women	CP or collagen-elastin mixture for 8 weeks	Wrinkles, texture, hydration, elasticity, microbiota	Wrinkles improved by 12.00% with CP and 14.83% with the mixture; texture by 15.21% and 16.87%; hydration increased by 4.36 and 4.48 units; and elasticity increased by 0.10 units ($p<0.05$). The mixture showed no significant advantage over CP alone.
Žmitek et al. (2024)	Europe; 90 randomized, 87 completed the study	5 g collagen + vitamin C ± hyaluronic acid for 16 weeks	Density, texture, wrinkles, hydration, elasticity	Dermal density increased by 16.3% in the CP group at week 16 ($p<0.001$), and wrinkle volume decreased by 13.8% compared with placebo ($p<0.001$). Hydration and elasticity did not differ significantly; adding hyaluronic acid did not provide a consistent benefit over collagen alone.

Clinical Effectiveness and Safety

Hydration showed the most consistently favourable direction of effect. Multiple collagen studies reported increased skin water content, and several also reported reduced TEWL or increases in NMF and ceramide, indicating changes in barrier-related physiology rather than surface moisture alone (Jung et al., 2021; Miyanaga et al., 2021; Tak et al., 2021; Lee et al., 2023; Morakul et al., 2024; Wang et al., 2025). However, effects were formulation-specific; Wisutthathum et al. (2026), Zague et al. (2025), and Žmitek et al. (2024) did not show a significant hydration advantage for every tested formulation. Elasticity and wrinkle outcomes were also frequently favourable, with several trials reporting improvements in R2/R5/R7 parameters, wrinkle depth, volume, roughness, or visual scores. Imaging-based studies reported changes in dermal density, echogenicity, or thickness, supporting effects beyond surface appearance in some formulations (Maia Campos et al., 2021; Reilly et al., 2024; Vleminckx et al., 2024; Wang et al., 2025; Lin et al., 2026).

Glutathione evidence was smaller and centred on pigmentation. Duperray et al. (2022) reported improved L^* , ITA° , and dark-spot size with reduced glutathione plus L-cystine; Wahab et al. (2021) found changes in melanin index and brightness with combined oral-topical treatment; and Sitohang et al. (2021) found non-significant trends with a multi-ingredient oral formulation. These designs limit attribution to oral glutathione alone. Across studies, short-term tolerability was generally acceptable. Serious product-related adverse events were not a recurring pattern, while reported complaints were mostly mild and transient.

VOSviewer Mapping

Network mapping placed skin hydration, collagen peptides, skin elasticity, skin aging, hydrolyzed collagen, and dermal density near the centre. Overlay mapping suggested a shift from earlier topics such as photodamage and ceramide toward newer work on dermal density, peptide formulation, delivery technology, and persistence of effects. Density visualization identified skin hydration as

the strongest hotspot, followed by collagen peptides and skin elasticity; glutathione remained peripheral because fewer eligible clinical studies were available.

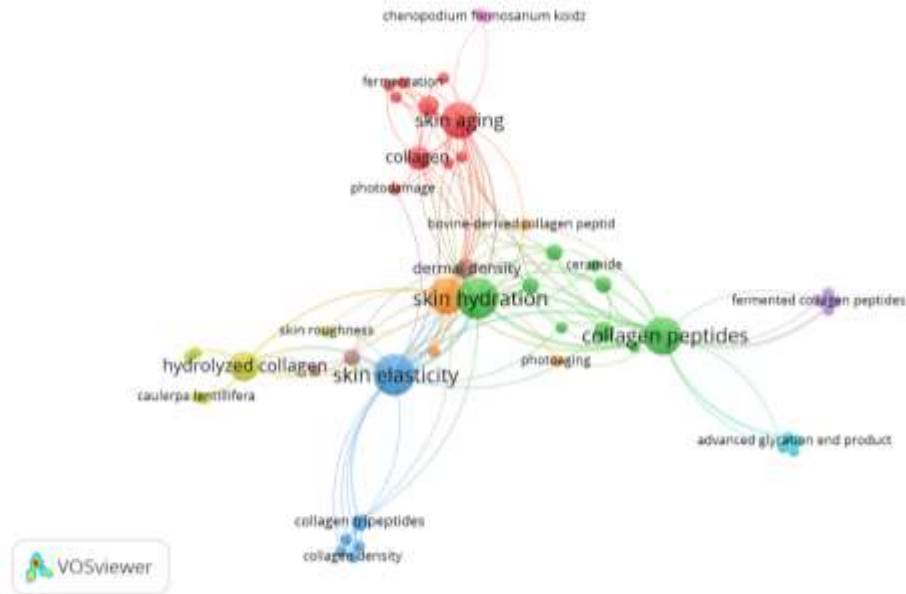


Figure 2. Network Visualization of Oral Collagen and Glutathione Supplementation for Skin Health

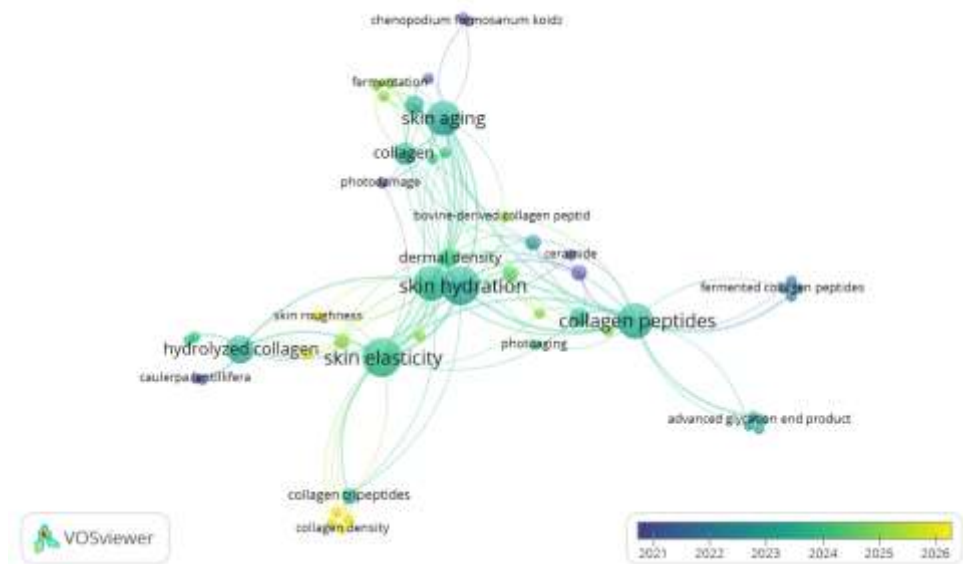


Figure 3. Overlay Visualization of Oral Collagen and Glutathione Supplementation for Skin Health

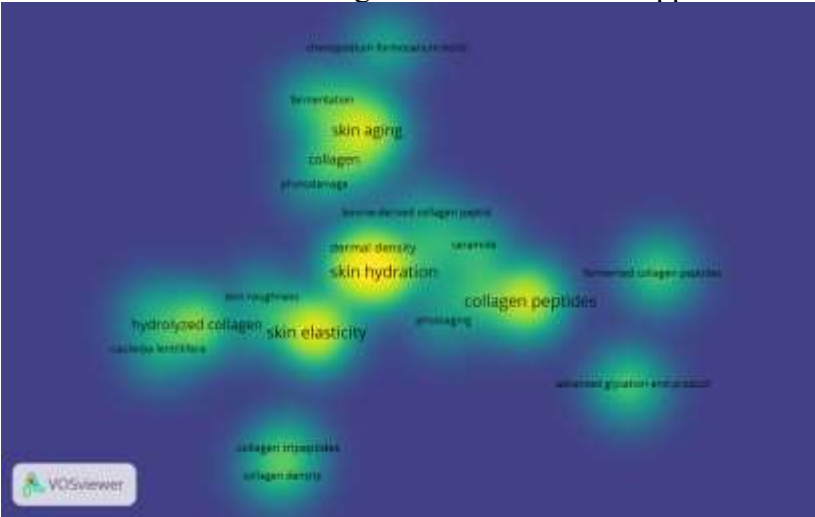


Figure 4. Density Visualization of Oral Collagen and Glutathione Supplementation for Skin Health

DISCUSSION

Collagen Supplementation

The synthesis indicates that collagen has the strongest evidence for hydration, elasticity, wrinkles, and selected dermal-structure outcomes. Hydration findings were supported by TEWL, NMF, and ceramide measurements in several trials, while tissue imaging in other studies showed increased dermal density or thickness. Mechanistically, collagen-derived peptides may be absorbed and influence fibroblast and extracellular-matrix responses, although clinical effects remain dependent on peptide type, dose, formulation, and measurement method (Chae et al., 2023; Fisher et al., 2023; Inacio et al., 2024). The findings are consistent with previous systematic reviews and meta-analyses reporting improvements in hydration and elasticity but also substantial heterogeneity. Importantly, pooled benefits may attenuate when analyses are restricted to higher-quality or non-industry-funded trials, indicating that statistical significance alone should not be interpreted as uniform effectiveness across all collagen products (Pu et al., 2023; Myung & Park, 2025; Moltó-Balado & Simeó-Monzó, 2026).

Glutathione and Combination Formulations

Glutathione studies differed from collagen studies because pigmentation-related outcomes predominated. Improvements in melanin index, brightness, or dark spots were reported in some trials, but evidence was limited by small numbers of studies and frequent use of L-cystine, vitamin C, alpha-lipoic acid, zinc, topical glutathione, or other co-interventions. Positive findings therefore support the tested formulation more directly than glutathione as an isolated oral ingredient (Sitohang et al., 2021; Wahab et al., 2021; Duperray et al., 2022).

Safety and Evidence Quality

Most studies were methodologically strong according to the operational JBI summary, but allocation concealment and blinding were not always fully reported. Safety findings support short-term tolerability rather than long-term safety because most interventions lasted only 4–16 weeks and participants were predominantly healthy adults. The evidence base was also weighted toward women and Asian populations, and multi-ingredient products complicate attribution of effects to individual components. The VOSviewer pattern mirrored the clinical synthesis by showing a dense collagen-hydration-elasticity cluster and smaller branches for pigmentation, glutathione, glycation, delivery systems, and microbiota.

CONCLUSION

Oral collagen supplementation has a stronger clinical evidence base than oral glutathione for skin health. The most consistent collagen benefits were observed for hydration, barrier function, elasticity, wrinkles, and selected measures of dermal structure, while glutathione evidence was more closely related to pigmentation, melanin index, brightness, and dark spots. Short-term safety was generally acceptable for the tested formulations. Most included studies were of good methodological quality, and VOSviewer mapping identified skin hydration, collagen peptides, skin elasticity, and skin aging as the dominant research themes.

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