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Oral Supplementation for Brittle Nails: What Does the Evidence Really Support? A Narrative Review

Jozelio Freire De Carvalho ^{1*}, MD Elizabeth Hautz ², Celso Roberto Cruz Da Colonia Junior ³

¹ Institute of Health Sciences, Federal University of Bahia, Salvador, Bahia, Brazil

¹ Afya Educação Médica, Salvador, Bahia, Brazil

² IBMR University Center, Rio de Janeiro, RJ, Brazil

³ Mathematics Institute, Catholic University of Salvador, Salvador, Bahia, Brazil

* Corresponding Author: Jozelio Freire de Carvalho

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Abstract

Background: Brittle nail syndrome is a common condition characterized by increased nail plate fragility, splitting, and breakage. Although oral supplements are widely marketed for nail health, evidence supporting individual substances, optimal doses, and combination regimens remains uncertain.

Objective: To critically review the clinical evidence for oral supplementation in brittle nails and onychoschizia, focusing on the substances evaluated, doses, treatment duration, magnitude of nail improvement, and methodological strength of the available studies.

Methods: A narrative review with a structured literature search was conducted using PubMed/MEDLINE and Google Scholar from database inception through September 2026. Clinical studies evaluating oral nutritional or nutraceutical interventions for brittle nails, onychoschizia, or nail fragility were considered. Data on intervention, dose, study design, sample size, treatment duration, nail-related outcomes, and methodological limitations were extracted and descriptively synthesized.

Results: Biotin was the most extensively investigated individual supplement. Biotin 2.5 mg/day was associated with improvement in nail firmness and hardness in 91% of evaluable patients in an uncontrolled study and with an approximately 25% increase in nail plate thickness in a microscopy-based study. Biotin 10 mg/day combined with topical hydroxypropyl chitosan resulted in $\geq 50\%$ clinical improvement in 80% versus 53% with topical treatment alone. However, a biotin dose-response relationship has not been established. A recent retrospective study reported $>50\%$ improvement in all patients receiving biotin 1 mg plus pyridoxine 100 mg/day, although confirmation in controlled trials is required. Choline-stabilized orthosilicic acid providing approximately 10 mg/day of silicon demonstrated improvement in a randomized placebo-controlled study. Bioactive collagen peptides (2.5 g/day) increased nail growth by 12% and reduced broken nails by 42% in an uncontrolled prospective study. Favorable findings were also reported for MSM, solubilized keratin-containing preparations, and L-cystine-containing multi-ingredient formulations, although attribution to individual components was frequently impossible.

Conclusions: Several oral interventions show potential benefit for brittle nails, but the overall evidence remains limited and heterogeneous. Biotin 2.5 mg/day has the largest direct clinical evidence base, while stabilized orthosilicic acid is supported by comparatively stronger controlled methodology. Higher biotin doses have not been demonstrated to provide greater efficacy. Current evidence favors targeted supplementation and correction of documented nutritional deficiencies rather than indiscriminate multi-micronutrient use. Larger randomized, placebo-controlled, dose-ranging, and head-to-head trials are needed.

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Keywords: brittle nails, brittle nail syndrome, onychoschizia, nail fragility, biotin, collagen peptides, silicon, nutraceuticals, dietary supplements

Introduction

Brittle nail syndrome is a common nail disorder characterized by increased fragility of the nail plate, frequently presenting as distal lamellar splitting (onychoschizia), longitudinal ridging and fissuring (onychorrhexis), irregularity of the nail surface, and an increased tendency to break. Nail plate brittleness may affect up to 20% of the population, particularly women and individuals

older than 50 years. Although often regarded primarily as a cosmetic problem, brittle nails may cause pain, interfere with daily activities, and negatively affect quality of life.¹

The pathogenesis of brittle nails is multifactorial. Repeated wetting and drying, frequent exposure to detergents, solvents and nail polish removers, manicures, and mechanical trauma may alter nail plate hydration and intercellular cohesion. Brittle nails may also occur secondary to dermatologic or systemic disorders and nutritional deficiencies. Consequently, identification and correction of an underlying cause remain important before empirical supplementation is considered.^[1, 2]

Despite the widespread use of oral supplements marketed for nail health, the scientific basis for many of these products remains uncertain. Commercial preparations may contain biotin, amino acids, collagen peptides, keratin, silicon, zinc, iron, selenium, vitamins, and various combinations of micronutrients. However, the physiological participation of a nutrient in nail formation does not necessarily demonstrate that supplementation improves nail strength in individuals without a corresponding deficiency.^[2, 3]

Biotin is probably the best-known oral supplement used for brittle nails. Early clinical studies reported improvements in nail firmness, hardness, and nail plate thickness with 2.5 mg/day. However, these studies were generally small and uncontrolled, and subsequent reviews have emphasized the need for larger controlled trials and determination of the optimal dose.⁴ More recently, higher doses and combinations of biotin with other nutrients have been investigated. Other interventions, including bioactive collagen peptides, stabilized orthosilicic acid, methylsulfonylmethane (MSM), solubilized keratin, sulfur-containing amino acids, and multimicronutrient formulations, have also produced potentially favorable results.^[3]

The available studies differ considerably in design, sample size, treatment duration, formulation, and outcome assessment. Moreover, some of the most favorable results have been obtained with multi-ingredient preparations, making it impossible to determine which component or interaction between components was responsible for the observed effect. Recent reviews therefore continue to characterize the overall evidence supporting nail supplements as limited and methodologically heterogeneous.^[1, 3, 4]

The aim of this narrative review was to critically summarize the available clinical evidence on oral supplementation for brittle nails and onychoschizia, with particular emphasis on the specific substance or formulation studied, oral dose, duration of treatment, magnitude of improvement in nail parameters, and methodological limitations of the supporting evidence. A secondary objective was to identify interventions that warrant further controlled investigation and to distinguish potentially useful supplementation from empirical micronutrient administration unsupported by clinical evidence.

Methods

Review Design and Literature Search

This study was conducted as a narrative review with a structured literature search focusing on oral nutritional and nutraceutical interventions for brittle nail syndrome, onychoschizia, and related manifestations of nail fragility. PubMed/MEDLINE and Google Scholar were searched from database inception through September 2026. Reference lists of relevant reviews and eligible primary studies were also

manually screened to identify additional publications.

Search terms included combinations of: “brittle nails,” “brittle nail syndrome,” “onychoschizia,” “onychorrhexis,” “nail fragility,” “nail plate,” “oral supplementation,” “dietary supplement,” “nutraceutical,” “biotin,” “pyridoxine,” “vitamin B6,” “collagen,” “collagen peptides,” “keratin,” “silicon,” “orthosilicic acid,” “methylsulfonylmethane,” “MSM,” “cystine,” “cysteine,” “amino acids,” “zinc,” “iron,” “selenium,” “vitamins,” and “micronutrients.”

Additional targeted searches were performed for individual supplements identified during the review process and for combinations of these compounds.

Eligibility Criteria

Studies were considered eligible when they: (1) included human participants with brittle nails, onychoschizia, onychorrhexis, increased nail fragility, or another clearly defined abnormality of nail strength or quality; (2) evaluated an orally administered nutritional supplement, nutraceutical, vitamin, mineral, amino acid, protein-derived product, or combination formulation; and (3) reported a clinical, patient-reported, instrumental, microscopic, or quantitative outcome related to nail growth, thickness, hardness, strength, brittleness, splitting, breakage, surface characteristics, or overall nail condition.

Randomized controlled trials, controlled clinical studies, prospective studies, retrospective studies, and clinically informative case series were considered. Studies in which nail outcomes represented a secondary endpoint were included when the nail data could be independently evaluated.

Studies exclusively evaluating topical therapies were excluded, except when topical treatment served as a comparator or was administered concomitantly with an oral intervention in a manner that allowed assessment of supplementation.

Data Extraction and Synthesis

For each eligible clinical study, the following information was extracted whenever available: oral substance or formulation, daily dose, study design, number of participants, treatment duration, nail-related outcome, magnitude of response, statistical significance, and relevant methodological limitations.

Studies were organized primarily according to the oral intervention rather than chronologically, allowing multiple studies evaluating the same substance, particularly biotin, to be considered together.

Objective outcomes, including nail plate thickness, hardness, growth rate, surface roughness, and validated or semiquantitative clinical scores, were preferentially reported when available. Subjective investigator- or patient-reported improvement was retained when objective measurements were unavailable.

Given the substantial clinical and methodological heterogeneity among studies, particularly regarding interventions, doses, treatment duration, and outcome definitions, no meta-analysis was performed. Results were synthesized descriptively.

Results

Overview of the Evidence

The clinical literature evaluating oral supplementation for brittle nails was limited and heterogeneous. Interventions

included biotin, pyridoxine, bioactive collagen peptides, silicon, MSM, solubilized keratin, and multi-ingredient formulations containing amino acids, vitamins, and minerals. Study designs ranged from randomized controlled trials to prospective uncontrolled studies and retrospective series. Sample sizes were generally small.

Outcome measures were similarly heterogeneous and included nail plate thickness, hardness, surface roughness, growth rate, splitting or breakage frequency, clinical grading scores, and subjective patient- or investigator-reported improvement.

Biotin

Biotin was the most frequently investigated individual supplement.

Floersheim administered biotin 2.5 mg/day to 71 patients with brittle fingernails. Among 45 evaluable patients, 41 (91%) demonstrated definite improvement, characterized by firmer and harder nails, after a mean treatment duration of 5.5 ± 2.3 months.^[5]

Colombo *et al.* subsequently investigated structural changes using scanning electron microscopy. In patients evaluated before and after biotin supplementation, 2.5 mg/day was associated with an approximately 25% increase in nail plate thickness, together with improvement in microscopic evidence of nail plate fragmentation.^[6]

Hochman *et al.* retrospectively evaluated patients with brittle nails prescribed daily biotin. Among 35 evaluable patients, 22 (63%) showed clinical improvement, whereas 13 (37%) reported no change.^[7]

A higher biotin dose was evaluated by Chiavetta *et al.* in a randomized, assessor-blinded trial involving 50 patients. Biotin 10 mg/day combined with hydroxypropyl chitosan nail lacquer was compared with lacquer alone for 4 months. Mean Onychodystrophy Global Severity Score decreased by 62% with combined treatment versus 57% with lacquer alone. A reduction of at least 50% occurred in 80% versus 53%, respectively (p=0.05).^[8]

More recently, Shemer *et al.* evaluated biotin 1 mg/day, pyridoxine 100 mg/day, and their combination in patients with idiopathic fingernail onychoschizia. Biotin monotherapy produced complete response (>90% improvement) in 10% and partial response (>50% improvement) in an additional 45% of patients.^[9]

No well-characterized clinical trial specifically evaluating biotin 5 mg/day as monotherapy for brittle nail syndrome was identified.

Pyridoxine and Biotin–Pyridoxine Combination

In the study by Shemer *et al.*, pyridoxine 100 mg/day for 3 months produced complete response in 11.1% and partial response in 38.9% of patients.^[9]

In contrast, biotin 1 mg/day plus pyridoxine 100 mg/day produced complete response in 69.6% and partial response in the remaining 30.4% of patients. Thus, all patients receiving combination therapy achieved greater than 50% improvement. No adverse events were recorded during the study.^[9]

Bioactive Collagen Peptides

Hexsel *et al.* evaluated 2.5 g/day of specific bioactive collagen peptides in 25 participants for 24 weeks. Treatment was associated with a 12% increase in nail growth rate, a 42%

decrease in the frequency of broken nails, and global clinical improvement in 64% of participants.^[10]

Silicon

Barel *et al.* evaluated oral choline-stabilized orthosilicic acid in a randomized, double-blind, placebo-controlled trial involving 50 women with photodamaged skin. After 20 weeks, nail brittleness decreased significantly from baseline in the active-treatment group, whereas no significant corresponding change occurred in the placebo group. The formulation provided approximately 10 mg/day of silicon.^[11]

Methylsulfonylethane

MSM has been evaluated at 1 and 3 g/day. In a double-blind study involving 63 women, both doses improved expert-rated nail appearance and patient-perceived nail health and strength. Improvements in nail shine and overall appearance were detectable within the first weeks of treatment.^[12]

These data remain preliminary, and the evidence supporting MSM for brittle nails is substantially less developed than that available for biotin.^[3]

Solubilized Keratin-Containing Formulation

Beer *et al.* conducted a randomized, double-blind, placebo-controlled trial involving 50 women. Participants received a formulation containing 500 mg/day of solubilized keratin together with vitamins and minerals or placebo for 90 days. Significant improvements in nail strength and appearance were reported in the active-treatment group compared with placebo.^[13]

Because the intervention was a multi-component formulation, the effect cannot be attributed specifically to keratin.

Amino Acid and Multimicronutrient Formulation

Sparavigna *et al.* conducted a randomized trial evaluating a biomineral formulation containing L-cystine, L-arginine, glutamic acid, vitamin C, vitamin E, vitamin B6, biotin, zinc, iron, and copper in women with onychoschizia.^[14]

After 3 months, oral supplementation increased nail hardness by approximately 43% and reduced nail surface roughness by approximately 18%. Combined oral and topical treatment produced an approximately 50% increase in hardness.^[14]

The study demonstrated measurable changes in nail physical properties but did not permit identification of the contribution of individual ingredients.

Discussion

The present review demonstrates a striking discrepancy between the widespread commercial use of oral supplements for brittle nails and the relatively small clinical evidence base supporting these products. Recent reviews reach a similar conclusion: several compounds show favorable signals, but the evidence is limited by small samples, heterogeneous endpoints, uncontrolled designs, and multi-ingredient formulations.^[1, 3, 4]

Biotin: The Most Studied Intervention, But Without An Established Dose–Response Relationship

Biotin remains the best studied individual oral supplement. The most consistent historical evidence involves 2.5 mg/day, with reported improvements in firmness and hardness and an objectively documented increase in nail plate thickness.^[5–7]

However, these classic studies were predominantly uncontrolled and therefore susceptible to selection bias, regression to the mean, changes in nail-care practices, and spontaneous variation.

The available dose range is particularly interesting. Biotin has been evaluated at 1, 2.5, and 10 mg/day, but these doses have never been adequately compared head-to-head.^[5, 8, 9] No convincing clinical study specifically supporting 5 mg/day was identified.

The randomized study using 10 mg/day demonstrated a higher proportion of patients achieving $\geq 50\%$ improvement when biotin was added to topical HPC, but the mean improvement in OGSS was similar between groups (62% vs 57%).^[8] Thus, current evidence does not establish that 10 mg/day is superior to 2.5 mg/day.

Accordingly, 2.5 mg/day currently represents the biotin dose with the most consistent direct clinical documentation, rather than necessarily the optimal biological dose.

An additional consideration is laboratory interference. Pharmacological biotin supplementation may interfere with biotin-dependent immunoassays and can produce clinically misleading laboratory results, including interference with certain troponin assays.^[15] This issue becomes particularly relevant when higher doses are used.

Biotin and Pyridoxine: A Potentially Important Combination

The 2025 study by Shemer *et al.* provides one of the most provocative observations in the recent literature.⁹ Biotin 1 mg/day and pyridoxine 100 mg/day individually produced relatively modest complete-response rates, whereas their combination resulted in complete response in 69.6% and at least partial response in every treated patient.

The marked difference raises the hypothesis of an additive or synergistic interaction. However, the retrospective design, small sample size, and absence of placebo control prevent definitive conclusions.

The 100-mg/day pyridoxine dose also deserves caution when considering prolonged supplementation because chronic excessive vitamin B6 exposure has been associated with sensory neuropathy. Consequently, future studies should determine whether lower pyridoxine doses maintain the apparent benefit when combined with biotin.

Silicon

Choline-stabilized orthosilicic acid is noteworthy because its supporting study used a randomized, double-blind, placebo-controlled design, which compares favorably with much of the biotin literature.^[11]

The improvement in nail brittleness after supplementation with approximately 10 mg/day of silicon suggests potential benefit. Earlier reviews have consequently identified biotin 2.5 mg/day and silicon 10 mg/day as among the few doses for which specific clinical data are available.^[12]

Nevertheless, evidence remains based on a small number of studies, and results obtained with choline-stabilized orthosilicic acid should not automatically be extrapolated to other forms of silicon with different bioavailability.

Collagen Peptides

Bioactive collagen peptides at 2.5 g/day produced a 12% increase in nail growth and a 42% reduction in broken nails after 24 weeks.^[10] The reduction in breakage is particularly

relevant because it directly addresses one of the major clinical manifestations of brittle nail syndrome.

However, the study was open-label and uncontrolled. Furthermore, nail keratin is not composed of collagen; therefore, a potential effect of collagen supplementation is unlikely to represent direct incorporation into the nail plate. Proposed explanations involving amino acid availability or bioactive peptide signaling remain plausible but incompletely established.

Sulfur-Containing Compounds And Amino Acids

The high sulfur content of keratin provides a biological rationale for investigating sulfur-containing amino acids and compounds. Disulfide bonds contribute to keratin stability, making L-cystine particularly attractive as a candidate for nail-strengthening formulations.

In the randomized study by Sparavigna *et al.*, a formulation containing L-cystine and other amino acids together with vitamins and minerals increased nail hardness by approximately 43% within 3 months.¹⁴ However, the multi-ingredient design makes it impossible to determine the independent contribution of L-cystine.

MSM represents another sulfur-containing intervention. Both 1 and 3 g/day produced improvements in nail appearance in a small double-blind study, but these findings require replication in independent controlled trials using validated measures of brittle nail severity.^[3, 12]

Keratin-Containing Formulations

The randomized placebo-controlled study of a formulation containing 500 mg/day of solubilized keratin plus vitamins and minerals demonstrated improvements in nail strength and appearance.^[13]

This represents an interesting clinical signal but should not be interpreted as proof of efficacy of isolated keratin because several nutrients were administered simultaneously. Moreover, ingested keratin undergoes gastrointestinal digestion; therefore, claims of direct incorporation of orally administered intact keratin into the nail plate require caution.

Replacement of Deficiencies Versus Empirical Supplementation

A critical distinction should be made between correction of nutritional deficiency and supplementation of adequately nourished individuals.

Iron and zinc deficiencies can adversely affect nail structure and growth, and appropriate replacement is indicated when deficiency is documented or strongly suspected.^[1-3] However, this does not establish that additional iron or zinc improves idiopathic brittle nails in individuals with adequate nutritional status.

The same principle applies to other micronutrients commonly incorporated into commercial “hair and nail” preparations. Evidence supporting routine empirical supplementation with vitamins C or E, selenium, copper, or other micronutrients in adequately nourished patients is insufficient.^[2]

This distinction is particularly relevant for selenium, because excessive intake may itself produce hair and nail abnormalities. Therefore, adding numerous micronutrients to a formulation simply because they participate in normal keratin biology is not equivalent to evidence-based supplementation.

Toward An Evidence-Informed Formulation

Taken together, the available evidence suggests that a rational formulation should favor a small number of components with direct clinical evidence or strong mechanistic justification, rather than indiscriminate multivitamin supplementation.

Among individual agents, biotin 2.5 mg/day currently has the largest direct clinical experience.^[5-7] Choline-stabilized orthosilicic acid providing approximately 10 mg/day of silicon has the methodological advantage of placebo-controlled evidence.^[11] Bioactive collagen peptides at 2.5 g/day demonstrated measurable effects on nail growth and breakage, although in an uncontrolled study.^[10]

L-cystine is biologically attractive and was included in a randomized trial demonstrating substantial improvement in nail hardness, but its independent efficacy has not been established.^[14] MSM and solubilized keratin formulations provide additional signals but currently have less robust evidence.^[3, 12, 14]

The biotin-pyridoxine combination deserves particular attention because of the magnitude of response reported in 2025.^[9] Nevertheless, this finding should be regarded as hypothesis-generating until reproduced prospectively, and the pyridoxine dose requires careful consideration.

Limitations

This review has several limitations. It was designed as a narrative review with a structured search rather than a formal systematic review. The available literature itself is also limited by small sample sizes, heterogeneous definitions of brittle nails, different treatment durations, and substantial variation in outcome assessment.

Some studies relied on subjective improvement, whereas others measured nail thickness, hardness, roughness, growth, breakage, or composite clinical scores. These endpoints cannot be considered interchangeable.

Several studies also investigated multi-component products, preventing identification of the active ingredient. Publication bias is possible, particularly in the nutraceutical field, and some studies involved commercially formulated products.

These limitations, together with substantial clinical and methodological heterogeneity, preclude meaningful meta-analysis and prevent determination of a single optimal oral regimen.

Future Research

Future research should prioritize randomized, placebo-controlled and dose-ranging trials using standardized definitions and objective nail outcomes.

For biotin, a direct comparison of 1, 2.5, 5, and 10 mg/day would be particularly informative and could determine whether a dose-response relationship exists.

The promising biotin-pyridoxine findings should be replicated prospectively, preferably evaluating lower pyridoxine doses. Similarly, simplified combination studies involving evidence-supported candidates such as biotin, L-cystine, and bioavailable silicon could determine whether combination therapy provides additive benefit over individual components.

Future trials should incorporate standardized measures including nail plate thickness, hardness, splitting frequency, growth rate, and validated brittle-nail severity scores. Because fingernail growth is slow, follow-up periods of at

least 4–6 months would provide a more appropriate assessment of newly formed nail plate.

Conclusion

Oral supplementation may improve brittle nails, but the strength of evidence varies substantially among interventions. Biotin, particularly at 2.5 mg/day, remains the most extensively documented individual supplement, although much of the evidence derives from small and older studies. Higher biotin doses have not been demonstrated to provide superior efficacy.

Choline-stabilized orthosilicic acid and bioactive collagen peptides have shown promising clinical effects, while L-cystine, MSM, solubilized keratin formulations, and the biotin-pyridoxine combination warrant further investigation. Iron, zinc, and other micronutrients should primarily be used to correct documented or suspected deficiencies rather than routinely incorporated into empirical supplementation.

Overall, current evidence favors a targeted rather than indiscriminate supplementation strategy. Larger randomized, placebo-controlled, dose-ranging, and head-to-head trials are required to establish the optimal substance, dose, duration, and combination of oral interventions for brittle nail syndrome.

Declarations

Funding

The authors received no specific funding for this work.

Conflicts of Interest

The authors declare that they have no conflicts of interest relevant to the content of this article.

Ethical Approval

Ethical approval was not required because this study is a narrative review of previously published literature and did not involve human participants, identifiable patient data, or experimental procedures.

Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Data Availability

No new datasets were generated or analyzed during the current study. All information discussed in this review was obtained from previously published sources cited in the manuscript.

Use of Artificial Intelligence

Generative artificial intelligence (ChatGPT, OpenAI) was used to assist with translation of author-prepared text from Portuguese into English and with English-language editing for grammar, clarity, and readability. The authors critically reviewed and edited all AI-assisted content and take full responsibility for the accuracy, integrity, and final content of the manuscript. Artificial intelligence was not used as an author and did not independently determine the scientific conclusions of the review.

Table 1: Clinical evidence for oral supplementation in brittle nails and onychoschizia

Substance/ formulation	Oral dose	Study/design	N	Duration	Main nail outcome
Biotin	1 mg/day	Shemer <i>et al.</i> ; retrospective comparative study [9]	20 biotin	3 months; assessment at 6–9 months	10% complete + 45% partial response; 55% achieved >50% improvement
Biotin	2.5 mg/day	Floersheim; clinical study [5]	71; 45 evaluable	5.5 ± 2.3 months	91% definite improvement in firmness/hardness
Biotin	2.5 mg/day	Colombo <i>et al.</i> ; scanning electron microscopy [6]	32; paired subgroup	Several months	Approximately 25% increase in nail plate thickness
Biotin	Daily supplementation	Hochman <i>et al.</i> ; retrospective [7]	35 evaluable	Variable	63% clinical improvement
Biotin	5 mg/day	No adequate primary study identified	—	—	Evidence insufficient
Biotin	10 mg/day + HPC lacquer	Chiavetta <i>et al.</i> ; randomized, assessor-blinded [8]	50	4 months	OGSS –62% vs –57%; ≥50% reduction in 80% vs 53%
Pyridoxine	100 mg/day	Shemer <i>et al.</i> [9]	18	3 months	11.1% complete + 38.9% partial response
Collagen peptides	2.5 g/day	Hexsel <i>et al.</i> ; prospective open-label [10]	25	24 weeks	+12% growth; –42% broken nails; 64% clinical improvement
Silicon (choline-stabilized orthosilicic acid)	≈10 mg/day silicon	Barel <i>et al.</i> ; randomized, double-blind, placebo-controlled [11]	50	20 weeks	Significant improvement in nail brittleness vs baseline; no corresponding placebo change
MSM	1 g/day	Muizzuddin & Benjamin; double-blind [12]	32	Up to 16 weeks	Significant improvement in nail appearance/shine and perceived strength
MSM	3 g/day	Muizzuddin & Benjamin; double-blind [12]	31	Up to 16 weeks	Significant improvement in nail appearance/shine and perceived strength
Solubilized keratin + micronutrients	Keratin 500 mg/day + vitamins/minerals	Beer <i>et al.</i> ; randomized, double-blind, placebo-controlled [13]	50	90 days	Significant improvement in nail strength and appearance vs placebo
Biotin + pyridoxine	Biotin 1 mg + B6 100 mg/day	Shemer <i>et al.</i> [9]	23	3 months	69.6% complete + 30.4% partial response; 100% achieved >50% improvement
L-cystine + amino acids + vitamins/minerals	Multi-ingredient formulation	Sparavigna <i>et al.</i> ; randomized [14]	50 randomized	3 months	+43% hardness; –18% roughness; combined oral/topical ≈+50% hardness

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