EFFECTS OF 5% CENTELLA ASIATICA EXTRACT CREAM FOR SKIN WHITENING

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ABSTRACT
Fair skin has traditionally been associated with beauty, prestige, and social advantage in many Asian cultures, leading to a strong demand for skin-lightening products. Melanin synthesis, regulated primarily by the enzyme tyrosinase, plays a critical role in determining skin pigmentation, and inhibiting this pathway forms the basis of many whitening agents. Conventional treatments include hydroquinone, arbutin, kojic acid, niacinamide, and ascorbic acid, alongside physical methods such as lasers, chemical peels, and cryotherapy. However, concerns regarding safety and toxicity have shifted attention toward herbal alternatives. Centella asiatica (Gotu Kola), widely recognized for its anti-inflammatory, antioxidant, and skin-hydrating properties, has recently been investigated for its potential tyrosinase-inhibiting and skin-whitening effects. Literature suggests that Centella asiatica, when combined with other active compounds, demonstrates tyrosinase-inhibiting activity and skin-lightening potential. However, evidence on its independent efficacy remains limited. This study aims to evaluate the whitening effect and user satisfaction of a topical Centella asiatica cream, thereby contributing to the evidence base for safe and affordable herbal agents in cosmetic dermatology.
Keywords: Centella asiatica, Gotu Kola, Skin Whitening, Hyperpigmentation, Melanin Index, Tyrosinase Inhibitor, Natural Cosmetic

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INTRODUCTION

Skin complexion is a key determinant of beauty and social perception, especially in Asian cultures where fair skin is historically associated with higher social status, wealth, and desirability. This cultural value has driven the global demand for skin-lightening products, including both topical and oral agents, with tyrosinase inhibitors occupying a central role in cosmetic development (Pillaiyar et al., 2017). Human skin color is largely determined by genetics, but external factors such as ultraviolet (UV) exposure, hormonal regulation, and diet also influence pigmentation. Central to this process is the enzyme tyrosinase, which catalyzes the hydroxylation of tyrosine to L-DOPA and its subsequent oxidation to dopaquinone, critical steps in melanin biosynthesis (Chang, 2012). Excessive tyrosinase activity leads to increased melanin production and hyperpigmentation, making it an attractive therapeutic target.Current therapeutic approaches to hyperpigmentation include chemical agents such as hydroquinone, kojic acid, niacinamide, arbutin, and ascorbic acid derivatives, in addition to procedural interventions such as chemical peels, cryotherapy, and laser therapy (Gillbro & Olsson, 2011; Kumari et al., 2018). However, many synthetic products are associated with long-term side effects including cytotoxicity, irritation, and ochronosis, which has prompted growing interest in natural and plant-derived alternatives with safer profiles. One such botanical extract is *Centella asiatica*, traditionally used in Asian medicine for wound healing, anti-inflammation, and cognitive enhancement. Preclinical and clinical studies have suggested that its triterpenoid compounds exhibit antioxidant, anti-inflammatory, and anti-tyrosinase properties, thereby reducing melanin synthesis and improving skin tone (Arora et al., 2018; Ha et al., 2010). Despite these promising findings, most investigations have evaluated *Centella asiatica* in combination with other active ingredients, and little is known about its efficacy as a standalone topical whitening agent. This study therefore aims to evaluate the effect of 5% *Centella asiatica* extract cream on skin whitening, side effects, and patient satisfaction.

LITERATURE REVIEWS

Melanin synthesis is a complex biological process regulated by melanocytes in the basal epidermis. Within these cells, melanosomes act as specialized organelles where tyrosinase, the rate-limiting enzyme, catalyzes the hydroxylation of tyrosine to L-DOPA and its oxidation to dopaquinone. The type of melanin produced—eumelanin or pheomelanin—determines pigmentation intensity, with eumelanin providing photoprotection while pheomelanin is less effective and may contribute to oxidative stress under ultraviolet (UV) exposure (Gillbro & Olsson, 2011). UV radiation is one of the strongest external stimulators of melanogenesis, enhancing tyrosinase activity and reducing natural inhibitory mechanisms, which explains the tanning response and the persistence of hyperpigmentation after chronic sun exposure (Kameyama et al., 1996).

Conventional depigmenting agents include hydroquinone, arbutin, kojic acid, niacinamide, and azelaic acid, many of which act through direct tyrosinase inhibition or melanosome transfer suppression. While effective, their long-term use is limited by cytotoxicity, irritation, and contact dermatitis. This has increased interest in plant-derived compounds with safer profiles. Among these, *Centella asiatica* has gained attention for its broad dermatological benefits, including antioxidant, wound-healing, and anti-inflammatory effects, along with potential tyrosinase-inhibitory activity (Arora et al., 2018; Bylka et al., 2013). Preclinical studies have shown that Centella asiatica extracts reduce melanin production in a dose-dependent manner (Ha et al., 2010), while early clinical data indicate improvements in hyperpigmentation and skin brightness when incorporated into topical formulations (Dewi et al., 2023). These findings suggest that *Centella asiatica* may serve as a promising natural alternative in skin-whitening products. Despite this evidence, the role of *Centella asiatica* as a sole active ingredient in skin whitening requires further investigation.

Pathophysiology

Hyperpigmentation results from dysregulated melanogenesis, characterized by increased tyrosinase activity and melanin overproduction within melanocytes. UV exposure, hormonal changes, and inflammation are major triggers, leading to enhanced synthesis of L-DOPA and dopaquinone and greater pigment transfer to keratinocytes (Ebanks et al., 2009). In addition, oxidative stress perpetuates melanocyte activation, and pheomelanin contributes to free radical formation, further exacerbating pigmentation (Gillbro & Olsson, 2011). Treatment strategies aim to interrupt these pathways through tyrosinase inhibition, suppression of melanosome transfer, antioxidant activity, or accelerated epidermal turnover. *Centella asiatica* is postulated to influence pigmentation primarily via anti-tyrosinase and antioxidant mechanisms, making it a biologically plausible candidate for safe and effective skin whitening.

***Centella asiatica* extract**

General Information: *Centella asiatica* (L.) Urban, commonly known as Gotu Kola or Tiger Grass, is a perennial herbaceous plant belonging to the Apiaceae family. Indigenous to tropical and subtropical regions of Asia, Africa, and Central America, it has been revered as a "panacea" in traditional medicinal systems across China, India, and Sri Lanka for over 3,000 years. Its formal recognition is evidenced by its inclusion in numerous pharmacopoeias, including the Indian, European, and British, with the official drug standardized to contain a minimum of 6.0% total triterpenoid derivatives expressed as asiaticoside (Bylka et al., 2013). In Ayurvedic practice, it is valued for restoring memory and longevity, while in Oriental medicine it is used to overcome physical and mental fatigue (Arora et al., 2018). Traditionally, it has been applied topically for centuries to treat wounds, burns, eczema, and other dermatological conditions (Bylka et al., 2013).

Chemical Constituents: The primary biologically active compounds in *C. asiatica* are triterpenoid saponins, notably asiaticoside, madecassoside, and their sapogenins, asiatic acid and madecassic acid (Bylka et al., 2013). The plant also contains a variety of other beneficial compounds, including polyphenols, flavonoids (such as quercetin, kaempferol, rutin, and apigenin), and volatile oils (e.g., caryophyllene, farnesol, elemene), which contribute to its broad pharmacological activities (Yasurin et al., 2015).

Preparation of Standardized Extracts: Pharmacological and clinical studies utilize both undefined aqueous/alcoholic extracts and well-defined, titrated extracts. Key standardized extracts include TECA (Titrated Extract of *Centella asiatica*), TTFCA (Total Triterpenic Fractions of *Centella asiatica*), and CATTF (*Centella asiatica* Total Triterpenic Fraction). These are commercially known as Madecassol®, Centellase®, or Blastoestimulina®, typically containing approximately 40% asiaticoside and 60% of a mixture of asiatic and madecassic acids (Bylka et al., 2013).

Biological Activities: *C. asiatica* exhibits a remarkably broad spectrum of pharmacological activities, including antioxidant, anti-inflammatory, anti-aging, antimicrobial (antibacterial, antiviral, antifungal), anti-allergic, anti-cancer, and anti-hypertensive properties. It demonstrates significant wound healing, skin moisturizing, and memory improvement effects, and has been traditionally used for treating mental fatigue, bronchitis, asthma, kidney disorders, urethritis, hypertrophic scars, and leukorrhea (Bylka et al., 2013).

Anti-Tyrosinase Activity: The extract's potential as a skin-lightening agent is linked to its anti-tyrosinase activity (Ha et al., 2010). Clinical studies have demonstrated that formulations containing *C. asiatica* extract significantly reduce the melanin index in human skin, improving tone and reducing hyperpigmentation (Saraf et al., 2012; Dewi et al., 2023). In vitro research has confirmed that both ethanolic and aqueous extracts inhibit tyrosinase activity and melanin synthesis in a dose-dependent manner, with efficacy enhanced by ultrasonification during extraction. The most effective extracts reduced melanin production to approximately 84% of control levels, performing comparably to ascorbic acid (Ha et al., 2010).

Toxicity : *C. asiatica* is generally considered non-toxic with rare side effects at recommended doses. However, topical commercial products can cause reactions in some individuals; Madecassol® has been associated with delayed hypersensitivity like eczema after prolonged use, while Centellase® has caused faster-onset reactions like blistering and itching. These differences highlight that formulation and concentration can influence the safety profile (Bylka et al., 2013).

RESEARCH METHODOLOGY

Twenty subjects, aged between 25 and 45 years with Fitzpatrick skin types III to V, who met all inclusion criteria, were enrolled in the study. Volunteers were thoroughly informed about the research purpose, detailed procedures, and anticipated risks and benefits. Participants completed and signed an informed consent form prior to enrollment. A comprehensive history was obtained, including general information, previous medical history, and any conditions relevant to the study. The test product was a cream containing 5% *Centella asiatica* aqueous extract (HETEROSIDES®, Product Code: 80142C, SEPPIC SAS, France). HETEROSIDES® is a standardized aqueous extract of *Centella asiatica* leaves, composed mainly of triterpenoid saponins including asiaticoside, madecassoside, asiatic acid, and madecassic acid. According to ISO 16128 guidelines, it is classified as of 100% natural origin. The extract is supplied as a cream-colored crystalline powder, water-soluble, and was incorporated into the cream base following a controlled production process (hydration, homogenization, emulsification, and cooling) to ensure homogeneity and stability. The final formulation contained 5% w/w extract. Before beginning the study, a patch test was performed by applying the 5% *Centella asiatica* extract cream to the subject's arm for at least 24 hours. During this period, activities that could cause excessive sweating were prohibited. The test site was reexamined for any reactions between 48 and 96 hours after application. Volunteers showing positive patch test results (score ++ or higher) were excluded from the study.

Participants applied the cream twice daily to the entire face for 12 weeks. Additionally, they were provided with a mild facial cleanser and a sunscreen with SPF 50 and PA+++ for use throughout the study period.

Efficacy was assessed at baseline, week 4, week 8, and week 12 using two objective tools: the Mexameter® MX18 for melanin index measurement and the VISIA® Complexion Analysis System for photographic evaluation of pigmentation. Safety was monitored by recording adverse events, including erythema, pruritus, or allergic reactions, at each follow-up visit. Patient satisfaction was evaluated at week 12 using a standardized questionnaire scored from -1 (worsening) to +4 (excellent improvement). All assessments were performed by three independent dermatologists to minimize observer bias.

RESEARCH RESULTS

Twenty healthy volunteers aged 25-4 years with Fitzpatrick skin type III to V and compatible with all the inclusion criteria were registered. All twenty volunteers complete this study. This study enrolled 20 volunteers (6 males, 14 females) with a mean age of 29.9±3.3 years (range: 26-37 years). Occupational distribution comprised 15 students, 3 employees, and 2 housewives. All participants reported a history of cosmetic product usage but no recent skin-whitening treatments. Daily sun exposure between 10:00-16:00 averaged 105± 40.5 minutes (range: 30-180 minutes). Fitzpatrick skin typing classified 14 participants as Type III and 6 as Type IV. No underlying medical conditions were reported. Half of the cohort (n=10) used dietary supplements, while the remainder (n=10) consumed no regular medications. All subjects had histories of UV exposure-a recognized exacerbating factor for melanogenesis.

Table 1 Statistical analysis of melanin index score that applied 5% *Centella asiatica* extract cream measured by Mexameter® MX 18 at baseline,4th wk,8th wk and 12th wk

melanin index score at baseline,4th,8th and 12th week (n=20)	Mean	Std. Deviation
Baseline	298.16	9.16
4th week	293.83	10.09
8th week	288.84	9.97
12th week	281.85	9.80

p-value determined by repeated measurement ANOVA< 0.001

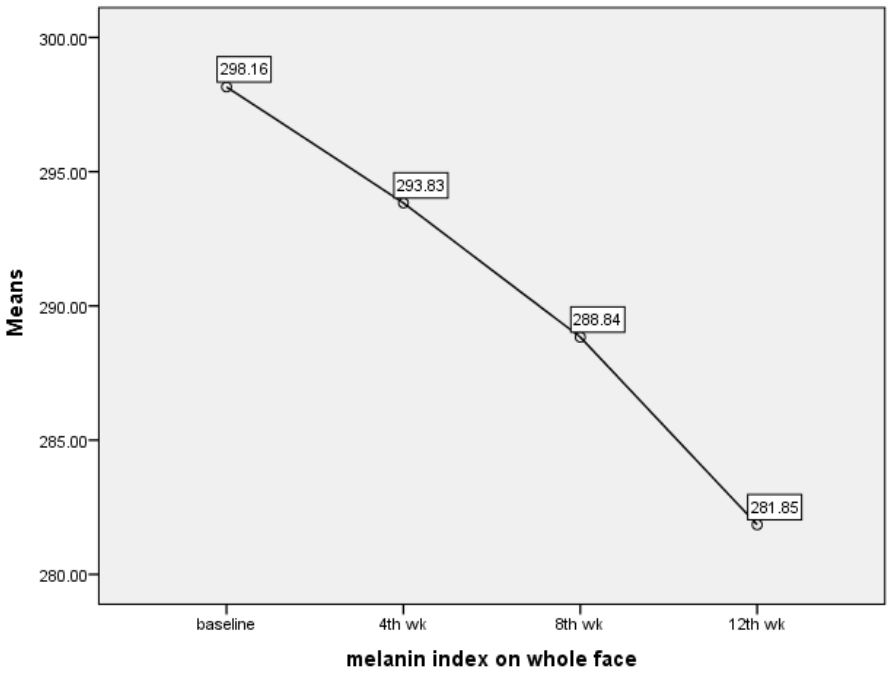

Figure 1 Line graph showing melanin index scores at baseline, follow-up visits 4th, 8th, and 12th weeks after last treatment session.

A statistical analysis demonstrated that the application of a 5% *Centella Asiatica* extract cream significantly reduced the mean melanin index of the total face over a 12-week period. The mean score decreased progressively from a baseline of 298.16 ± 9.16 to 293.83 ± 10.09 at week 4, 288.84 ± 9.97 at week 8, and 281.85 ± 9.80 at week 12. This reduction observed at each measurement interval was found to be statistically significant ($p < 0.001$).

Table2 Multiple comparison (post Hoc Test) of Melanin Index Score that applied 5% *Centella asiatica* extract cream at baseline, 4th, 8th and 12th week

Duration	Pair comparison	Mean difference	SD	p-value
Baseline	4th week	4.32	3.00	<0.0001
	8th week	9.32	4.25	<0.0001
	12th week	16.31	5.76	<0.0001
4th week	8th week	5.00	3.30	<0.0001
	12th week	11.98	5.06	<0.0001
8th week	12th week	6.99	3.76	<0.0001

Note: Multiple comparison determines by the paired t test.
*The mean difference is significant at the 0.05 level.

Post-hoc multiple comparisons revealed that the mean melanin index score for the total face area demonstrated a statistically significant reduction from baseline at each follow-up interval ($p < 0.0001$). The mean decreases were 4.32 at week 4, 9.32 at week 8, and 16.31 at week 12, indicating a progressive and dose-dependent lightening effect over the treatment period.

Dermatologist Evaluation Score

Table 3 Statistically Analysis of dermatologist evaluation score compared on 4th, 8th and 12th week

dermatologist evaluation score			
Improvement	**Week4**	**Week8**	**Week12**
-1 = worse	-	-	-
0 = no change	2	0	-
1 = 1-25% fairness improvement	10	3	-
2 = > 25-50% moderate improvement	8	13	14
3 = > 50-75% good improvement	-	4	6
4 = > 75-100% excellent improvement	-	-	-

The dermatologist evaluation scores, presented in Table 3, demonstrate a progressive improvement in skin fairness over the 12-week study period. At Week 4, the majority of subjects (90%) exhibited minimal improvement: 50% (n=10) showed 1-25% fairness improvement and 40% (n=8) showed >25-50% moderate improvement, while 10% (n=2) showed no change. No subjects exhibited worsening or higher levels of improvement at this stage. By Week 8, a notable shift toward greater improvement was observed: 65% (n=13) achieved >25-50% moderate improvement and 20% (n=4) showed >50-75% good improvement, while minimal improvement (1-25%) decreased to 15% (n=3). No subjects remained unchanged or showed higher improvement tiers. At Week 12, moderate improvement (>25-50%) was observed in 70% (n=14) of subjects, and good improvement (>50-75%) increased to 30% (n=6). No subjects were rated as having no change, worsening, minimal improvement (1-25%), or excellent improvement (>75-100%) at the final assessment. These results indicate a clear trend of increasing efficacy over time.

Patient Satisfaction Score

Table 5 Patient satisfaction score on 12th week (n=20)

Patient Satisfaction score	**Week12**
-1 = worse	-
0 = No satisfaction, no change	-
1 = Little satisfaction	-
2 = Moderate satisfaction	12
3 = Very satisfied	8
4 = Extremely satisfied	-

Analysis of patient satisfaction at Week 12 demonstrated that 40% (n=8) were 'very satisfied' with the 5% *Centella asiatica* extract cream, contrasted with 60% (n=12) reporting 'moderate' satisfaction.

Adverse effects

Throughout the treatment period, no adverse effects were observed or reported in any participant using the 5% *Centella asiatica* extract cream. This finding confirms the favorable safety profile of the formulation at the tested concentration.

DISCUSSION & CONCLUSION

Skin whitening, also referred to as skin lightening or brightening, is widely practiced across the world, particularly in Asia, where fairer skin is frequently associated with beauty, youthfulness, and higher social status (Gillbro & Olsson, 2011). Many individuals pursue treatments to reduce hyperpigmentation caused by melasma, sun exposure, or post-inflammatory changes. Although agents such as hydroquinone, kojic acid, and arbutin are effective, they are limited by adverse effects including irritation, dermatitis, and even exogenous ochronosis with prolonged use. Given these limitations, attention has shifted toward herbal and plant-based alternatives, which are perceived to be safer and gentler on the skin. One such natural remedy is *Centella asiatica,* a traditional medicinal herb with well-documented anti-inflammatory, antioxidant, and wound-healing properties. Previous in vitro study Ha et al. (2010) confirms its rich composition of triterpenoids (asiaticoside, madecassoside, asiatic acid) and flavonoids, compounds well-documented to possess potent antioxidant, anti-inflammatory, and wound-healing properties. Previous research also evaluated *Centella asiatica* in combination with other active ingredients, making it difficult to know its individual contribution. This study investigate *Centella* alone at 5% concentration to determine its true whitening potential, safety, and patient satisfaction.

Potential Mechanisms of Action: The skin-whitening effects observed in this study are consistent with several proposed biological mechanisms of *Centella asiatica*. Its triterpenoid saponins, particularly asiaticoside and madecassoside, directly inhibit tyrosinase activity, thereby blocking the conversion of tyrosine to melanin precursors (Ha et al., 2010). In addition, flavonoids such as quercetin and kaempferol act as potent antioxidants, reducing reactive oxygen species (ROS) that are known to upregulate melanogenesis. Recent evidence also suggests that *Centella asiatica* may downregulate microphthalmia-associated transcription factor (MITF), a key regulator of tyrosinase and related melanogenic enzymes, further suppressing melanin synthesis (Dewi et al., 2023). Its anti-inflammatory properties, mediated by asiatic and madecassic acids, may also reduce post-inflammatory pigmentation by dampening cytokine-driven melanocyte stimulation. Finally, its ability to promote collagen synthesis and accelerate keratinocyte turnover may facilitate faster removal of melanin-containing cells, contributing to an even skin tone. Together, these multimodal pathways provide biological plausibility for the clinical whitening effects demonstrated in this trial.

This study employed a pre-test/post-test experimental design to evaluate the efficacy and safety of a topical 5% *Centella asiatica* extract cream for facial skin whitening in adults with Fitzpatrick skin types III-V over a 12-week treatment period.

A total of 20 volunteers were enrolled in this clinical study. The participant demographic profile was characterized by a mean age of 29.9 years (SD ±3.3), spanning from 26 to 37 years, with a gender distribution of 30% male (n=6) and 70% female (n=14). The majority of the cohort (75%) were categorized as students, while the remainder were employed (15%) or identified as housewives (10%). All subjects reported regular use of cosmetic products but confirmed no recent history of skin-whitening treatments. Participants demonstrated considerable daily sun exposure during peak hours (10:00-16:00), averaging 105 minutes (±40.5 SD) with a range of 30-180 minutes. According to the Fitzpatrick classification, the majority (70%, n=14) were categorized as skin type III, while the remaining 30% (n=6) were type IV. No underlying medical conditions were reported among participants. Half of the cohort (n=10) reported using dietary supplements, while the other half (n=10) did not take any

regular medications. All subjects had histories of UV exposure, establishing a uniform risk profile for melanogenesis activation across the study population.

The primary outcome measure, the melanin index measured by Mexameter® MX18, demonstrated a highly significant reduction over the 12-week study period. The mean melanin index decreased progressively from a baseline of 298.16 ± 9.16 to 293.83 ± 10.09 at week 4, 288.84 ± 9.97 at week 8, and 281.85 ± 9.80 at week 12 ($p < 0.0001$, Repeated Measures ANOVA). The post-hoc analysis further clarified this progression, revealing that the reduction was not only significant from baseline but also between each subsequent follow-up visit. For instance, the mean difference between baseline and week 12 was 16.31, which was substantially larger than the difference between baseline and week 4 (4.32). This indicates a cumulative, time-dependent effect of the *Centella asiatica* cream, suggesting that prolonged use yield progressively better whitening results.

The dermatologist evaluation scores provided a complementary clinical perspective to the objective Mexameter data. The results showed a clear trend towards improvement. At week 4, 90% of participants showed some degree of improvement (50% minimal, 40% moderate), while 10% showed no change. By week 12, all participants demonstrated improvement, with 70% showing moderate improvement (>25-50% reduction in hyperpigmentation) and 30% achieving good improvement (>50-75% reduction). Patient satisfaction at week 12 was positively correlated with the clinical results. A majority of participants (100%) reported satisfaction, with 60% expressing "moderate satisfaction" and 40% reporting being "very satisfied." The absence of any reports of "no satisfaction" or "worse" underscores the product's acceptability and perceived efficacy from the user's perspective. Throughout the 12-week period, no adverse effects such as irritation, erythema, contact dermatitis, or paradoxical hyperpigmentation, were observed or reported by any participant.

Conclusions

This study found that 5% *Centella asiatica* extract cream is effective and safe for facial skin whitening in individuals with Fitzpatrick skin types III-V. Over 12 weeks, participants showed a significant reduction in melanin index and progressive improvement in dermatologist assessments, with most reporting moderate to high satisfaction. No adverse effects were observed, highlighting its excellent safety profile. Overall, *Centella asiatica* cream offers a promising natural alternative for gradual and irritation-free skin lightening.

Suggestions

Based on the findings of this study, 5% *Centella asiatica* extract cream can be considered a safe and effective natural option for gradual skin whitening, particularly for individuals with sensitive skin or intolerance to conventional agents. However, the study has limitations, including a relatively small sample size, restriction to Fitzpatrick skin types III-V, and a short follow-up period of 12 weeks. These factors limit the generalizability of the results to broader populations and prevent conclusions about long-term safety and efficacy. For future research, larger randomized controlled trials are recommended, with inclusion of participants across a wider range of skin types and backgrounds. Direct comparisons with standard treatments such as hydroquinone or kojic acid would help clarify relative effectiveness. Further studies should also investigate higher concentrations of *Centella asiatica*, potential synergistic effects in combination formulations, and long-term safety profiles beyond 12 weeks to better establish its full clinical potential.

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