



Perspective

Glutathione in dermatology: A bright future or fading hype?

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ABSTRACT

Glutathione, a potent endogenous antioxidant, has garnered significant attention in dermatology for its purported skin-lightening and anti-aging benefits. While its mechanisms – primarily inhibition of tyrosinase and modulation of melanogenesis – suggest potential efficacy, clinical evidence remains mixed. Several studies have demonstrated its ability to reduce pigmentation and improve skin health when administered orally or topically, yet inconsistencies in outcomes and concerns over bioavailability persist. Furthermore, the safety of intravenous administration remains controversial, with reports of adverse effects prompting regulatory warnings. Different dosing schedules, duration of use, and the longevity of effects remain areas of ongoing investigation. This viewpoint critically examines the current evidence on glutathione's dermatological applications, weighing its benefits against potential risks. Given the ethical and medical implications, further high-quality research is needed to establish standardized protocols, optimal dosages, and long-term safety profiles.

Keywords: Anti-aging, Anti-oxidant, Glutathione, Skin-lightening

INTRODUCTION

Glutathione, a tripeptide composed of glutamine, cysteine, and glycine, is a powerful endogenous antioxidant essential for cellular detoxification, immune function, and maintenance of redox balance. Recently, it has gained popularity in dermatology for its purported skin-lightening and anti-aging benefits. However, despite its widespread use, the scientific community remains divided on its efficacy and long-term safety. In addition, its role in dermatological conditions beyond hyperpigmentation, such as atopic dermatitis and psoriasis, is an emerging area of research.

This viewpoint critically evaluates the current evidence on glutathione's role in dermatology, highlighting both its potential benefits and limitations.

MECHANISMS OF ACTION

Glutathione influences skin pigmentation primarily through inhibition of tyrosinase, the rate-limiting enzyme in melanin biosynthesis.^[1] It also shifts melanogenesis toward the production of pheomelanin (a lighter pigment) over eumelanin (a darker pigment), thereby contributing to a brighter skin tone.^[2] In addition, its strong antioxidant properties counteract oxidative stress-induced melanogenesis, further supporting its role in skin lightening.^[3] Studies suggest that oral and topical formulations can modulate these pathways, but the extent of clinical benefit remains

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debated.^[4] Emerging formulations, such as liposomal glutathione, aim to enhance bioavailability and efficacy, representing a promising avenue for future dermatological applications.

CLINICAL APPLICATIONS: WHAT DOES THE EVIDENCE SAY?

Multiple clinical studies have evaluated glutathione's efficacy for skin lightening. A randomized controlled trial by Weschawalit *et al.* (2017) demonstrated that oral glutathione (250 mg/day) significantly reduced melanin index after 4 weeks of administration, supporting its potential as a depigmenting agent.^[2] Similarly, Handog *et al.* (2016) reported skin-lightening effects in Filipino women following the use of glutathione, though the degree of lightening varied among individuals.^[3]

Topical applications of glutathione have also shown promise. A study by Etnawati *et al.* (2019) evaluated skin care formulations containing reduced glutathione (0.1–0.5%) and reported significant improvements in skin brightness and reduction in hyperpigmented lesions over 8 weeks.^[4] These findings suggest that both oral and topical glutathione formulations may have beneficial dermatological effects, though optimal dosing and duration of treatment remain areas for further research. A summary of key clinical studies is provided in Table 1.

Other dermatological applications: Beyond skin lightening, glutathione has been studied for its anti-aging properties. It is believed to improve skin elasticity, reduce wrinkles, and enhance overall skin health by mitigating oxidative damage.^[5] A systematic review by Dilokthornsakul *et al.* (2019) highlighted evidence suggesting that glutathione contributes to improved skin hydration and elasticity, though more extensive trials are necessary to confirm these benefits.^[5]

Several additional studies have examined the synergistic effects of glutathione with other antioxidants, such as vitamin C and alpha-lipoic acid, suggesting enhanced efficacy in reducing oxidative stress and improving skin health.^[6-8] Furthermore, emerging research explores its role in photoprotection by reducing ultraviolet-induced damage and suppressing inflammatory responses in skin cells.^[9]

SAFETY AND ADVERSE EFFECTS

While oral and topical glutathione is generally considered safe, concerns have been raised about intravenous (IV) administration, which is commonly used in esthetic clinics despite limited regulatory approval. The use of IV glutathione for skin lightening has been associated with potential adverse effects, including renal dysfunction, thyroid dysfunction, and severe dermatologic reactions.^[10] Health authorities, including the Food and Drug Administration and the Philippine Dermatological Society, have issued warnings against its unregulated use due to safety concerns.^[11,12]

Furthermore, the long-term effects of chronic glutathione supplementation remain unknown. Sachdev *et al.* (2022) emphasized the need for longitudinal studies to evaluate its metabolic and dermatologic impact, particularly in populations with extended use.^[13] The possibility of rebound hyperpigmentation upon discontinuation has also been suggested, warranting cautious and regulated use.^[14] The variability in responses to different dosing schedules also underscores the need for standardized guidelines.

CONTROVERSIES AND LIMITATIONS

Despite its increasing popularity, the efficacy of glutathione remains controversial. Several studies have reported inconsistent outcomes, with some showing minimal or no significant impact on skin pigmentation.^[1,5] The variability in individual responses, differences in formulation bioavailability, and lack of standardized protocols contribute to the ongoing debate.^[15]

In addition, ethical concerns arise regarding the promotion of skin-lightening agents, as these may reinforce colorism and unrealistic beauty standards.^[16] Dermatologists must consider these social implications when recommending glutathione-based treatments.

FUTURE PERSPECTIVES

Future research should focus on optimizing glutathione delivery methods to enhance efficacy and safety. Liposomal glutathione, a formulation designed to improve bioavailability, has emerged as a promising alternative, potentially allowing for better absorption and prolonged effects.^[17] In addition, combination therapies incorporating

Table 1: Summary of key studies on glutathione in dermatology.

Study	Form	Dose	Duration	Outcome
Weschawalit <i>et al.</i> (2017) ^[2]	Oral	250 mg/day	4 weeks	Significant skin-lightening
Handog <i>et al.</i> (2016) ^[3]	Oral	500 mg/day	12 weeks	Improved melanin index
Etnawati <i>et al.</i> (2019) ^[4]	Topical	0.1–0.5%	8 weeks	Reduced hyperpigmentation
Dilokthornsakul <i>et al.</i> (2019) ^[5]	Systemic review	Various	Various	Mixed results, efficacy debated

glutathione with other antioxidants, such as vitamin C and alpha-lipoic acid, warrant further exploration for synergistic benefits. Advanced research methodologies, including omics-based approaches, may also provide deeper insights into individual responses to glutathione treatment.

CONCLUSION

Glutathione presents an intriguing avenue for dermatological applications, particularly in skin-lightening and anti-aging therapies. While emerging evidence supports its efficacy in oral and topical forms, the safety of IV administration remains questionable. Given the inconsistencies in clinical outcomes and the lack of long-term safety data, caution is warranted before widespread endorsement. Future research should focus on high-quality, well-controlled studies to establish definitive conclusions regarding its dermatological benefits and risks.

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