

Glabridin

Glabridin is an isoflavan-type flavonoid monomer extracted from the roots of *Glycyrrhiza glabra*. It is a naturally lipophilic brightening active ingredient with multi-mode benefits including potent tyrosinase-inhibiting activity, melanogenesis suppression, anti-inflammatory redness relief, antioxidant and anti-photoaging effects. It takes effect at low concentrations with extremely low irritation and serves as a core raw material for high-end brightening systems. Different from glycyrrhizic acid / liquiritin, glabridin produces no hormone-like side-effects.

It simultaneously ameliorates hyperpigmentation, erythema and photo-aging-related sallowness, and is suitable for sensitive-skin and post-aesthetic-procedure formulations.

Trade Name	Glabridin
INCI Name	GLABRIDIN
CAS Number	59870-68-7
EC Number	611-908-7
Appearance	98 % high-purity grade: white crystalline powder; 40 % / 10 % grades: pale-yellow crystalline powder
Purity	≥99%
Solubility	Insoluble in water and glycerol; freely soluble in ethanol, propylene glycol, 1,3-butanediol, DMSO and oils; solubilization with polyols / surfactants is required
Recommended Dosage & Formulation pH	Brightening serums / lotions / creams: 0.05 %-0.10 %; pH 4.0-6.5
Storage	Store hermetically protected from light under dry ambient conditions (10-30 °C); shield from light and oxygen. Shelf-life of unopened original packaging: 36 months. Sensitive to ultraviolet radiation and oxygen; formulate with vitamin E and sodium phytate for stabilization.
Regulatory Compliance	Listed in China Catalogue of Used Cosmetic Raw Materials; included in EU CosIng database; safety assessment passed by US CIR; compliant for spot-removing & brightening cosmetic ingredients.

Human Skin Safety and Tolerance

48-hour occlusive patch test: No erythema, edema or stinging observed among subject

groups treated with 0.05%, 0.1 % and 0.5 % concentrations.No delayed adverse response in the 72-hour follow-up.

Abraded-skin irritation test: Irritation potential on post-procedure abraded and barrier-compromised skin shows no significant difference from blank vehicle control. It alleviates irritation-related erythema triggered by alpha-hydroxy acids and retinol.

Phototoxicity/photosensitization test: No photosensitization or phototoxicity upon UVA/UVB irradiation. No risk of rebound hyperpigmentation when used in daytime with sunscreen.

Repeated Open Application Test (ROAT) for sensitization: Sensitization rate <0.3 %, no contact-sensitization potential. Free of hormone-related side-effects such as edema or elevated blood pressure (distinguished from glycyrrhizic acid).

12-week long-term clinical trial on sensitive skin: Continuous application of 0.05% glabridin significantly reduced erythema index among subjects with rosacea and inflammatory flushing; no dryness, desquamation or stinging was reported.

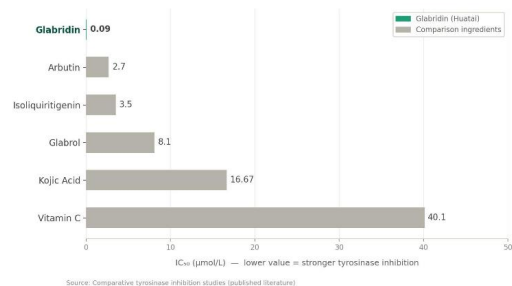
Long- term use at concentrations $\leq$ 0.05 % carries extremely low risk for all skin types. 0.1 % is the maximum safe loading level for leave - on cosmetic products. Avoid total combined loading exceeding 0.1 % in multi- brightening-ingredient formulations.

In-Vitro Efficacy Assays

Study 1: Potent Tyrosinase Inhibition Assay (Core Brightening Target)

- **Model** – Mushroom tyrosinase and human recombinant tyrosinase; IC₅₀ (half- maximal inhibitory concentration) as evaluation criterion.

- **Key data** – Glabridin IC₅₀ = 0.09 μ mol/L; kojic acid 16.67 μ mol/L, arbutin 2.7 μ mol/L, pure vitamin C 40.1 μ mol/L. Under identical test conditions its tyrosinase-suppressing potency is 185- fold that of kojic acid, 30- fold that of arbutin, and 445- fold that of pure vitamin C.



- **Inhibition mechanism** – Mixed-mode non-competitive inhibition. Instead of occupying substrate-binding sites, glabridin binds to the copper-ion catalytic centre of tyrosinase to alter protein conformation and permanently decrease enzymatic catalytic capacity. It also down-regulates key melanogenic enzymes TRP- 1 / TRP- 2.

Lower bar-chart IC₅₀

values correspond to lower required concentration for tyrosinase suppression and stronger brightening potency.

Glabridin delivers activity at trace dosages, with IC₅₀ markedly lower than mainstream commercial brightening agents.

Study 2: Melanogenesis Inhibition Assay in B16F10 Melanoma Cells

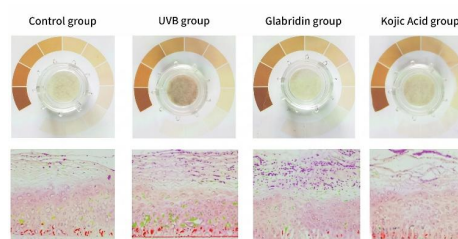
Massive epidermal melanin deposition occurs in the UVB- challenged model group. Under equal concentrations, melanin deposition in the glabridin-treated group is lower than in the

kojic-acid group with obvious epidermal pigment lightening.

- **Cell model** – α -MSH-stimulated hyperpigmented B16F10 cells

- **Gradient concentrations** – 0.2 μ M, 1 μ M, 5 μ M glabridin; 48 h treatment

- **Assay results** – The 5 μ M group achieved a 21.9 % reduction in total cellular melanin content, with significant down-regulation of intracellular tyrosinase activity. It concurrently suppresses the MITF transcription factor (master switch for melanogenesis) to block melanin biosynthesis at source, and inhibits dendrite outgrowth to reduce melanosome transfer from melanocytes toward keratinocytes.



At 5 μ M, total cellular melanin content decreased by 21.9 %, accompanied by significant down-regulation of intracellular tyrosinase activity. Meanwhile, it suppresses the MITF transcription factor (master regulator of melanogenesis), blocks melanin biosynthesis at the source, and inhibits dendrite outgrowth to reduce melanosome transfer from melanocytes to keratinocytes.

Study 3: Anti- Inflammatory & Soothing In- Vitro Assay (Inflammation- induce d pigmentation pathway)

- **Model** – UVB- irradiated human keratinocytes and LPS- induced inflammatory stimulation model

- **Detection targets** – NF- κ B signalling pathway, pro- inflammatory mediators TNF- α , IL- 6, COX- 2

- **Assay conclusion** – 0.05 μ M glabridin inhibits the release of 62 % of pro- inflammatory cytokines. It blocks inflammation- triggered MC1R receptor activation to reduce post- inflammatory hyperpigmentation (PIH), and alleviates cutaneous erythema and burning caused by UV- irradiation, chemical peeling and retinol treatment.

At 0.05 μ M, glabridin inhibits 62 % of pro- inflammatory- cytokine release. It blocks inflammation- triggered MC1R receptor activation to mitigate post- inflammatory hyperpigmentation (PIH), and alleviates cutaneous erythema and burning flushing induced by ultraviolet radiation, chemical peeling and retinol treatment.

Study 4: Antioxidant & Free- Radical- Scavenging Assay

- **Detection systems** – DPPH, ABTS and metal- ion- chelating model

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At 10 μ mol/L, metal- ion- chelating rate reaches 67.3 %. Formulation addition at 0.05 % lowers skin lipid peroxidation value by 42.7 %. Its bis- phenolic- hydroxyl structure scavenges UVA / blue- light- generated ROS free- radicals and suppresses AGE- related glycation- mediated sallowness for anti- photoaging benefits.

Study 5: Anti- Photoaging Cellular Protection Assay

- **Treatment** – Human fibroblasts pre- incubated with 0.03 % glabridin for 24 h prior to UVB irradiation

- **Read-out markers** – γ -H2AX DNA- damage biomarker, ROS level, collagen expression

Cellular UV-induced DNA damage reduced by 38 %. It suppresses matrix metalloproteinase MMP- 1 to mitigate collagen breakdown, help preserve skin elasticity and fade sun- induced fine lines and photo- aging- related roughness.

Transdermal Permeation Profile

Glabridin is a lipophilic small- molecule isoflavonoid ($\text{LogP} \approx 3.5$) capable of penetrating intercellular lipid spaces of the stratum corneum to reach melanocytes within the epidermal basal layer.

- **Permeation distribution** – Enriched across full epidermis; partial fraction reaches superficial dermis, directly acting on melanocytes, keratinocytes and fibroblasts.
- **Limitation** – Crystallization readily occurs in pure aqueous solutions. Solubilization via ethanol / polyols / nanoliposomes is required to improve transdermal delivery; nanoliposome encapsulation elevates basal- layer accumulation by 3.2- fold.
- **Synergistic combination** – Co- formulation with niacinamide extends skin residence time and realizes dual- pathway brightening: “enzymatic inhibition plus melanosome- transport blockade”.

Comprehensive Multi- Functional Skincare Mechanisms

• Potent Up- stream Spot- Fading & Brightening (Core Differentiated Advantage)

Unlike niacinamide which only blocks melanosome transfer, glabridin acts at the upstream stage of melanogenesis;

Exerts potent non- competitive inhibition against tyrosinase and TRP- 1 / TRP- 2 to block dopa- oxidation- driven melanin formation;

Down- regulates MITF and MC1R melanogenic transcription proteins and reduces autonomous melanin production by melanocytes;

Inhibits melanocyte dendrite extension and lowers melanosome- transfer efficiency toward keratinocytes.

• Anti- Inflammatory Redness Relief & Prevention of Inflammatory Rebound Hyperpigmentation

Blocks NF- κ B inflammatory signalling cascade and suppresses pro- inflammatory cytokines TNF- α and IL- 6. Rapidly soothes erythema triggered by post- aesthetic- procedure irritation, chemical peeling and retinol. Mitigates erythematous acne marks and rosacea- related flushing, and reduces inflammation- provoked hyperpigmentation at source.

- **Broad-Spectrum Antioxidation for Sallowness and Photo- Aging Improvement**

Blocks NF- κ B inflammatory signalling cascade and suppresses pro- inflammatory cytokines- TNF- α and IL- 6. Rapidly soothes erythema triggered by post- aesthetic- procedure irritation, chemical peeling and retinol. Mitigates erythematous acne marks and rosacea- related flushing, and reduces inflammation- provoked hyperpigmentation at source.

- **Photodamage Repair and Retardation of Fine Lines and Laxity**

Protects fibroblast DNA against UV- mediated injury; down- regulates collagen- degrading enzyme MMP- 1 and reduces degradation of type I / III collagen. Long- term application ameliorates photo- aging- related roughness, dry fine lines and skin laxity.

- **Gentle Stabilization & Mitigation of Side- Effects from Irritant Actives**

When combined with high- concentration acids, retinol and pure vitamin C, it alleviates dryness, stinging and desquamation and improves the mildness of brightening formulations. Suitable for sensitive and thin- barrier skin.

Human Clinical Efficacy Studies

Study 1: 56- Day Human Brightening & Spot- Fading Clinical Trial

- **Test sample** – Brightening serum containing 0.04 % glabridin, applied full- face twice daily

- **Assessment instruments** – Mexameter melanin- index meter,

VISIA imaging system, skin colorimeter for ITA° and L* lightness value

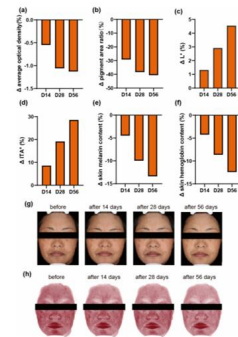


FIGURE 1 • 1 Analysis of the facial parameters percentage change before and after 14 days, 28 days, and 56 days range of the female with ITA° 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 98, 100. (a) Average optical density (OD) (%), (b) Pigmented area ratio (%), (c) A.U. (%), (d) ITA° (%), (e) Skin transparency index (%), (f) A.U. (%), (g) Representative images of skin whitening results, (h) Representative images of skin whitening results. n = 30.

Day 14: Melanin index (MI) decreased by 8.12 %; skin- brightness L* value increased by 2.7 %.

Day 56: Pigmented- area proportion reduced by 40.59 %; ITA° skin- transparency index elevated by 9.84 %. Visible fading of melasma and erythematous acne marks. No adverse reactions including irritation, rebound hyperpigmentation or dryness were observed.

Study 2: UVB- Induced Erythema Repair Controlled Clinical Trial (28 erythema- prone sensitive- skin subjects)

- **Groups** – 0.05% glabridin lotion versus blank placebo; daily application after

UVBchallenge

- **Trial duration** –Continuous 28- day treatment

At week 28, erythema index (EI) decreased by 13.99 %; transepidermal water loss (TEWL) reduced by 18 %. Significant improvement observed for barrier- fragile skin and seasonal flushing.

Study 3: 12- Week Anti-Sallowness Anti- Photoaging Clinical Trial (29 early- mature subjects aged 30- 48 years)

Continuous 12 - week use of 0.03 % glabridin cream increased skin - elasticity parameter R2 by 14.2 %. Noticeable improvement in glycation- mediated facial sallowness and sun- induced roughness.

Recommended Addition- Level Reference Table

Product Category	Recommended Concentration	Core Functional Goals
Brightening & spot- fading serums, ampoule stock solutions	0.03%–0.1%	Stubborn acne marks, melasma, sun- induced dullness
Soothing- repair post- aesthetic- procedure masks	0.005%–0.03%	Redness relief, prevention of rebound hyperpigmentation, mitigation of peeling- agent irritation
Anti- aging firming creams, daytime sun- care products	0.01%–0.05%	Anti- photoaging, sallowness reduction, sun-spot prevention
Sebum- control anti- acne gels, toners	0.01%–0.04%	Inflammatory papules, erythematous acne marks, inflammatory dullness

Formulation- Processing Considerations

- **Dissolution process:** Pre- solubilize in polyols(ethanol / propylene glycol) at low temperature of 40- 50 °C, then incorporate into emulsified systems after cooling below 40 °C. Prolonged high- temperature heating is prohibited, asit causes oxidative discoloration and activity loss.

- **pH control:** Stable pH range 4.0- 6.5. Avoid strong- alpha- hydroxy- acid systems below pH3 and strongly alkaline systems above pH9, which trigger rapid degradation and deactivation.
- **Stabilization system:** Must co- formulate with 0.1 %- 0.5 % tocopherol (vitaminE) plus sodium phytate- EDTA to isolate oxygen and metal ions and prevent oxidative yellowing.
- **System compatibility:** Prioritize anhydrous- polyol, water- in- oil and nanoliposome delivery systems. Crystallization readily occurs in high- water- phase formulations; solubilizers must be added.
- **Incompatibility notes:** Avoid long- term co- existence with raw- materials containing high- levels of free iron / copper ions and high- concentration free alpha- hydroxy acids (pH < 3).

Authoritative Synergistic Formulation Combinations

Synergistic Ingredient	Mechanism of Action	Recommended Usage Concentration
Niacinamide	Glabridin exerts upstream tyrosinase inhibition; niacinamide blocks melanosome transport while repairing skin barrier and reducing irritation, achieving full- cascade brightening	Glabridin 0.03- 0.08 % + Niacinamide 2- 4 %
Tranexamic Acid	Tranexamic- acid blocks inflammatory pro- melanogenic signalling; glabridin delivers enzymatic inhibition plus redness- relieving activity, effective for severe post-inflammatory hyperpigmentation and erythematous acne marks	Glabridin 0.02- 0.05 % + Tranexamic Acid 2- 3 %
3- O- Ethyl Ascorbic Acid	Dual tyrosinase- inhibitory effect; EAA reduces pre- formed melanin, glabridin provides anti- inflammatory protection against rebound hyperpigmentation for amplified spot- fading and brightening efficacy	Glabridin 0.01- 0.03 % + Retinol 0.1- 0.3 %
Retinol	Glabridin mitigates retinol- caused desquamation and erythema irritation; retinol boosts collagen- synthesis anti- aging performance, synergistically fading photo- aging spots and fine lines	Glabridin 0.01- 0.03 % + Retinol 0.1- 0.3 %
Panthenol + Ceramide	Reinforce stratum- corneum barrier, improve glabridin transdermal penetration for mild brightening formulas for	Glabridin 0.02- 0.05 % + Ceramide 0.1- 0.5 %

	sensitive skin	
Ferulic Acid + Vitamin E	Build antioxidant matrix to stabilize glabridin, dual free-radical scavenging against UV- induced oxidative stress for long- term anti- sallowness and anti- photoaging benefits	Glabridin 0.03 % + Vitamin E 0.3 % + Ferulic Acid 0.05 %

Raw- Material Key Summary

• Core Differentiated Advantages

High- potency brightening at trace dosage: Its tyrosinase-

suppressing activity greatly surpasses kojic acid, arbutin and vitamin- C derivatives.

It takes effect at concentrations as low as

0.01 % without requiring high- concentration tolerance build- up.

Full- cascade brightening: Inhibits upstream melanogenic enzymes, down- regulates MITF and blocks melanosome transport, distinguishing it from single- pathway brightening actives.

Combined brightening- and- anti- inflammation:

Simultaneously ameliorates pigmentation and erythema, addressing two major pain- points: post- inflammatory hyperpigmentation and post- aesthetic- procedure rebound darkening.

Ultra- low- irritation with broad compatibility: Non- cytotoxic, non- photosensitizing.

Neutralizes irritation caused by acids / retinol. Compatible with dry- sensitive, oily- acne - prone and thin- barrier skin.

Anti- photoaging & antioxidant: Scavenges free- radicals and inhibits glycation, combining brightening and anti- aging benefits and suitable for daytime sunscreen formulations.

• **Overview of Core Efficacy:** Broad pH- tolerance window. Long- term storage is

stable. Suitable for brightening and anti- aging formulations without discoloration or fading. Also, sun spots, acne marks and uneven sallow complexion.

Anti-inflammatory redness relief: Blocks pro-inflammatory cytokines, soothes erythema and burning sensation and prevents inflammation- driven hyperpigmentation.

Antioxidation for sallowness improvement: Scavenges UVA / blue-light- derived free-radicals, suppresses AGE formation and alleviates sleep- deprivation and photo- aging-related dull yellow complexion.

Photodamage repair: Protects fibroblast DNA, reduces collagen degradation and fades sun-induced fine lines, roughness and laxity.

Gentle stabilization: Mitigates irritation triggered by acids, retinol and high- concentration vitamin C; delivers brightening- and- repair benefits for post- aesthetic- procedure and sensitive skin.

• Suitable User Profiles

Subjects suffering sallow dull complexion, acne marks, melasma, sun spots and post-inflammatory hyperpigmentation;
Fragile skin prone to erythema and rebound hyperpigmentation after chemical peeling or aesthetic-medical treatments;
Individuals with rosacea, seasonal dry-sensitivity and intolerance toward high-potency irritant
brightening actives;
Persons exposed to long-term outdoor UV-radiation and screen blue-light suffering photo-aging roughness and sun-spot formation;
All-skin-type daily-care users pursuing mild spot-fading without building tolerance to high-strength actives.

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