

UP302

UP302, fully known as dimethoxytolyl-4-propylresorcinol, is a highly potent skin-brightening active belonging to the diarylpropane class. Its prototype originates from the extract of the Chinese medicinal plant *Dianella ensifolia*. After over a decade of molecular optimization and scaled-up artificial synthesis, following the implementation of the Regulations on Supervision and Administration of Cosmetics, it became the first domestically registered raw material for a new brightening and spot-fading use (NMPA Raw Material Registration No. 20250001) completed through re-evaluation of an already-used ordinary raw material, with over 18 years of global evidence-based research accumulation. Relying on its multi-dimensional pathways of dual tyrosinase regulation + anti-glycation + anti-inflammation and anti-darkening, it serves as a core ingredient for high-end spot-fading, anti-yellowing, and post-aesthetic procedure repair formulations.

UP302 has a complete panel of toxicological, skin irritation, sensitization, and phototoxicity tests. It is listed in China's Catalogue of Used Cosmetic Ingredients (2021 Edition) and the EU cosmetic ingredient inventory, and is compliant for use in spot-fading special-certificate products, daily brightening serums, and post-aesthetic procedure repair lotions. Early plant-extracted raw materials had limited purity and high cost; modern synthesis processes can stably achieve a 98.0% high-purity grade with irritating by-products eliminated, greatly improving skin tolerability. A compliant addition range of 0.2%–0.6% fully delivers brightening efficacy, specifically targeting glycation-induced sallowness, sun-induced hyperpigmentation, post-acne PIH, senile spots, melasma, and post-procedure darkening, suitable for all skin types, sensitive skin, and post-procedure repair product lines.

Product Information

Product Name	UP302
INCI Name	DIMETHOXYTOLYL PROPYLRESORCINOL
CAS No.	869743-37-3
EC No.	N/A
Appearance	Light brown to off-white powder
Purity	≥98.0%
Solubility	Soluble in organic solvents such as methanol and ethanol
Recommended Use Level and Formulation pH	Facial leave-on serum: 0.2%–0.5%; body leave-on lotion: 0.05%–0.15%; pH: 4.5–5.5
Storage	Store in original sealed container at 10–30°C; protect from light, high temperature, and moisture.
Regulatory Status	Globally recognized

Human Skin Tolerability

Safety assessment based on MOS values: Compared with 1% kojic acid (MOS=88), 1% UP302 achieves a topical MOS value as high as 421. MOS ≥ 100 is judged safe for topical use. At the same addition concentration, its safety threshold is significantly higher than that of kojic acid and phenylethyl resorcinol, with ample safety margin for long-term facial use.

Human Repeat Closed Patch Test for evaluating allergy/skin irritation/skin sensitization: (0.2%, 0.4%, 0.6% in corn oil base); continuous closed patch for 21 days; UP302 showed no persistent erythema, edema, or itching, and was judged to be a non-irritating, non-sensitizing active.

Chamber scratch test for evaluating skin irritation propensity: (0.2%, 0.6% in petrolatum base) on scratched skin; compared with the blank saline control group, no significant redness, swelling, stinging, or peeling irritation reactions were observed, with extremely low irritation potential on compromised skin, suitable for post-aesthetic procedure and thin/sensitive skin repair and brightening formulations.

In Vitro Enzyme Inhibitory Activity

- **Enzyme** — Mushroom tyrosinase
- **Substrate** — L-DOPA
- **Test substances** — UP302, 4-butylresorcinol, phenyl ethyl resorcinol, kojic acid, arbutin
- **Measurement** — Spectrophotometry; spectral range 490 nm
- **Performance quantification** — Half maximal inhibitory concentration (IC₅₀), i.e., the concentration required to inhibit 50% of enzyme activity

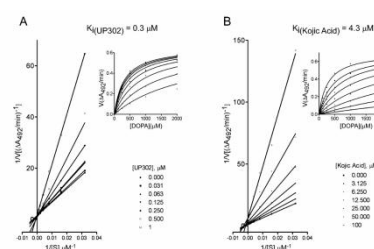


Fig. 3. Kinetics of Mushroom Tyrosinase Inhibition by UP302 and Kojic Acid
A series of substrate-velocity plots were taken at increasing concentrations of L-DOPA as a substrate in the presence of UP302 (A) or Kojic Acid (B). The curves were fit using a non-linear regression method. K_d values were calculated from global (shared) fit using GraphPad Prism software. Lineweaver-Burk plots for the inhibition of mushroom tyrosinase by UP302 or Kojic acid.

UP302 is a reversible competitive tyrosinase inhibitor. At equimolar concentrations, its enzyme-inhibitory activity is 22 times that of kojic acid, with melanin-inhibitory efficacy superior to kojic acid, arbutin, and phenylethyl resorcinol; only weaker than 4-butylresorcinol. With its unique dual pathway of accelerated tyrosinase degradation, its overall efficacy surpasses ordinary single-target resorcinols.

In Vitro Melanin Inhibitory Activity

- **Cells** — B16-F1 mouse melanoma cells, human primary melanocytes
- **Incubation time** — At 37°C, 5% CO₂, continuous culture with treatment for 72 h; cell viability assay incubated for 24 h
- **Test substance** — UP302
- **Measurement** — 590 nm
- **Performance quantification** — Half maximal effective concentration (EC₅₀), i.e., the concentration required to inhibit 50% of melanin synthesis

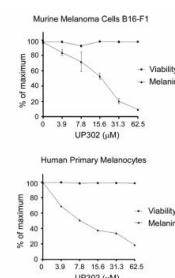


Fig. 6. The Effects of UP302 on Melanin Production and Viability of B16-F1 Cells and Primary Human Melanocytes
Mouse melanoma cells B16-F1 and primary human melanocytes were treated with increasing concentrations of UP302 for 72 h. At the end of treatment cell viability was assessed using a tetrazolium conversion assay (MTT). Production of melanin was measured by taking absorbance of culture media (B16-F1 cells), or by extracting intracellular melanin from pooled cells with KOH (primary human melanocytes) as outlined in Experimental.

UP302 exhibits no cytotoxicity at effective melanin-inhibitory concentrations. At 0.6 mM, the melanin synthesis inhibition rate reaches 86%, efficiently blocking melanin accumulation without damaging melanocytes, and does not induce redness or sensitivity due to cytotoxicity.

In Vitro Spot-Fading Efficacy Test on 3D Human Skin Equivalent (MelanoDerm)

- **Model** — MelanoDerm™ MEL-300-B 3D reconstructed human epidermal skin (containing high-pigment donor-derived human keratinocytes + human melanocytes, air-liquid interface culture, simulating the real human epidermal topical environment)
- **Test samples** — UP302 (0.1% in propylene glycol base), 1% kojic acid positive control, blank vehicle (80% propylene glycol)
- **Observation method** — Day-14 endpoint macroscopic tissue photography + quantitative detection of melanin content in tissue
- **Application method** — Daily topical application, continuous culture for 14 days
- **Evaluation indicators** — Degree of skin pigmentation, total tissue melanin content, epidermal cell integrity

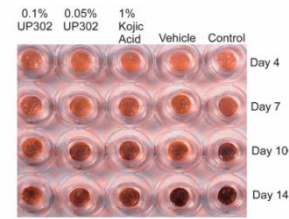


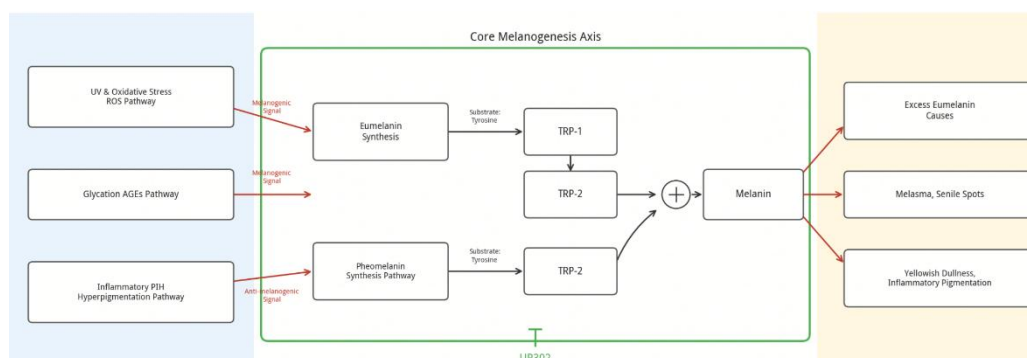
Fig. 7. The Effects of UP302 and Kojic Acid on Melanin Production in Reconstructed Skin Tissue
Samples of reconstructed skin were treated for up to 14 d with indicated concentrations of UP302, Kojic acid, or vehicle (80% propylene glycol). At the end of treatment tissues were fixed in formalin. The samples were photographed altogether at the end of the 14 d experiment.

After 14 consecutive days of topical application, the 0.1% UP302 group showed visibly significant pigment fading in 3D skin, with photographic evidence demonstrating a lighter skin tone than the blank vehicle group. Quantitative melanin assays showed that the pigment-fading effect of 0.1% UP302 was equivalent to 1% kojic acid, achieving excellent melanin inhibition at low addition levels. Epidermal structure remained intact throughout, with no damage to melanocytes or keratinocytes, confirming that UP302 has no epidermal cytotoxicity at efficacious concentrations. Compared with simple cell suspension assays, 3D reconstructed skin more closely mimics the real environment of transdermal absorption and pigment production in human epidermis, directly supporting the actual topical brightening potential of UP302.

Multiple Pathways Affecting Melanogenesis

Distinct from traditional brightening ingredients with a single target, UP302 covers multiple core pathways of melanogenesis, melanin stability, glycation-induced melanogenesis, and inflammation-induced melanogenesis, simultaneously regulating both the eumelanin and pheomelanin synthesis branches:

Competitively binds to the copper cofactor of tyrosinase, inhibiting its catalytic activity; accelerates intracellular tyrosinase protein degradation, reducing the pool of functional enzyme at the source; scavenges ROS free radicals, reducing oxidative stress-stimulated melanin secretion; decomposes AGEs (advanced glycation end products), blocking glycation-induced dullness and melanogenesis; downregulates inflammatory factor release, inhibiting post-inflammatory hyperpigmentation (PIH); mildly inhibits TRP-1 and TRP-2 auxiliary melanogenic enzymes, achieving dual blockade of melanin maturation.



Recommended Synergists/Additives for Enhancing Skin Brightening/Even-Tone Effects

Synergist/Additive	Rationale/Mechanism	Use Level
Tranexamic Acid INCI: TRANEXAMIC ACID	Inhibits UV- and inflammation-induced release of melanogenic factors, blocking PIH formation; synergizes upstream-downstream with UP302's 'enzyme inhibition + enzyme degradation' pathway, reducing formulation irritation and post-acne darkening.	2%
Niacinamide INCI: NIACINAMIDE	Blocks melanosome transfer to keratinocytes, intercepting epidermal deposition of synthesized melanin; forms a closed loop with UP302's source-level melanin inhibition, accelerating skin brightening and fading superficial pigmented spots.	3%
Acetylzingerone INCI: ACETYL ZINGERONE	Chelates core copper ions of tyrosinase to assist enzyme inhibition; broad-spectrum antioxidant, repairs photo-damage, soothes redness, and improves freckles and solar dullness.	1%
VC Derivatives (A2G/VC MAP) INCI: ASCORBYL GLUCOSIDE	Fast- and slow-acting antioxidant combination, enhances UP302 formulation stability, and strengthens anti-yellowing and brightening effects.	2%~5%
Licorice (Glycyrrhiza glabra) Root Extract INCI: GLYCYRRHIZA GLABRA ROOT EXTRACT	Inhibits inflammatory pathways to reduce redness, balances the irritation of highly active brightening ingredients, suitable for sensitive skin and post-procedure repair formulations.	0.1%~0.5%

A Truly Multifunctional Skin-Brightening Active Ingredient

Safe and Effective Skin Brightening Agent / Even-Tone Active

- Over a decade of global human evidence-based data, with a complete panel of toxicology, irritation, and sensitization tests; the only resorcinol derivative in China with dual special certificates for both raw material and product brightening.
- High-purity synthesis process with no irritating by-products; compliant for use by pregnant women, sensitive skin, and post-procedure skin.
- Listed in China's New Raw Material Catalogue and EU cosmetic ingredient inventory; compliant for addition in major global markets.

Brightening

- Dual regulation of tyrosinase (activity inhibition + accelerated degradation), with melanin-inhibitory efficacy surpassing kojic acid, arbutin, and phenylethyl resorcinol.
- Unique anti-glycation pathway, specifically targeting facial sallowness and dullness caused by late nights, sugary diets, and photoaging — a target absent in traditional brightening ingredients.
- Potently prevents post-inflammatory hyperpigmentation, suitable for acne-prone skin, post-procedure skin, and skin prone to darkening.
- Lipophilic molecular structure with strong skin penetration; higher epidermal utilization at the same concentration.

Anti-Aging and Additional Anti-Aging Benefits

- Efficiently scavenges skin ROS oxidative free radicals, reduces DNA oxidative damage, and repairs photo-aged cells.
- Increases endogenous glutathione (GSH) levels in skin, strengthening the intrinsic antioxidant barrier.
- Decomposes AGE glycation products, inhibits glycosylation cross-linking, and improves yellowing, roughness, sagging, and dullness.
- Inhibits UV-induced oxidative degradation of collagen and elastin, delaying signs of photoaging such as spots, uneven skin tone, and rough, aged skin.

Key Publications

1. Hertel C. 1-(2,4-Dihydroxyphenyl)-3-(2,4-dimethoxy-3-methylphenyl) propane, a Novel Tyrosinase Inhibitor with Strong Depigmenting Effects [J]. Chemical & Pharmaceutical Bulletin, 2008, 56 (9):1292-1296.
2. Zhu L. Preclinical pharmacokinetic study of the novel tyrosinase inhibitor UP302 [D]. National Institutes for Food and Drug Control, 2011.
3. Kondo T, Hearing VJ. Complex regulation of melanin synthesis in melanocytes [J]. Expert Review of Dermatology, 2011,6 (1):97-108.