# Progress of Biological Whitening Technology

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**Abstract:** Biological whitening technology has emerged as a sustainable and eco-friendly alternative to conventional chemical-based whitening methods. This review summarizes recent progress in biological whitening agents (e.g., microbial enzymes, plant-derived compounds, and bioactive peptides) and their mechanisms of action, including melanin inhibition, tyrosinase activity modulation, and oxidative stress reduction. Key advancements include the utilization of lactic acid bacteria for skin brightening, ligninolytic enzymes for textile whitening, and genetic engineering to enhance microbial pigment-degrading efficiency. Challenges such as low stability, high production costs, and scalability limitations are discussed, along with potential solutions like nano-encapsulation and metabolic pathway optimization. Future directions emphasize the integration of synthetic biology, AI-driven enzyme design, and circular economy principles to expand applications in cosmetics, food preservation, and environmental remediation. In this paper, a series of biological whitening technology is discussed.
***Keywords*:** Biological whitening, melanin inhibition, microbial enzymes, sustainable biotechnology, tyrosinase inhibitors

## 1. Introduction

Melanin is a black or brown polymer, which is widely distributed in animals, plants and microorganisms. There are three basic types of human melanin: pheomelanin, eumelanin, and neuromelanin[1]. In recent years, with the increasing demand of skin whitening all over the world, there are more and more studies on melanin depigmentation. The most important enzyme in the melanin biosynthetic pathway is tyrosinase, which is the only enzyme absolutely necessary for melanin production[2].

Traditional drugs, including corticosteroids, hydroquinone, and aminomercuric chloride, reduce skin tone by inhibiting melanocyte maturation or interfering with the melanogenesis process. However, most of these drugs can cause side effects, including a tingling sensation, contact dermatitis, irritation, high toxicity, and sensitivity [3]. Some natural whitening agents are introduced, and the mechanism of these whitening agents on melanogenesis based on their efficacy is discussed. In addition, the current research methods used to evaluate the biological activity of compounds were reviewed.

## 2. Types and mechanisms of whitening agents

Melanin production is a complex process involving a series of chemical and enzymatic pathways[4]. Regulation at any level of this process will be an important way to whiten the skin, so there are many types of skin whitening agents for different mechanisms, and the synthesis and mechanism of action of various whitening agents are shown in Table 1. Tyrosinase (TYR), tyrosine-related protein-1 (TRP-1) and TRP-2 (dopachrome tautomerase) are mainly involved in the conversion of tyrosine to melanin[6-8].

**Table 1. Comparison between skin whitening agents.**

| Whitening agent | Biosynthesis pathway | Whitening mechanism | References |
|---|---|---|---|
| Arbutin | 1. from benzene using designed E. coli cells harbor-ing P450-BM3 mutant and arbutin synthase.<br>2. with a high concentration of glycoside donor sucrose, amylosucrase (amy-1) could completely glycosylate hydroquinone to α-arbutin. | Inhibiting the activities of tyrosinase. | [5]<br>[8]<br>[9] |
| Azelaic Acid | 1.The transformation consists of a three-step multiple-enzyme cascade. In the first step, the lipoxygenase St-LOX1 catalyzes the hydroperoxidation of linoleic acid, which is followed by the subsequent cleavage of the nascent hydroperoxy moiety by the action of a hydroperoxidelyase Cs-9/13HPL to yield 9-oxononanoic acid. In the last step, 9-oxononanoic acid is oxidized by an endogenous E. coli oxidoreductase to azelaic acid. | 1. a rather weak competi-tive inhibitor of tyrosinase.<br>2. cytotoxic effect on melanocytes. | [10]<br>[2] |
| Kojic Acid | 1. a natural metabolite produced by fungi. | 1. the potential inhibition of cellular NF-κB activity.<br>2. Inhibiting the activities of tyrosinase. | [11-12] |
| Hydroquinone | 1. E. coli mono-cultures and co-cultures for the HQ biosynthesis from simple carbon substrate glucose. | 1. Inhibits tyrosinase<br>2. Cytotoxic to melanocyte. | [2] |
| Ascorbic Acid (vitamin C) | 1. fruits and vegetables. | 1. Reduce back o-dopaquinone to dopa<br>2. Antioxidsnt. | [2] |

## 3. Enzymatic Decolorization of Melanin

Several oxidases and peroxidases have been tested for melanin decolorization, such as laccase, horseradish peroxidase, manganese peroxidase, and lignin peroxidase[13-16]. Lignin peroxidase is a promising catalyst for melanin decolorization because of its high oxidation-reduction ability[17]. In addition, the in situ generation and supply of H2O2 by glucose oxidase (Gox) in combination with LiPH 8 catalyzed melanin decolorization inhibits the inactivation[18]of LiPH 8 by excess H2O2. Since Gox can continuously generate and input low concentration of H2O2 using glucose and molecular oxygen in the air, the maximum decolorization of melanin can be achieved. Jia et al. designed, optimized and validated a novel glucose oxidase-perhydrolase-in situ chemical oxidation cascade to produce peracetic acid for melanin decolorization[19]. Therefore, the method can provide excellent application prospect for whitening cosmetics.

## 4. Modification Strategies of Various Whitening Agent

Topical treatments face some obstacles such as the low stability of the whitening agents, therefore, encapsulation of these agents is essential. Natural skin lightening agents are effectively incorporated into lipid vesicles, cyclodextrins, emulsions, solid lipid nanoparticles , nanostructured lipid carriers, and chitosan nanoparticles. Liposomes are known for their biodegradability, biocompatibility, low toxicity, and ability to encapsulate lipophilic and hydrophilic drugs. They can also enhance skin penetration and control the release of encapsulated drugs[20-21].

Manosroi et al. (2005) prepared a hydroxypropyl-β-CD/azelaic acid complex by synergistic evaporation and freeze-drying to improve the solubility of azelaic acid and measured its release through three synthetic membranes. Ansari et al. (2011) prepared resveratrol loaded β-CD nanocells by a cross-linked freeze-drying technique to improve the solubility, stability, and permeability of resveratrol[21-22].

There are many types of emulsions, oil-in-water (O/W) emulsions, oil-in-water (W/O) emulsions, anhydrous emulsions, microemulsions , nanoemulsions and multiple emulsions. Gallarate et al. dissolved arbutin and kojic acid respectively in O/W microemulsions containing natural surfactants (lecithin and alkyl glycosides) to improve their photostability[22].

## 5. Problems and Countermeasures in Evaluation of Whitening Cosmetics

Tyrosinase is the rate-limiting enzyme for melanin production and thus is the most prominent target for inhibition of pigmentation. A number of tyrosinase inhibitors have been identified, but most lack clinical efficacy, because they are based on mushroom tyrosinase (mTyr) as the target, which has been shown to have catalytic activity and substrate specificity significantly different from mammalian enzymes[23].

Mushroom and human tyrosinases differ significantly in catalytic activity and substrate specificity, and a large amount of literature has been devoted to the use of mushroom tyrosinase inhibitors in humans, but unfortunately, currently used inhibitors lack the substrate affinity and selectivity needed for targeted application of human tyrosinase[24-27].

## 6. Conclusion

Whitening cosmetics play an important role in global cosmetics. Many tyrosinase inhibitors have been identified from natural and synthetic sources, but only a few have been used as skin lightening agents, mainly due to various safety concerns, cytotoxicity, solubility, stability, efficient absorption through the skin, etc. So, using biological technology to improve the safety of skin whitening agents, improve skin permeability and physical stability has become an effective means of melanin decolorization.

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