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# A REVIEW ON NATURAL SKIN LIGHTENING AGENTS

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## ABSTRACT

Natural bleaching agents are the natural metabolites mostly obtained from plants as well as from other natural sources implied to reduce or alter melanin production in the human body. Many natural compounds exert their efficiency as skin lightening agent, i.e., vitamin C, E and niacinamide flavonoids, phenolic compounds, arbutin, kojic acid, azelaic acid, Mulberroside F, Aloin, aloesin, Glabridin, liqriritin, N-acetyl glucosamine has found as a substantial compound obtained from a natural source and could be used reduce skin condition that causes hyperpigmetation. Natural bleaching agents could be better alternatives to synthetic bleaching agents due to their biocompatatibily to the human skin.

## Keywords: Tyrosinase, Melanin, Bleaching agent, Hyperpigmentation, Skin lightening.

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## INTRODUCTION

Natural bleaching agents are compounds obtained from natural source implied to provide esthetic look and even tone. Skin-lightening agents would be used to improve skin tone, fading of dark skin spots, and alleviate other skin conditions. The most favored pathway of skin-lightening agents is by hampering the biosynthetic pathways of melanin production and inhibition of tyrosinase. However, melanin is a protective natural pigment accountable for the characteristic color of skin, hair, and eye. Melanin is produced in our body by specialized cells called melanocytes situated in the stratum germinativum or basal layer, uneven distribution and deposition of melanin may lead to defile natural appeal of the skin. Natural skin lightening agent are preferred over their synthetic counterparts due to their lower toxicity and side effects. The review aims to highlight the natural and safer alternative agents that would help to improve various skin conditions [1,2].

# NATURAL INGREDIENTS AS SKIN LIGHTENING AGENTS

#### Arbutin

Arbutin is a naturally occurring glycosylated hydroquinone, chiefly found as beta-arbutin, in the leaves of plants bearberry, blueberry, and cranberry belonging to families Ericaceae. Arbutin accolades as globally accepted and widely recommended skin-lightening agent. Bearberry or *Arctostaphylos uva-ursi* has been used as a rich source of natural arbutin since ancient times. Another form of arbutin is alpha-arbutin could be synthesized enzymatically from hydroquinone or  $\beta$ -arbutin [3-5]. Alpha arbutin has been proven more stable, safe, effective, and better alternative to hydroquinone and beta arbutin. Arbutin has shown potential anti tyrosinase activity by competitive inhibition of tyrosinase biosynthesis, an enzyme responsible for melanin synthesis in melanocytes this action leads to suppression in melanin production and lightening of skin coloration. Arbutin would be used for hyperpigmentation, melasma, freckles, senile lentigines, post-inflammatory hyperpigmentation, sunspots, and uneven skin tone [6-8].

#### Kojic acid

Kojic acid is an organic acid that is primarily produced by a fungus of genus *Aspergillus* as metabolite, concurrently it could be generated through fungi ferment. Kojic acid was first isolated in 1907 by Saito from mycelia of *Aspergillus oryzae* grown on steamed rice. In 1912 Yabuta gave it the name kojic acid. Certain other genus capable to produce kojic acid are *Penicillium* and *Acetobacter* [9-13]. Kojic acid is

globally accepted and impressively used by cosmetic formulators for a variety of skin conditions, i.e., sun spots, uneven skin tone, melasma, hyperpigmentation, it also offers protection against ultraviolet rays. Kojic acid and its derivatives impede melanin production by inhibiting tyrosinase a fundamental enzyme in melanin biosynthesis. Hindrance in melanin production reflects as skin brightening, 1% concentration of kojic acid in cosmetics was recommended as safe by CIR [14-18].

#### Azelaic acid

Azelaic acid is a natural dicarboxylic acid compound found in barley, wheat, and rye. It is also produced instinctually by *Malassezia furfur*, a yeast that resides on normal skin. Azelaic acid might be effective against multiple skin conditions, i.e., lightening of dark spots, hyperpigmetation, melasma, to retain even skin tone, acne scars, and other skin conditions [19,20]. Azelaic acid reduces melanin production by inhibiting of tyrosinase enzyme selectively responsible for the production of melanin in our body [21,22].

#### Mulberroside F

Mulberroside F is a stilbenoid isolated from *the* leaves of *Morus alba* commonly known as white mulberry naturally found in various tropical countries. The compound had shown a skin-lightening effect by suppressing the melanin biosynthesis and tyrosinase inhibitory action by obstructing the enzyme that converts dopa to dopachrome in melanin biosynthesis therefore inhibiting melanin production [23,24].

## Flavonoid and Polyphenolic compounds

Flavonoids and polyphenolic are the predominant group of variable compounds found ubiquitously in plant species. Those were well recognized for their antioxidant potential, epigallocatechin from green tea leaf extract, Hesperidin from citrus fruits such as lemon and orange, proanthocyanidins and anthocyanidins from pigmented vegetables and fruits, quinic acid, caffeic acid, and chlorogenic acid from tea and coffee beans, hydroxychavicol from *Piper betel* leaves extract isoflavones from soya beans, alfalfa, and clover, Umbelliferone found in various plants of family umbelliferae now *Apiaceae* and *Rutaceae* has been recognized for their substantial effect in melanogenis [25-31].

### Aloin and aloesin

Aloin also known as barbaloin is a prominent anthracene glycoside found in a wide variety of genus aloe known for its purgative and cosmetic effect for long age. It is a yellow to brown color compound with a bitter taste. Aloesin also known as aloe resin B is the resinous component present in aloe and has been shown great potential in wound healing, burns, and subdued melanogenesis by competitive inhibition of tyrosinase an enzyme fundamentally important in the biosynthesis of melanin. As skin lightening agent [9,32,33].

## Glabridin and liqriritin

Glabridin is an isoflavonoid majorly isolated from the root of plant *Glycyrrhiza glabra* commonly known as licorice belonging to family *Fabaceae*. Glabridin could be found as yellowish–brown powder in hydrophobic portion of the extract of root. Glabridin is a tyrosinase inhibitor that was shown to reduce UVB-raised pigmentation. Liqriritin one another compound isolated from the same plant potentially shows its ability to reduce hyperpigmentation [34].

#### Vitamin C and E

Vitamin C also dictated as L-ascorbic acid, is a water-soluble vitamin found in a variety of fruits and vegetables known for its antioxidant and free radical scavenging potential. Vitamin E was found in vegetable oils, fruits, cereals, vitamin E is fat-soluble vitamin with predominately used as an antioxidant in various skin and hair cosmetics. Vitamin C acts by interacting and reducing various oxidative steps involved in melanin formation thus inhibit melanogenesis. Furthermore, vitamin E would be acts by obstructing and interfering with lipid peroxidation of the membrane of melanocyte, furthur it would act by raise in cellular glutathione content as well as tyrosinase inhibition [35-39].

#### Niacinamide

Niacinamide or nicotinamide is a type of vitamin B-3, it is inseminated in many foods including green vegetables, cereals, milk, meat, fish, and eggs. Niacinamide impedes the interaction of keratinocytes and melanocytes, therefore obstructing melanogenesis. Furthermore it would alter protease-activated receptor involved in the transferring melanosomes from melanocytes into surrounding keratinocytes [40,41].

#### N-acetyl glucosamine

N-acetyl glucosamine is a natural monosaccharide found majorly in outer shells of shellfish lobster, shrimp, and crab. N-acetyl glucosamine would reduce the amount of melanin in melanocytes, therefore minimizing hyperpigmentation and improving skin tone. It might inhibit the conversion of pro-tyrosinase to tyrosinase moreover it affects the genetic expression in hyperpigmentation [41,42].

## CONCLUSION

Natural skin lightener would play a major role in a variety of skin conditions by maintaining the ratio of melanin in skin layers. Synthetic ingredients might cause deleterious reactions to the skin may not be safe to use. On the other side, natural alternatives are more biocompatible, safer, and friendly to use in the skin as well as to the environment. Limited data are available to ensure safety and efficacy. Furthermore, insight is needed to ensure safety and efficacy of these compounds. Further research is needed to find out more related compound from natural origin that would provide better and efficient alternative to the available product in the market.

#### REFERENCES

- Sugimoto K, Nishimura T, Nomura K, Sugimoto K, Kuriki T. Inhibitory effects of alpha-arbutin on melanin synthesis in cultured human melanoma cells and a three-dimensional human skin model. Biol Pharm Bull 2004;27:510-4.
- Chakraborty AK, Funasaka Y, Komoto M, Ichihashi M. Effect of arbutin on melanogenic proteins in human melanocytes. Pigment Cell Res 1998;11:206-12.
- Maeda K, Fukuda M. Arbutin: Mechanism of depigmetation in human melanocyte culture. J Pharmacol Exp Ther 1996;276:765-9.
- Lim YJ, Lee EH, Kang TH, Ha SK, Kim SM, Yoon TJ, et al. Inhibitory effects of arbutin on melanin biosynthesis of melanocyte stimulating hormone induced hyperpigmentation in cultured guinea pig skin tissues. Arch Pharm Res 2009;32:367-73.

- Garcia-Jimenez A, Teruel-Puche JA, Rodriguez-Lopez JN, Tudela J. Action of tyrosinase on beta and alpha arbutin: A kinetic study. PLoS One 2017;12:e0177330.
- Liu CQ, Deng L, Zhang P, Zhang SR, Liu L, Xu T, *et al.* Screening of high α arbutin produce strains and production of α arbutin fermentation. J Microb Biotechnol 2013;29:1391-8.
- Seo DH, Jung JH, Lee JE, Jeon EJ, Kim W, Park CS. Biotechnological production of α and β arbutins skin lightening agents, and their derivatives. Appl Biochem Biotechnol 2012;95:1417-25.
- 8. Tse TW. Hydroquinone for skin lightening: Safety profile, duration of use and when should we stop? J Dermatol Treat 2010;21:272-5.
- Sarkar R, Arora P, Garg KV. Cosmeceuticals for hyperpigmentation: What is available? J Cutan Aesthet Surg 2013;6:4-11.
- Phasha V, Senabe J, Ndzotoyi P, Okole B, Fouche G, Chuturgoon A. Review on the use of kojic acid a skin lightening. Cosmetics 2022;9:64.
- Bashir F, Sultana K, Khalid M, Rabia H, Khan H. Kojic acid: A comprehensive review on applications of kojic acid. Asian J Allied Health Sci 2021;6:13-7.
- Aytemir DM, Karakay G. Kojic acid derivatives. In: Medicinal Chemistry and Drug Design. London: Intech Open; 2012. p. 1-27.
- Van Tran V, Nguyen TL, Moon JY, Lee YC. Core-shell materials, nanoemulsions and lipid particles for delivery of antioxidants in cosmetics applications challenges and development strategies. Chem Eng J 2018;368:88-114.
- Chaudhary J. Production technology and applications of kojic acid. Annu Res Rev Biol 2014;4:3165-96.
- Feng W, Liang J, Wang B, Chen J. Improvement of kojic acid production in *Aspergillus oryzae* AR-47 mutant strain by combined mutagenesis. Bioprocess Biosyst Eng 2019;42:753-61.
- Masum MN, Yamauchi K, Mitsunaga T. Natural and synthetic tyrosinase inhibitors as skin-lightening agents. Rev Agric Sci 2019;7:41-58.
- Saeedi M, Eslamifar M, Khezri K. Kojic acid applications in cosmetic and pharmaceutical preparations. Biomed Pharmacother 2019;110:582-93.
- Chambers C. Opinion on kojic acid. Sci Committees Consum Prod 2008;SCCP /11182:1-79.
- National Centre for Biotechnology Information. Pub Chem Compound Summary for CID 2266, Azelaic Acid. Available from: https:// pubchem.ncbi.nlm.nih.gov/compound/azelaic-acid [Last accessed on 2023 May 19].
- Fitton A, Goa KL. Azelaic acid. A review of its pharmacological properties and therapeutic efficacy in acne and hyperpigmentary skin disorders. Drugs 1991;41:780-98.
- Mackrides PS, Shaughnessy AF. Azelaic acid therapy for acne. Am Fam Physician 1996;54:2457-9. Erratum in: Am Fam Physician 1997;55:1586.
- Novosel T, Rundle CW, Yu JD, Jacob SE. Art of prevention: The importance of bath time and avoiding extended exposure to irritating and allergenic chemicals. Int J Womens Dermatol 2019;5:152-4.
- 23. Mei M, Ruan JQ, Wu WJ, Zhou RN, Lei JP, Zhao HY, et al. In vitro pharmacokinetic characterization of mulberroside A, the main polyhydroxylated stilbene in mulberry (*Morus alba* L.), and its bacterial metabolite oxyresveratrol in traditional oral use. J Agric Food Chem 2012;60:2299-308.
- Lee SH, Choi SY, Kim H, Hwang JS, Lee BG, Gao JJ, et al. Mulberroside F isolated from the leaves of *Morus alba* inhibits melanin biosynthesis. Biol Pharm Bull 2002;25:1045-8.
- 25. Ribeiro AS, Estanqueiro M, Oliveira MB. Main benefits and applicability of plant extracts in skincare products. Cosmetics 2015;2:48-65.
- Katiyar SK, Singh SK, Rai M. Botanical, study of skin lightening agents. Int J Pharmacogn 2014;1:243-9.
- Saewan N, Jimtaisong A. Photoprotection from natural flavonoids. J Appl Pharm Sci 2013;3:129-41.
- Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: An overview. ScientificWorldJournal 2013;2013:162750.
- 29. Katiyar SK, Afaq F, Perez A, Mukhtar H. Green tea polyphenol (-)-epigallocatechin-3-gallate treatment of human skin inhibits ultraviolet radiation-induced oxidative stress. Carcinogenesis 2001;22:287-94.
- Lee HJ, Lee WJ, Chang SE, Lee GY. Hesperidin, a popular antioxidant inhibits melanogenesis via Erk1/2 mediated MITF degradation. Int J Mol Sci 2015;16:18384-95.
- Casagrande R, Georgetti SR. Protective effect of quercetin containing topical formulations against UVB induced oxidative stress in mice. J Photochem Photobiol B Biol 2006;84:21-7.
- Choi S, Park YI, Lee SK, Kim JE, Chung MH. Aloesin inhibits hyperpigmentation induced by UV radiation. Clin Exp Dermatol 2002;27:513-5.

- Hanif N, Al-Shami AM, Khalid KA, Hadi HA. A review on plant-based skin lightening agents. J Phytopharmacol 2020;9:54-60.
- Yokota T, Nishio H, Kubota Y, Mizoguchi M. An inhibitory effect of glabridin from liquorice extracts on inflammation and melanogenesis. Pigment Cell Res 1998;11:355-61.
- Espinal-Perez LE, Moncada B, Castanedo-Cazares JP. A double-blind randomized trial of 5% ascorbic acid vs. 4% hydroquinone in melasma. Int J Dermatol 2004;43:604-7.
- Hakozaki T, Takiwaki H, Miyamoto K, Sato Y, Arase S. Ultrasound enhanced skin-lightening effect of vitamin C and niacinamide. Skin Res Technol 2006;12:105-13.
- Thiele JJ, Hsieh SN, Ekanayake-Mudiyanselage S. Critical review of Vitamin E: Its current use in cosmetic, clinical dermatology. Dermatol Surg 2005;31:805-13.
- Farris PK. Cosmeceutical Vitamins: Vitamin C Procedures in Cosmetic Dermatology Series: Cosmeceuticals. Philadelphia, PA: Elsevier, 2005.

p. 51-6.

- 39. Hayakawa R, Ueda H, Nozaki T, Izawa Y, Yokotake J, Yazaki K, et al. Effects of combination treatment vitamins E and C on chloas maand pigmented contact dermatitis. A double blind controlled clinical trial. Acta Vitaminol Enzymol 1981;3:31-8.
- Hakozaki T, Minwalla L, Zhuang J, Chhoa M, Matsubara A, Miyamoto K, *et al*. Effect of niacinamide on reducing cutaneous pigmentation and melanosome transfer. Br J Dermatol 2002;147:20-31.
- 41. Kimball AB, Kaczvinsky JR, Li J, Robinson LR, Matts PJ, Berge CA, et al. Reduction in facial hyperpigmentation after use of moisturizers with a combination of topical niacinamide and N-acetyl glucosamine: Results of a randomized, double-blind, vehicle-controlled trial. Br J Dermatol 2010;162:435-41.
- Bissett DL, Robinson LR, Raleigh PS, Miyamoto K, Hakozaki T, Li J, et al. Reduction in the facial hyperpigmentation by topical N-acetyl glucosamine. J Cosmet Dermatol 2007;6:20-6.