Hae et al., Int J Clin Nutr Diet 2019, 5: 141
https://doi.org/10.15344/2456-8171/2019/141

International Journal of
Clinical Nutrition & Dietetics

Mini Review Open Access

Tyrosinase Inhibitors from Natural Source as Skin-Whitening Agents and the Application of Edible Insects: A Mini Review

Gam Da Hae, Jae Min Jo, Song Yi Kim and Jin Woo Kim*

Department of Food Science, Sunmoon University, Asan city, Chung Nam, 380-701, South Korea

Abstract

Tyrosinase is a key enzyme for synthesis of melanin pigments which is present in plants and animals. Several synthetic and naturally occurring tyrosinase inhibitors have been studied for skin whitening but the development of natural agents is becoming more important due to the disadvantages of synthetics such as high cytotoxicity, insufficient penetrating power, and low activity. Despite the benefits of insects as an alternative protein source, considering the reluctance of eating insects and problematic food security, it is easier to use insects as products for the skin than edible food sources. However, among the various plant and animal sources, a few insects have been investigated to test the content of tyrosinase inhibitors. According to recent research, mealworm has great potential as a source of bioactive compounds which could be used as cosmetics, food, and pharmaceutical agents. Especially, because it is known that mealworm extract has tyrosinase inhibition activity, mealworm extracts could be wildly used as cosmetics materials.

Publication History:

Received: January 19, 2019
Accepted: February 18, 2019
Published: February 20, 2019

Keywords:

Alzheimer's disease, Amyloid-β, Dementia, Memory, Neuroprotection

Introduction

The world's rapid population growth led to the global food shortage, especially animal protein sources. Other factors such as competition between humans and livestock over crops, and environmental problems are raising concern, with insects gaining more attention as an alternative protein source. Insects are used as a food source for their environmental benefits over conventional animals. Insects such as plastic-eating mealworms effect the environment by contributing in waste biodegradation [1]. The growth of insects does not require large areas of land compared to the domestication of livestock, allowing people to save resources, such as cattle ranching, which produces greater amounts of greenhouse gases and NH3 emissions [2, 3]. Furthermore, growing insects is more efficient because of the shorter growth period. In the case of mealworms, they hatch within 4 to 20 days and rapidly reach the larval period.

Insects have a relatively higher content of fat and protein than conventional livestock, specifically fish and beef. Previous research shows that 100 mg of insects provide more than 100% of the daily consumption requirements of vitamins and minerals. Also, insects have a lower proportion of cholesterol and are high in many vital minerals, vitamins, lipids, and carbohydrates [4]. Amino acid composition, such as Leucine, Lysine, and Isoleucine within mealworms meet both the requirements of domestic animals and human beings. In terms of fatty acid, 43.2 g (per 100 g of protein) of oleic acid, 30.2 g of Linoleic acid, and 16.7 g of palmitic acid were found respectively in mealworm larvae [5]. Such benefits are leading to an increase in insect consumption as food sources. More than 1500 species in 300 ethnic groups of 113 countries are known to supply food for an estimated population of 2 billion people, especially in developing countries with high demands of edible insects like Southern, Central Africa, and Southeast Asia [6]. In the case of mopane caterpillars, about 9.5 billion are harvested, producing worth US $85million. The Netherlands has a supply chain, practicing farming and marketing in a large scale. Trade of insects as edible products has also increased between various countries such as Central African Republic to Belgium or France, and Mexico to the United States [2].

Despite the advantages of alternative proteins, eating insects is still considered socially uncomfortable and such issues remain to be solved. Therefore, there will be more benefits of using edible insects for skin products than for food sources for their high production rate throughout the world and verified safety.

Whitening Cosmetics

During several decades, the medical and cosmetic industries have been focusing research on treating skin disorders. A number of studies have approved that the extracts and isolated compounds from numerous natural sources and synthetics have great potency in antioxidant and skin-whitening activity. Recently, tyrosinase inhibitors have become important, in depigmentation ingredients of medical and cosmetic products [7]. Tyrosinase is a copper-containing enzyme involved in the formation of melanin pigments in mammals [8]. Melanin is a phenolic bipolymer, and is distributed widely in animal skin and hair to protect the skin against UV radiation from the sun and reactive oxygen species. Meanwhile accumulation of an excessive level of melanin pigmentation causes dermatological disorders, such as melasma, freckles, age spots and other forms of hyperpigmentation. Tyrosinase is mainly involved in two distinct reactions of melanin synthesis; first, the hydroxylation of tyrosine to 3, 4-dihydroxyphenylallanine (DOPA) and second, the conversion of DOPA to the corresponding dopaquinone. Dopaquinone undergoes several reactions to eventually form melanin [9]. Also, tyrosinase catalyzes the oxidation of phenolic compounds to the corresponding quinones which is responsible for the enzymatic browning in vegetables and fruits. It plays an important role in the developmental and defensive functions of insects as involved in wound healing, parasite encapsulation and sclerotization. Synthetic and naturally occurring polyphenols, including flavonoids or stilbenoid, free radical scavengers, and copper chelators, are known to inhibit tyrosinase [10].

Even though numerous synthetic tyrosinase inhibitors have been reported, only a few of them such as arbutin and kojic acid are commercially used, mainly due to disadvantages like high cytotoxicity, insufficient penetrating power, low activity and low stability [11]. In addition, vitamin C and its derivatives can be used as whitening agents; the levels of tyrosinase inhibitory activity in these compounds

***Corresponding Author:** Prof. Jin Woo Kim, Department of Food Science, Sunmoon University, Asan city, Chung Nam, 380-701, South Korea; E-mail: kimjw1028@sunmoon.ac.kr

Citation: Hae GD, Jo JM, Kim SY, Kim JW (2019) Tyrosinase Inhibitors from Natural Source as Skin-Whitening Agents and the Application of Edible Insects: A Mini Review. Int J Clin Nutr Diet 5: 141. doi: https://doi.org/10.15344/2456-8171/2019/141

are still not high enough for broad use [12]. The use of traditional whitening products like hydroquinone, corticosteroids and mercury containing products has been prohibited, because these compounds have been found to be potentially mitogenic on account of their cytotoxicity to melanocytes [13,14]. Hence, there is a great demand for the development of natural skin whitening agents, which are free from harmful side effects.

Whiting Materials

The extracts and isolated compounds of numerous natural sources, in particular botanical sources, were well characterized with anti-tyrosinase activities and have been accepted as skin lightening agents [15-17]. Tyrosinase inhibitory activity is generally expressed as the IC_{50} (The half maximal inhibitory concentration) value measured using the dopachrome microplate-assay and kojic acid as the reference standard. Table 1 shows the IC_{50} values of the plant extracts and animal extracts reported and the values of synthetic inhibitors currently in commercial use. [18-24,26-28] Separated fraction from camellia pollen indicated the activity, IC_{50} value of 0.05 mg/ml [22]. Thai mango seed kernel extract (IC_{50} value of 98 μg/ml) and its major phenolic principle exhibited inhibitory on tyrosinase [23]. In addition to what is shown in the table, many plant extracts have already been reported to inhibit tyrosinase and testified acute oral toxicity. Chen et al. [24] demonstrated that isolated product from the Chinese herbal plant. *Gastrodia elata* attenuated 20% melanin content of human melanocytes without cell toxicity. The toxicity studies showed that the product did not have cytotoxicity in mice and zebrafish in vivo analysis and effectively reduced melanogenesis without adverse effects. Far Eastern sea cucumber *(Stichopus japonicus*) extracts were screened for their tyrosinase inhibition [28]. The 70% ethanolic extract (IC_{50} value of 0.49 to 0.61 mg/mL) was more capable in inhibiting tyrosinase activity than the water extract (IC_{50} value 1.80 to 1.99 mg/mL). These extracts were known to inhibit the production of L-DOPA and dopachrome by tyrosinase as well as plant extracts. Ethyl-α-D-glucopyranoside and adenosine, isolated from the extracts, were identified as key tyrosinase inhibitors. It was found that the inhibitory activity of animal extract, silkworms and sea cucumbers, was not lower than that of plant extracts and synthetic compounds, and IC_{50} values were dependent on extraction concentration and solvent. Reviews of potent tyrosinase inhibitors derived from various plants as well as animals have initiate to study tyrosinase inhibition of insects, especially edible insects, which are recognized as safe food source.

Whitening Materials from Insect

Little information is available on tyrosinase inhibitory activity of insects so fat. Reports show that the activity of peroxidase inhibitors, also known as tyrosinase inhibitors, involve in inhibiting melanization of insect extracts. Tsukamoto et al. [25] have isolated three low molecular weight protein inhibitors from the pupal extract of houseflies. The inhibitors which are heat and pH stable, showed competitive inhibition of phenoloxidase activity. Phenoloxidase inhibitor extracted and purified from larvae of *Manduca sexta* was directed toward the melanogenic pathway [26]. Methanolic Pupa extract of the *Muga* silkworm showed higher free radical scavenging activity and anti-tyrosinase activity (IC_{50} value of 15.05 μg/ml) [27]. Antityrosinase activity of the extract was highly correlated with DPPH (2, 2-diphenyl-1-picrylhydrazyl) scavenging activity.

Among the few insect studies, there have been reports of tyrosinase inhibition of silkworm. However, mealworm, the rising source as an edible insect commercially reared around many countries, has only been reported on antioxidant activity [29, 30] but not on tyrosinase inhibition yet. Based on nutritional researches of mealworm as an edible insect, it has been necessary to study it as a valuable resource of cosmetics containing tyrosinase inhibitor, fatty acids and vitamins, which have an activity of whitening, moisturizing and regenerating skin. Further research into investigation on variety of extraction processes to extract the whitening materials will be performed and the performance will be evaluated. According to a recent research by Yu et al., the following results were obtained from mealworm extracts using organic solvents: total phenolic compounds of 5.41 mg GAE/g dry weight (DW), radical scavenging activity of 91.8 μg/mL, and tyrosinase inhibition activity of 82.4%. These results suggest that mealworm contains bioactive compounds including phenolic compounds that were proved to have evident cosmetic, pharmaceutical, and medical care function such as antioxidant and tyrosinase inhibitions activities in many plant extracts [31]. Therefore, mealworm has great potential as a source of bioactive compounds which could be used as cosmetics, food, and pharmaceutical agents.

Competing Interests

The authors declare that they have no competing interests.

	IC_{50}	extract solvent
Camellia pollen	0.05 mg/mL	ethanol
Thai mango seed kernel	98.63 μg/mL	ethanol
Blumea balsamifera DC leave	0.319 mg/mL 0.345 mg/mL	hexane
Euphorbia lathyris L	0.28 mg/mL	methanol
Peel of *Citrus* Fruit	2427.0 μg/mL	methanol
Far Eastern sea cucumber	0.49 to 0.61 mg/mL 1.80 to 1.99 mg/mL	ethanol
Pupae of Muga silk worm	15.05 μg/ml	methanol
Sericin extract of silkworm	8 to 19 μg/ml	water
Kojic acid	22.45 μg/ml	
Arbutin	2.29 mg/mL	

Table 1: Tyrosinase inhibitory activity of natural extracts and synthetic compounds [18-24,26-28].

References

1. Yang Y, Yang J, Wu WM, Zhao j, Song Y, et al. (2015) Biodegradation and mineralization of polystyrene plastic-eating mealworms: Part 1. Chemical and physical characterization and isotopic tests. Environ Sci Technol 49: 12080-12086.
2. Van Huis A, Van Itterbeeck J, Klunder H, Mertens E, Halloran A, et al. (2013) Edible insects - Future prospects for food and feed security. FAO Forestry.
3. Nakagaki BJ, DeFoliart GR (1991) Comparison of diets for mass-rearing Acheta domesticus with values reported for livestock. J Econom Entom 84: 891-896.
4. Micek J, Rop O, Borkovcova M, Bednarova M (2014) A Comprehensive Look at the Possibilities of Edible Insects as Food in Europe - a Review. Pol J Food Nutr Sci 64: 147-157.
5. Ravzanaadii N, Kim SH, Choi WH, Hong SJ, Kim NJ, et al. (2012) Nutritional Value of Mealworm, Tenebrio molitor as Food Source. Int J Indust. Entomol 25: 93-98.
6. Micek J, Rop O, Borkovcova M, Bednarova M (2014) A Comprehensive Look at the Possibilities of Edible Insects as Food in Europe. Pol J Food Nutr 64: 147-157.
7. Maeda K, Fukuda M (1991) In vitro effectiveness of several whitening cosmetic components in human melanocytes. J Soc Cosmet Chem 42: 361-368.
8. Whittaker JR (1995) In: Food Enzymes, Structure and Mechanism. Wong D, Chapman and Hall, New York.
9. Solano F, Briganti S, Picardo M, Ghanem G (2006) Hypopigmenting agents: an updated review on biological, chemical and clinical aspects. Pigment Cell Res 19: 550-557.
10. Chang TS (2009) An updated review if tyrosinase inhibitors. Int Mol Sc 10: 2400-2475.
11. Frenk E (1995) Treatment of melasma with depigmenting agents. Melasma: New Approaches to Treatment. Martin Dunitz, London.
12. Callender VD, Surin-Lord S, Davis EC, Maclin M (2011) Post inflammatory hyperpigmentation: Etiologic and therapeutic considerations. Am J Clin Dermatol 12: 87-99.
13. Briganti S, Camera E, Picardo M (2003) Chemical and Instrumental Approaches to Treat Hyperpigmentation. Pigm. Cell & Melanoma Res 16: 101-110.
14. Hermanns JF, Petit L, Martalo O, Pierard-Franchimont C, Cauwenbergh G, et al. (2000) Unravelling the patterns of subclinical pheomelanin-enriched facial hyperpigmentation: Effect of depigmenting agents. Dermatology 201: 118-122.
15. Hunt KJ, Hung SK, Ernst E (2010) Botanical extracts as anti-aging preparations for the skin: a systematic review. Drugs Aging 27: 973-985.
16. Antignac E, Nohynek GJ, Re T, Clouzeau J, Toutain H, et al. (2011) Safety of botanical ingredients in personal care products/cosmetics. Food Chem Toxicol 49: 324-341.
17. Baumann L, Woolery-Lloyd H, Friedman A (2009) ''Natural'' ingredients in cosmetic dermatology. J Drugs Dermatol 8: 5-9.
18. Lim TY, Lim YY, Yule CM (2009) Evaluation of antioxidant, antibacterial and anti-tyrosinase activities of four Macaranga species. Food chemistry 114: 594-599.
19. Saewan N, Koysomboon S, Chantrapromma K (2011) Anti-tyrosinase and anti-cancer activities of flavonoids from Blumea balsamifera DC. Joural of Medic Plants Res 5: 1018-1025.
20. Masamoto Y, Ando H, Murata Y, Shimoshi Y, Tada M, et al. (2003) Mushroom Tyrosinase Inhibitory Activity of Esculetin Isolated from Seeds of Euphorbia lathyris L. Biosci Biotechol Biochem 67: 631-634.
21. Sasaki K, Youshizaki Y (2002) Nobiletin as a Tyrosinase Inhibitor from the Peel of Citrus Fruit. Biol Pharm Bull 25: 806-808.
22. Yang FY, Lai XY, Lai GY, Jian ZD, Ni H, et al. (2016) Purification and characterization of a tyrosinase inhibitor from camellia pollen. J func foods 27: 140-149.
23. Nithitanakool S, Pithayanukul P, Bavovada R, Saparpakorn P (2009) Molecular Docking Studies and Anti-Tyrosinase Activity of Thai Mango Seed Kernel Extract. Molecules 14: 257-256.
24. Chen WC, Tseng TS, Hsiao NW, Lin YL, Wen ZH, et al. (2015) Discovery of highly potent tyrosinase inhibitor, T1, with significant anti-melanogenesis ability by zebrafish in vivo assay and computational molecular modeling. Scientific reports 5: 7995.
25. Tsukamoto T, Ichimaru Y, Kanegae N, Watanabe K, Yamaura I, et al. (1992) Identification and isolation of endogenous insect phenoloxidase inhibitors. Biochem Biophys Res Commun 184: 86-92.
26. Suguraran M, Nellaiappan K (2000) Characterization of a new phenoloxidase inhibitor from Manduca sexta. Biochem biophyl res comm 268: 379-383.
27. Deori M, Boruah DC, Devi D, Devi R (2014) Antioxidant and antigenotoxic effects of pupae of the muga silkworm Antheraea assamensis. Food Biosci 5: 108-114.
28. Husni A, Jeon JS, Um BH, Han NS, Chung D, et al. (2011) Tyrosinase inhibitory by water and ethanol extracts of far eastern sea cucumber, Stichopus japonicas. J Sci Food Agric 91: 1541-1547.
29. Kim IS, Yang MR, No GR, Kim DH, Bang WY, et al. (2015) Identification of antioxidant properties of various extracts from mealworm, Tenebrio molitor, development of functional food, Korean soc Biotech. Bioeng 10: 555.
30. Alves AV, Sanjinez-Argandona EJ, Linzmeier AM, Cardoso CAL, Macedo MLR, et al. (2016) Food Value of Mealworm Grown on Acrocomia aculeata Pulp Flour. PLOS ONE 11: e0151275.
31. Kim JJ, Kim KS, Yu BJ (2018) Optimization of Antioxidant and Skin-Whitening Compounds Extraction Condition from Tenebrio molitor Larvae (Mealworm). Molecules 23: 2340.