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Antioxidant, antimelanogenic, and skin-protective effect of sesamol

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Synopsis

Sesame contains high nutritional value and important bioactive lignans which are good for health-promoting effects including sesamol. Sesamol is found in trace amounts in sesame. The biological action from the trace amounts of sesamol found might indicate its efficacy. This paper presents a systematic study of the antimelanogenic and skin-protective effects (antioxidant) of sesamol and positive compounds. The results showed that sesamol had the most scavenging 2,2-Diphenyl-1-picrylhydrazyl hydrate ($DPPH^{\cdot}$) radical with an IC_{50} value < 14.48 μM. The antioxidant power (Ferric reducing antioxidant power value) of sesamol at a concentration of 0.1129 μM was 189.88 ± 17.56 μM $FeSO_4$. Sesamol inhibited lipid peroxidation with an IC_{50} value of 6.15 ± 0.2 μM. Moreover, sesamol possessed a whitening effect by inhibition of mushroom tyrosinase at an IC_{50} value of 1.6 μM and an inhibition of cellular tyrosinase with 23.55 ± 8.25% inhibition at a concentration of 217.2 μM. Sesamol exhibited high antioxidant and anti-tyrosinase activity compared to the positive control, kojic acid and β-arbutin. Sesamol from edible sesame seed could therefore have an alternative cosmeceutical purpose.

INTRODUCTION

Sesame is rich in proteins, dietary fiber, micronutrients, and bioactive phytochemicals. The seeds and their pressed oil contain important bioactive lignans sesamin, sesamolin, and sesamol. The presence of sesame lignans were reported to play a pivotal role in

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health-promoting effects. Sesamol is a phenolic compound that is metabolized from sesamolin by heat/hydrolysis and is mainly found in roasted sesame or in processed sesame oil (1). Sesamol is—by comparison with other active compounds such as sesamin and sesamolin—only a trace component whether it is found in the seed, roasted sesame oil, roasted sesame meal, or sesame lignin extract (1,2). Intensive studies of sesamol indicate that sesamol not only possesses a phytochemical value but also medicinal effects. Sesamol acts as a metabolic regulator; possesses chemopreventive, antioxidant, anti-lipid peroxidation, antimutagenic, antihepatotoxic (3), antibacterial, antifungal (4), anti-MMP-9 (5), anti-inflammatory activities (6); and prevents neurodegenerative diseases associated with aging such as Alzheimer's disease and stroke (3). In this study, we evaluated the potential of sesamol for an alternative use as a cosmeceutical.

Ultraviolet ray (UVR) plays an important role in skin aging as it initiates the generation of reactive oxygen species (ROS) that induce oxidative stress. Different types of UV radiation have different mechanisms of cell toxicity. The oxidative stress of skin will lead to the depletion of endogenous antioxidants both intra- and intercellular, enhancement of intracellular lipid peroxidation, and the induction of specific signal transduction pathways that modulate inflammatory, immunosuppressive, or apoptotic processes in the skin (7). Although skin possesses antioxidant systems, the free radicals were excessively generated by UV radiation; hence antioxidant defense is overwhelmed leading to skin damage at the cellular level. Oxidative stress causes destruction of the protein collagen, changes cellular renewal cycle, damages DNA, and promotes the release of proinflammatory mediators (cytokines) that trigger inflammatory skin disease. Moreover, the free radicals further undergo the pathogenesis of allergic reaction in the skin (8). The destruction at the dermis that contains collagen, fibrils, and elastin could affect the strength and flexibility of the skin. When disarrangement of the skin occurs, problems such as wrinkling and aging arise. These factors lead to increasing deterioration in skin texture, complexion, and function. Therefore, there is an urgent need for an effective antioxidant to protect the skin from the UV-induced damage. In addition, the exogenous antioxidants that can scavenge ROS and improve the antioxidant/pro-oxidant balance may benefit the skin.

The ROS generated can further activate melanocyte to produce more melanin pigment leading to pigmentary disorders such as melasma (9). Melasma is a hyperpigmentation disorder, and although there is no pain, it has a significant impact on the quality of life. Melasma is worsened by UV exposure and hormonal factors. A crucial part of prevention is photoprotection and avoidance of inducing factors (e.g., such as ROS, UV exposure, and hormonal factor) (10). Treatment of melasma is associated with the topical hypopigmenting agents like hydroquinone, tretinoin, and azelaic acid and its derivatives (11). Various studies attempted to find practical antioxidant and antimelanogenic compounds for skin application. A number of tyrosinase inhibitors have been reported from both natural and synthetic sources, but only a few of them are used as skin-whitening agents, primarily due to safety concerns. Among the skin-whitening agents, hydroquinone is one of the most widely prescribed (12,13). Notwithstanding, hydroquinone is considered to be a potent melanocyte cytotoxic agent which can induce mutations (14,15); consequently, the discovery of safe herbal or pharmaceutical depigmentation alternatives is needed.

To confirm the multifunctional effect of sesamol, this study investigated its potential antimelanogenic and skin-protective effects vis-à-vis its antioxidant properties and tyrosinase inhibition in the human melanoma (SK-MEL2) cell line.

MATERIALS AND METHODS

CHEMICALS

Sesamol was purchased from Spectrum Chemical (Gardena, CA); α-Tocopherol from Fluka Biochemika (Buchs, Switzerland); butylated hydroxy anisole (BHA) and butylated hydroxy toluene (BHT) from Fluka AG (Buchs, Switzerland); 2,2-Diphenyl-1-picrylhydrazyl hydrate ($DPPH^{\bullet}$) from Fluka (Buchs, Switzerland); 2,4,6-Tri(2-pyridyl)-1,3,5-Triazine (TPTZ) was from Tokyo Kasei Kogyo Co., Ltd. (Tokyo, Japan); thiobarbituric acid from Sigma-Aldrich chemie GmbH (Buchs, Switzerland); linoleic acid from Sigma-Aldrich chemie GmbH (Steinheim, Germany); dimethyl sulfoxide (DMSO) from Sigma (St Quentin Fallavier, France); ferric chloride ($FeCl_3.6H_2O$) and ferrous sulfate ($FeSO_4.7H_2O$) from Asia Pacific Specialty Chemical Limited (Seven Hills, Australia); mushroom tyrosinase, β-arbutin, and neutral red (NR) from Sigma–Aldrich Chemical Co. (St. Louis, MO); kojic acid from TCI (Tokyo, Japan); L-3,4-dihydroxyphenylalanine (L-DOPA) from Acros Organic Geel (Geel, Belgium); and, DMEM medium, fetal bovine serum (FBS), and penicillin/streptomycin from GIBCO (Grand Island, NY). The UV spectra were recorded on UV–Vis spectrophotometry from Shimadzu, UV-1700 PharmaSpec (Kyoto, Japan), while the microplate reader was from Anthos 2010 (Anthos Labtec Instruments, GmbH, Salzburg, Austria).

DETERMINATION OF $DPPH^{\bullet}$ RADICAL SCAVENGING ACTIVITY

The effect of sesamol on radical scavenging by DPPH was determined in comparison to three standard compounds—*viz.,* BHA, BHT, and α-tocopherol. Various concentrations of test compounds in methanol were added to a methanolic solution of the DPPH radical. The final concentration of DPPH was 0.02 mM. The mixture was shaken thoroughly and kept in the dark at room temperature for 30 min. The absorbance of the resulting solution was measured by UV–Vis spectrophotometry at 520 nm (16).

DETERMINATION OF FERRIC REDUCING ANTIOXIDANT POWER (FRAP)

The FRAP assay was assessed according to Benzie and Strain (17). The method was based on the reduction of the Fe^{3+}-TPTZ complex to the ferrous form (Fe^{2+}) at low pH. This reduction was monitored by measuring the change of absorbance at 600 nm, which was related to the combined or "total" reducing power of the existence of electron-donating antioxidants in the reaction mixture. Briefly, 50 µl of working FRAP reagent prepared daily was mixed with 200 µl of diluted test compounds. The stock solutions of the test compounds were dissolved in the DMSO. The absorbance at 600 nm was recorded after 8 min incubation at 37°C. FRAP values were obtained from the difference of absorptions in the reaction mixture with those from increasing concentrations of Fe^{3+} and were expressed as µmol of Fe^{2+}. The standard curve was linear between 15.625 and 250 µM $FeSO_4$ with $R^2 = 0.9603$.

DETERMINATION OF INHIBITION OF LIPID PEROXIDATION (LPO) USING THE THIOBARBITURIC ACID REACTIVE SUBSTANCES (TBARS) ASSAY

LPO was measured in terms of TBARS; according to the reaction with malondialdehyde equivalents formed from the peroxidation of lipids as described by Bae and Lee (18).

Sesamol, BHA, BHT, and α-tocopherol were dissolved in DMSO and diluted with 0.1 M PBS, pH 7.0. A volume of 50 µl test compound was added to each well of a 96-well plate. Lipid oxidation was initiated by adding 85 µl of linoleic acid solution in DMSO and shaken at 100 rpm, 40°C for 24 h. To the mixture, 100 µl of thiobarbituric acid (0.67%w/v in phosphate buffer) was added and incubated at 80°C for 1 h. After cooling down, 45 µl of chloroform was added to the mixture, which was then shaken at 20×g for 5 min. The clear solution was taken and read at 520 nm. The plot between the different concentrations (µg/ml) of the compounds and percentage inhibition of LPO were used to calculate the IC_{50} value, i.e., the concentration of compound needed to achieve a 50% inhibition of LPO.

DETERMINATION OF TYROSINASE INHIBITION ACTIVITY

Tyrosinase is the key enzyme in melanin biosynthesis; initiation of the reaction is by conversion of the amino acid tyrosine to other intermediates resulting in the melanin pigment. The inhibition of tyrosinase enzyme activity will lead to skin whitening. The inhibition of mushroom tyrosinase activity *in vitro* was performed as *per* Momtaz *et al.* (19), with minor modifications. Mushroom tyrosinase enzyme was added to each well of a 96-well plate to achieve a final concentration of 27 units/ml. The test compounds and positive control, kojic acid and β-arbutin (prepared in aqueous solution) were added into each well. The prepared substrate L-DOPA solution in the 0.1 M PBS (pH 6.8) was added to the reaction mixture yielding a final concentration of 4.5 mM. All of the reaction mixtures were incubated at room temperature (28°C) for 20 min and the absorbance was measured at 492 nm using a microplate reader. The concentration possessing a 50% tyrosinase inhibition compared to the control (in an absence of inhibitor) or IC_{50} value was calculated. Percent inhibition of tyrosinase activity was calculated as the following:

$$\%\ \text{Tyrosinase inhibition} = \left[(A - B) - (C - D)\right] \times 100 \Big/ (A - B)$$

Note: A = absorbance of blank solution with enzyme
B = absorbance of blank solution without enzyme
C = absorbance of sample solution with enzyme
D = absorbance of sample solution without enzyme

CELL CULTURE

The African green monkey kidney cell line (Vero) was maintained at the Centre for Research and Development of Medical Diagnostic Laboratories, Khon Kaen University, while SK-MEL2 was purchased from CLS-Cell Lines Service, Eppelheim, Germany. Both cell lines were maintained in Dulbecco's modified Eagle medium (DMEM) supplemented with 10% FBS, 1% penicillin/streptomycin and were cultured at 37°C in a humidified atmosphere at 5% CO_2.

DETERMINATION OF CYTOTOXICITY

SK-MEL2 and Vero cells in complete DMEM medium were added to each well of a 96-well plate (5×10^4 cells per well). After 24 h incubation at 37°C in 5% CO_2 incubator, 100 µl of sesamol and the positive control (melphalan) were added to each well and incubated for 48 h. The cells were centrifuged for 5 min at 675 ×*g* to obtain the cell pellet. Next, 190 µl of medium was removed from each well and 100 µl of freshly prepared NR solution (50 µg/ml of stock solution) was added to each well including the blanks (media combined with sample) and the controls (non-treated cells). The solution mixture was incubated at 37°C in an incubator with 5% CO_2 for 2 h. After incubation, the cells were pelleted by centrifugation for 5 min at 675 ×*g* and the 100 µl of NR and medium were discarded. The cells were rinsed with 150 µl PBS (pH 7.4) and centrifuged for 5 min at 675 ×*g*. Then, 200 µl of 0.33% HCl in isopropanol solution was added to each well—including the controls and blanks—followed by thorough mixing. Finally, the absorption of the solutions was measured at 520 nm and the concentration resulting in 50% cytotoxicity vs. the non-treated cells (IC_{50}) was calculated.

DETERMINATION OF CELLULAR TYROSINASE INHIBITION ACTIVITY

The inhibition of cellular tyrosinase activity was performed according to Sapkota *et al.* (16) with some modifications. The SK-MEL-2 cells were cultured at 9×10^5 cells/well in six-well plates then incubated at 37°C, 5% CO_2 for 24 h. The cells were subsequently treated (48 h exposure) with sesamol or positive controls, kojic acid and β-arbutin. After treatment, the cells were washed with ice-cold PBS and slowly lysed with 1 ml of PBS 0.1 M, pH 6.8, containing 1% Triton X-100, at room temperature for 30 min. Lysed cells were centrifuged at 10,000 ×g for 10 min. The supernatant that contained the tyrosinase enzyme was checked for protein content using the Lowry method and bovine serum albumin as the standard protein. Supernatant containing the same amount of tyrosinase enzyme was added to each well of the 96-well plate. Then L-DOPA in 0.1 PBS (pH 6.8) was added to each well to achieve a final concentration of 4.5 mM and incubated at 37°C for 18 h. The absorbance was measured at 475 nm and percentage inhibition calculated.

STATISTICAL ANALYSIS

The data were expressed as a mean ± S.D. (n = 3). Statistical differences between the treated and untreated groups were tested using a one-way ANOVA with a 95% confidence interval.

RESULTS

EFFECT OF SESAMOL ON RADICAL ANTIOXIDANT ACTIVITY

Skin exposure to UV radiation can generate radicals or trigger signaling pathways to induce melanin formation. This hyperpigmentation of melanin is a defense mechanism in the skin. Radical generation can, however, be disrupted by using sufficient effective antioxidant(s). The antioxidant activities of sesamol were therefore investigated in

Table I.
Effect of Sesamol, BHT, BHA and α-Tocopherol on Radical Scavenging Activity Using the DPPH Assay and Lipid-Peroxidation Using the TBAR Assay

	IC_{50} (μM)	
Compounds	DPPH assay	TBAR assay
Sesamol	<14.48[a]	6.15 ± 0.2[b]
BHT	21.78 ± 0.9[b]	9.53 ± 1.4[c]
BHA	40.50 ± 2.8[c]	1.55 ± 0.2[a]
α-Tocopherol	19.73 ± 4.6[b]	3.02 ± 0.7[a]

Results presented: mean ± S.D. (n = 3). Values with different superscripts in each column are significantly different (one-way ANOVA, $p < 0.05$).

comparison to the standard positive antioxidants (BHT, BHA, and α-tocopherol) using the DPPH, TBAR (Table I) and FRAP assays (Table II), which represent different mechanisms of antioxidant activities. The ability of sesamol to inhibit radical scavenging and lipid peroxidation are presented with the IC_{50} value. The results showed that sesamol exerted the strongest radical scavenging activity over against the positive controls with an IC_{50} value < 2 μg/ml (14.48 μM). Sesamol was able to inhibit lipid peroxidation more than BHT but not higher than BHA and α-tocopherol.

Total antioxidant activity based on reducing power was measured by FRAP. The standard curve created by $FeSO_4$ was plotted and was linear between 15.625 and 250 μM $FeSO_4$

Table II.
Effect of Sesamol, α-Tocopherol, BHA, and BHT on Reducing Power as Determined by the FRAP Method

Compounds	Concentration (mM)	FRAP value (μM $FeSO_4$)
Sesamol	0.0145	44.17 ± 2.22[a]
	0.0282	84.23 ± 4.59[b]
	0.0565	117.71 ± 14.51[c]
	0.1129	189.88 ± 17.56[d]
α-Tocopherol	0.0046	44.66 ± 4.12[a]
	0.0091	75.91 ± 4.35[b]
	0.0181	109.12 ± 9.07[c]
	0.0362	165.75 ± 10.70[d]
BHA	0.0111	10.75 ± 5.57[a]
	0.0216	29.55 ± 6.86[a,b]
	0.0433	45.59 ± 15.30[b]
	0.0866	70.91 ± 14.04[c]
BHT	0.0091	4.32 ± 2.94[a]
	0.0177	10.21 ± 5.47[a]
	0.0354	20.75 ± 3.62[b]
	0.0708	33.79 ± 5.63[c]

[a–d]Mean within a column of each compounds having the same superscripts are not significantly different ($p > 0.05$).

with $R^2 = 0.9603$. After considering the activity of each compound, sesamol exhibited a total antioxidant power (84.23 ± 4.59 μM $FeSO_4$) greater than BHT (20.75 ± 3.62 μM $FeSO_4$) and BHA (45.59 ± 15.30 μM $FeSO_4$), but lower than α-tocopherol (165.75 ± 10.70 μM $FeSO_4$), respectively (Table II). Taken together, our results on radical scavenging, lipid peroxidation activities, and reducing power indicate that sesamol possessed antioxidant activity with multiple mechanisms.

INHIBITORY EFFECT OF SESAMOL ON MUSHROOM TYROSINASE *IN VITRO*

The antimelanogenic activity of sesamol was principally evaluated on its inhibition of mushroom tyrosinase activity *in vitro*. The results showed that sesamol and kojic acid inhibited tyrosinase activity in a dose-dependent manner. The respective IC_{50} values for sesamol and kojic acid were 0.33 μg/ml (1.6 μM) and 6.15 μg/ml (67.6 μM) (Figures 1A and 1B.). The other positive control (β-arbutin) did not show any tyrosinase inhibitory activity (data not shown), despite using a concentration as high as 1000 μg/ml (3673 μM), indicating that sesamol blocked the tyrosinase enzyme with the strongest activity than the known whitening compounds, kojic acid and β-arbutin.

EFFECT OF SESAMOL ON CELLULAR TYROSINASE INHIBITION

To confirm the ability of sesamol on inhibition of tyrosinase enzyme in the cells, the cellular tyrosinase inhibitory activity was evaluated in the SK-MEL2 cell model. The concentration used in the cell-based assay was higher than that used in the inhibitory study of mushroom tyrosinase *in vitro* to ensure sufficient accumulation of the test compound in the cells. The result showed that 30 μg/ml (217 μM) sesamol inhibited cellular tyrosinase activity 23.55 ± 8.25%, whereas 600 μg/ml (4222 μM) kojic acid only inhibited tyrosinase 33.88 ± 1.43% (Figure 2). Although kojic acid was used at higher concentration (4222 μM) than sesamol (217 μM), kojic acid showed a tyrosinase inhibitory activity (33.88 ± 1.43%) not significantly different than sesamol (23.55 ± 8.25%) ($p = 0.243$). By comparison, although β-arbutin was used as high as 3673 μM, it could only inhibit cellular tyrosinase enzyme at 8.26 ± 8.78% (Figure 2). These results indicate that sesamol has potential as a whitening agent and possesses better activity than the currently used whitening compounds, kojic acid and β-arbutin.

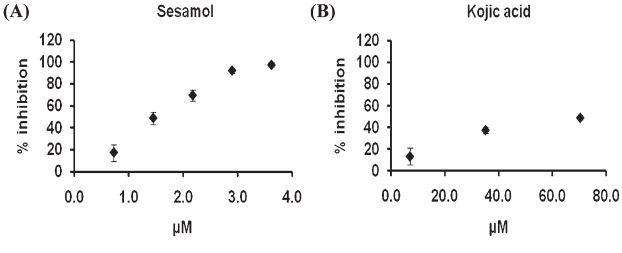

Figure 1. Effect of (A) sesamol and (B) kojic acid on mushroom tyrosinase inhibition. Data are presented as mean ± S.D. (n = 3).

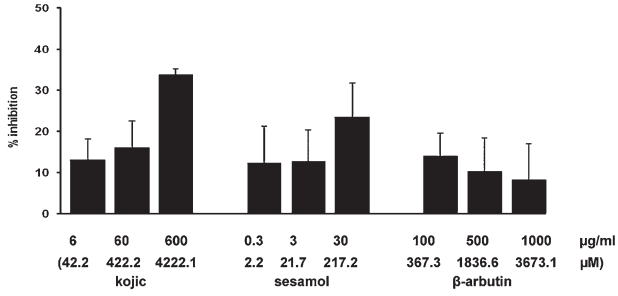

Figure 2. Inhibition effects of kojic acid sesamol and β-arbutin on cellular tyrosinase enzyme. Data are presented as mean ± S.D. (n = 3).

EFFECT OF SESAMOL ON CELL CYTOTOXICITY

To test the possibility of a clinical use for sesamol as a skin application, the cytotoxicity of sesamol was investigated *in vitro* in both normal (Vero) and melanoma (SK-MEL2) cell lines. The Vero cell line was used to represent normal cells. Cytotoxicity was evaluated using a colorimetric NR assay (20). Viable cells accumulate and bind neutral red within the lysosomes, but dead cells cannot because of the fragility of the lysosomal membrane and irreversible molecular alterations in the dead cells (21). Figure 3 shows that sesamol barely affected cell viability. Although as much as 800 µg/ml (5792 µM) sesamol was used, the cytotoxicity to Vero cell was only 22% after 48 h treatment. Similar non-cytotoxicity to the Vero cell line was observed for the positive control β-arbutin and kojic acid, which possessed a cytotoxicity of only 4% and 7%, respectively. The SK-MEL2 cell line was used to represent melanocytes. The cytotoxicity of the test compounds on the growth of SK-MEL2 was found to be non-cytotoxic when using concentrations up to 400 µg/ml (Figure 3). A 40% cytotoxicity was observed in the sesamol-treated SK-MEL2 cell line at concentration of 600 µg/ml (4344 µM) (Figure 3), while β-arbutin and kojic acid did not possess any cytotoxicity. Sesamol thus possesses a cytotoxicity IC_{50} value of 4406.5 µM in the SK-MEL2 cell line (Figure 3). Notwithstanding, the concentration used to create the tyrosinase inhibition effect *in vitro* was much lower than the concentration used in this cellular assay. Sesamol therefore may not be cytotoxic at the effective whitening concentrations used in the melanoma cell line. Further experiment on the normal melanocyte cells should be conducted to confirm non-toxicity of sesamol.

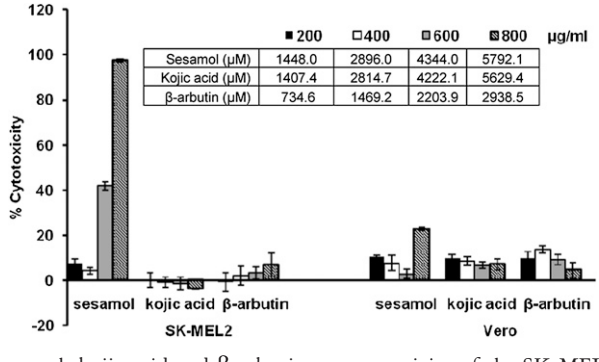

Figure 3. Effect of sesamol, kojic acid and β-arbutin on cytotoxicity of the SK-MEL2 and Vero cell lines after 48 h treatment. Data are presented as mean ± S.D. (n = 3).

DISCUSSION

Oxidative stress is induced by various factors leading to oxidation of biomolecules (e.g., lipids, proteins, and DNA) and pathological status (22). Under certain physiological conditions, when the level of ROS increases more than the intracellular antioxidant capacity, oxidative stress will occur. The tyrosinase enzyme in melanogenesis also increases the oxidative risk in physiological systems (23). Therefore, antioxidant is beneficial for antiaging. Our study demonstrates that sesamol can play an important role as an antioxidant because it possesses radical scavenging, lipid peroxidation prevention, and reducing power. Our results confirm the radical scavenging of sesamol as reported by Suja *et al.* (24) and Hayes *et al.* (25). Moreover, sesamol has the strongest lipid peroxidation prevention among our tested compounds. Occurring in cell membranes, lipid peroxidation releases arachidonic acid, which is involved in the inflammatory response (26). Sesamol can hereby protect the cell membrane which is composed of a lipid bilayer from lipid peroxidation and might also prevent the inflammatory process from decreasing arachidonic acid. Chen and Ahn (27) reported that sesamol inhibited lipid oxidation in UV-induced lipid oxidation in the following order: quercetin > rutin = caffeic acid = ferulic acid = sesamol > catechin. The advantage of a reducing ability is the capacity to neutralize free radicals and to stabilize and stop harmful chain reactions (17). In this study, sesamol possessed the reducing ability according to the results of the FRAP assay.

Melanogenesis is a natural mechanism—the product of melanocytes. Melanin is a pigment for preventing UV-induced skin damage and that acts as a photoprotectant (28). The abnormal accumulation of melanin leads to hyperpigmentation which is a main concern in cosmetics. Anti-tyrosinase agents are therefore important ingredients in cosmeceuticals for skin whitening. Skin aging can be classified as intrinsic and photo albeit both processes induce skin wrinkling. UV radiation generates ROS that can induce a transcription factor that promotes collagen destruction by upregulating enzymes, matrix metalloproteinases (MMPs). These MMPs induce collagen destruction, resulting in wrinkle formation. Laxity and fragility of the skin are also caused by ROS-activated hyaluronidase and elastase, which block hyaluronan and elastin formation, respectively (29). Since ROS causes photo and intrinsic aging, protection from UV radiation and antioxidant homeostasis is crucial. Based on the results of this study, sesamol can supplement antioxidants, which can inhibit ROS via multiple mechanisms, and it acts as photoprotection. So, sesamol can be successfully used against the skin wrinkling associated with photoaging.

In this study, cellular toxicity was determined in the human melanoma cell line (SK-MEL2) and the normal (Vero) cell line by using the NR assay after treating them with various compounds for 48 h. The known whitening agents—kojic acid and β-arbutin—and sesamol had negligible cytotoxicity on the SK-MEL2 and Vero cell lines. It should be noted that the concentration of sesamol that can inhibit cellular tyrosinase was much lower than the cytotoxic concentration.

This study demonstrated that sesamol inhibits tyrosinase activity against mushroom tyrosinase and human melanoma tyrosinase in a dose-dependent manner. These data were found to be in agreement with the previous studies regarding mushroom tyrosinase inhibition of sesamol (30). Tyrosinase inhibition of sesamol at the first and second step of melanin biosynthesis is reportedly due to competitive and non-competitive inhibition, respectively (31). β-Arbutin was previously reported to have no inhibition effect on mushroom tyrosinase but had an inhibition effect against melanoma tyrosinase (32). It has

been suggested that the cellular tyrosinase inhibition of β-arbutin is due to the intracellular conversion of arbutin to hydroquinone via the hydrolysis reaction by bacteria on the skin of humans (33). It is evidenced that the glycosidic linkage of arbutin structure could be cleaved in the cellular assay resulting in the tyrosinase inhibitory activity (34). Moreover, previous study reported that α-arbutin, which is the other isomer form, was also found to be active based on cell-based assay (35). β-Arbutin was reported to possess lesser tyrosinase inhibitory effect than α-arbutin (35). Our study found that β-arbutin exhibited low tyrosinase inhibitory effect which is in agreement with this report.

CONCLUSIONS

Evidence clearly shows that sesamol possesses high antioxidant properties and anti-tyrosinase activity. Importantly, sesamol was less cytotoxic in the human melanoma cell line (SK-MEL2). This study illustrates that sesamol—a lignan from edible sesame—could be used for cosmeceutical purposes. The molecular mechanisms underlying the antimelanogenic effect *in vitro* and *in vivo* and the safety of sesamol *in vivo* need clarification.

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