ACS OMEGA

Open Access

http://pubs.acs.org/journal/acsodf

Review

Searching for Natural Plants with Antimelanogenesis and Antityrosinase Properties for Cosmeceutical or Nutricosmetics Applications: A Systematic Review

Published as part of the ACS Omega virtual special issue "Phytochemistry".

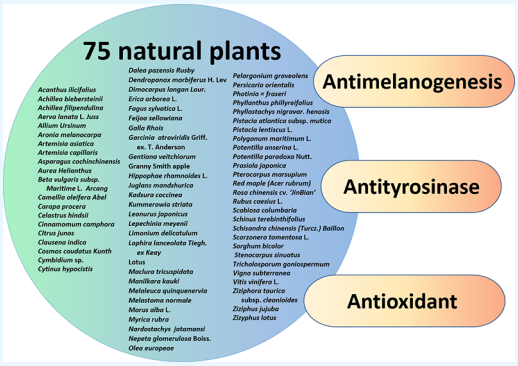
Xin Yee Tung, Jia Qi Yip, and Lai Ti Gew*

Cite This: *ACS Omega* 2023, 8, 33115−33201

Read Online

ACCESS | Metrics & More | Article Recommendations

ABSTRACT: Excessive UV radiation (UVR) exposure has been shown in studies to be a major risk factor for most melanomas, causing premature skin aging as well as immune system suppression due to the increased production of hydrogen peroxide (H_2O_2) and other reactive oxygen species (ROS) during the melanogenesis process. Although several compounds with antioxidant and antityrosinase activities are widely used in the cosmetic industry, like kojic acid, hydroquinone, ascorbic acid, and arbutin, their use has been limited due to their adverse effects on the skin and cytotoxic issues. Recently, attempts have been made to develop new natural skin-lightening products by using plant extracts that are less toxic and exhibit numerous biological properties with great market demand. In this study, information on the depigmentation effects of various natural plant species was gathered from the SCOPUS database according to the PRISMA guidelines. A total of 414 records were retrieved, and finally, 76 articles were included in the qualitative synthesis by fulfilling all the inclusion criteria. In this review, we discuss the extraction methods and biological assays of 75 highly potential plant species, including the olive, yuzu, longan, and lotus. We concluded that the use of natural plants as skin-whitening agents is highly effective as there is a significant correlation between the content of polyphenolic compounds, antimelanogenesis, antityrosinase, and antioxidant activities. However, it is worth noting that the use of extraction methods or types of solvents is very important in determining the biological activities of plants.



1. INTRODUCTION

Melanin is a pigment that is responsible for skin color as well as the protection of skin from ultraviolet (UV) damage, and free radicals from the sun are thought to be responsible for the majority of pigmentation disorders, especially hyperpigmentation.[1] There are two common types of melanin, eumelanin and pheomelanin. It is produced by the melanocytes in the membrane-bound compartments known as melanosomes and transported to keratinocytes through melanogenesis.[2,3] However, excessive synthesis and accumulation of melanin can cause abnormal hyperpigmentation, freckles, melasma, and other pigmentation disorders.[2]

Melanogenesis is a complex process regulated by the microphthalmia-associated transcription factor (MITF) and tyrosinase and tyrosinase-related proteins (TRPs).[1] This process is triggered by a variety of stimuli such as UV radiation (UVR) and α-melanin-stimulating hormone (α-MSH) in melanocytes.[2] Stimulation of α-MSH binds to melanocortin 1 receptor (MC1R) on the melanocytes' surface, thereby increasing the intracellular cytoplasmic cyclic AMP (cAMP) concentration.[4,5] High cAMP levels activate the protein kinase A (PKA) cascade, which leads to the phosphorylation of cAMP response element-binding protein (CREB) and in turn induces the expression of MITF.[2,5] Activation of MITF, which is a crucial transcription factor, increases melanin synthesis by promoting expression of tyrosinase and TRPs.[2,6] Tyrosinase is one of the key enzymes in the melanin biosynthesis pathway.[5] Tyrosinase plays a significant role in the initial steps of melanin production by catalyzing the hydroxylation of L-tyrosine into 3,4-dihydroxy-L-phenylalanine (L-DOPA), followed by oxidation of L-DOPA to dopaquinone and finally the production of melanin.[7,8] Hence, inhibition of tyrosinase activity can be used to achieve skin hypopigmentation because it catalyzes the rate-limiting steps in melanogenesis.[1]

Received: May 15, 2023
Accepted: July 25, 2023
Published: September 6, 2023

Repeated short-term exposure to UVR causes erythema of the skin and subsequently activates the melanocytes. This leads to increased tyrosinase activity and melanin production.[9] As a result, darkening of skin color known as tanning which is a type of hyperpigmentation occurs.[9] Excessive long-term exposure to UVR leads to premature aging of the skin, immune system suppression, and development of skin cancers such as melanoma skin cancers.[9,10] Additionally, UVR exposure increases the production of hydrogen peroxide (H_2O_2) and other reactive oxygen species (ROS) during the melanogenesis process, which induce melanocytes to undergo oxidative stress.[1,3] Consequently, melanin production will be increased due to the formation of ROS, producing key signals that stimulate melanogenesis.[6] It can be concluded that ROS scavengers and tyrosinase inhibitors can act as antimelanogenesis agents.[1] It is also widely recognized that UV-induced ROS generation plays a role in the pathogenesis of a variety of skin disorders, including aging, wrinkles, photosensitivity, and cancer.[11] Several compounds that are melanin inhibitors are utilized widely in cosmetic industries including kojic acid, hydroquinone, ascorbic acid, and arbutin.[2] These compounds possess antioxidant and antityrosinase activities.[12] However, their use has been limited because they can cause adverse effects on the skin and cytotoxic issues.[12]

Due to increasing health and environmental awareness, many researchers have recently been attempting to develop new natural skin-lightening products that contain phytochemicals, for instance, polyphenol, flavonoids, and carotenoids, to prevent excessive melanogenesis and hyperpigmentation.[13,14] Various phytochemicals and plant extracts have been discovered to be less toxic and exhibit numerous biological properties.[15] Thus, the studies involving the investigation of antimelanogenesis, antityrosinase, and antioxidant activities of plants are crucial to discovering their potential whitening benefits toward human skin. In this systematic review, the antimelanogenesis, antityrosinase, antioxidant, and other biological activities of various natural plant species for the development of natural product-based skin-lightening agents were summarized. This review provides information on the different extraction methods using various solvent systems to extract bioactive compounds from plant extracts, and the evaluation of their biological activities such as antimelanogenesis, antityrosinase, and antioxidant was reviewed and presented in Table 1.

2. METHODS

Preferred reporting items for systematic review and meta-analyses (PRISMA) were used as a standard to conduct the systematic review. This published standard allowed authors to gather all relevant information and used various inclusion and exclusion criteria to determine the articles that will be included in the review. It also ensures that all components of the research are reported accurately and transparently.[16] Article resources were searched using the Scopus database in May 2022. The first step of the systematic review process involved the development of a search string based on the identification of keywords from my research question and the use of Boolean Operators. The keywords used for this review were based on various plant species with antimelanogenesis and antityrosinase activities to produce a comprehensive review covering most aspects of these two activities, using the search string ("plant" OR "medicinal plant") AND ("anti-melanogenesis" OR "anti-tyrosinase"). As a result, a total of 414 records were successfully retrieved from the Scopus database.

No duplicated articles were found, and 414 records were further screened using several inclusion and exclusion criteria. The first criteria was the document type by focusing only on primary source research articles and excluded sources in the form of a review, erratum, book chapter, and conference paper. The second and third criteria were the publication stage and language, respectively, by selecting final articles only in English. Additionally, it should be noted that the timeline was chosen as a 5-year period (2017−2022). Based on these criteria, 181 articles were excluded. It is worth noting that only articles with full text were included. Search engines such as Google, Google Scholar, Elsevier, and ResearchGate were used to download the full texts. The screening stage of the articles was done based on the abstract, which indicates that articles with irrelevant content will be eliminated from this study based on the abstract screening.

After screening, a total of 185 articles were selected for the eligibility assessment process. For the eligibility assessment, the main contents of the articles were assessed thoroughly to ensure that relevant and sufficient information matches with the objectives of the review. Hence, 109 articles were eliminated due to lack of data and insufficient information on the evaluation of biological activities of plants and did not focus on the biological activities of individual plant species but rather a variety of plant species. Finally, the remaining 76 articles were included in the qualitative synthesis as shown in Figure 1.

3.0. RESULTS AND DISCUSSION

Table 1 shows the antimelanogenesis, antityrosinase, antioxidant, and other biological activities of various natural plant species. The plant parts, extraction methods, and biological assays used for investigation of biological activities were also recorded in the table.

Based on the strong evidence of biological activities of plant extracts, the studies that focus on the determination of melanin content, tyrosinase inhibition, and antioxidant activity can identify natural plants with potent depigmenting effects. To investigate the antimelanogenesis activity, the quantification analysis of melanin contents was measured using a specific melanoma cell line, while mushroom tyrosinase activity and cellular tyrosinase activity assays were generally used to evaluate antityrosinase activity. In addition, there were a variety of assays such as DPPH, ABTS, CUPRAC, and FRAP that can be performed to examine the antioxidant activity of plant extracts. Other biological activities including antiaging, antidiabetic, and anti-inflammatory activities also have been identified from the plant extracts.

3.1. Extraction Methods. Extraction is the crucial first step in the analysis of natural plants because it is important to extract the desired bioactive compounds from the plant materials for further separation and characterization.[17] Different solvent systems are available to extract the bioactive compounds from plants, and the solvent is chosen based on the polarity of the solute of interest.[17,18] The solute will dissolve properly in a solvent with polarity identical to the solute.[18] Solvents such as ethanol, methanol, ethyl acetate, water, chloroform, acetone, acetonitrile, dichloromethane, and butanol or nonpolar solvents such as hexane, benzene, and petroleum ether are commonly employed for extraction. In particular, ethanol and water are the most popular solvents used by biologists for extraction due to their lower toxicity and effectiveness in extracting bioactive compounds. However,

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. Extraction Method, Biological Assays, Antimelanogenesis, Antityrosinase, and Other Biological Activities[a]

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
Acanthus ilicifolius	Leaves	**Sample preparation**: Leaves were freeze-dried, grinded into fine powders, and subjected to extraction and purification	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-Arbutin as positive control	Antioxidant:	24
		Solvent extraction: 70% acetone−water	**Antioxidant**: DPPH, ABTS, and FRAP assays		**-Tyrosinase inhibition IC_{50}**:	a) DPPH assay:	
		Extracted crude extract separated by column chromatography, which first eluted with methanol−water and then 70% acetone−water to obtain condensed tannins (CTs)			CTs: 19.7 ± 0.13 μg/mL	-Ascorbic acid as standard	
		Temperature: 25 °C			Arbutin: 10.89 mg/mL	-EC_{50} (μg/mL): CTs: 104 ± 0.894 Ascorbic acid: 131.47 ± 1.90 **b) ABTS assay**: -Ascorbic acid as standard -EC_{50} (μg/mL): CTs: 86 ± 0.616 Ascorbic acid: 119.97 ± 0.463 **c) FRAP assay**: -Ascorbic acid as standard -EC_{50} (mg AAE/g): CTs: 758.28 ± 2.42 Ascorbic acid: NR	
Achillea biebersteinii	Flowers	**Solvent extraction**: Distilled H_2O, 75% EtOH, 50% EtOH, 25% EtOH	**Antimelanogenesis**: Melanin content assay using B16F10 murine melanoma cells	-Fractions 25 and 27 obtained from extracts using ASE decreased the melanin release from B16F10 cells	-Kojic acid as positive control	**Antioxidant**:	25
		Extraction method: Accelerated solvent extraction (ASE), maceration (M), ultrasonic-assisted extraction (UAE), shaking extraction (SE). Extracts were further fractionated by column chromatography	**Antityrosinase**: Mushroom tyrosinase inhibitory assay using L-DOPA as a substrate		**Mushroom tyrosinase activity**:	-Vitamin C as standard	
		Temperature: 60 °C, 80 °C, 100 °C, 120 °C, 140 °C, 160 °C, 180 °C	**Antioxidant**: DPPH assay		-Extracts obtained by ASE under 160 °C possessed the highest mushroom	-Extracts obtained by UAE. SE had better antioxidant activity than extracts obtained by ACE and M	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
					tyrosinase inhibitory activity. Hence, this extract was fractionated, with fractions 5, 6, and 7 showing 34.9, 24.3, and 31.5% inhibitory activity, respectively		
					Murine tyrosinase activity:		
					Fractions 25 and 27 showed significant murine tyrosinase inhibitory activity with approximately 80%		
Achillea filipendulina	Flower, leaves	**Isolation of essential oil**: Flowers and leaves subjected to hydrodistillation, and essential oil (EO) was collected	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	26
		Extraction method: maceration technique using EtOH	**Antioxidant**: DPPH, ABTS, and PM assays, metal chelating activity		**-Tyrosinase inhibition (mg KAE/g extract)**:	**a) DPPH assay (mg TE/g extract)**:	
			α-amylase, α-glucosidase, and cholinesterase inhibition: α-amylase, α-glucosidase and cholinesterase inhibition assays		Flowers-EtOH: 23.97 ± 0.84	Flowers-EtOH: 53.93	
					Leaves-EtOH: 24.41 ± 0.95	Leaves-EtOH: 51.70	
					Flower-EO: NR	Flower-EO: 25.87	
					Leaves-EO: NR	Leaves-EO: 22.13	
						b) ABTS assay (mg TE/g extract):	
						Flowers-EtOH: 43.47	
						Leaves-EtOH: 35.03	
						Flower-EO: 18.23	
						Leaves-EO: 15.40	
						c) PM assay (mg AAE/g extract):	
						Flowers-EtOH: 84.03	
						Leaves-EtOH: 70.17	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						Flower-EO: NR Leaves-EO: NR **d) Metal chelating assay: (mg EDTAE/g extract):** Flowers-EtOH: 37.13 Leaves-EtOH: 30.47 Flower-EO: NR Leaves-EO: NR **α-amylase inhibition (mmol ACE/g extract):** Flowers-EtOH: 1.91 ± 0.05 Leaves-EtOH: 1.75 ± 0.05 Flower-EO: 0.71 ± 0.04 Leaves-EO: 0.48 ± 0.02 **α-glucosidase inhibition (mmol ACE/g extract):** Flowers-EtOH: 2.84 ± 0.04 Leaves-EtOH: 2.97 ± 0.06 Flower-EO: 0.98 ± 0.03 Leaves-EO: 1.10 ± 0.07 **Cholinesterase inhibition (mg GALAE/g extract):** **AChE inhibition:** Flowers-EtOH: 2.46 ± 0.06 Leaves-EtOH: 2.31 ± 0.05 Flower-EO: 1.41 ± 0.07 Leaves-EO: 0.94 ± 0.06 **BChE inhibition:** Flowers-EtOH: 3.65 ± 0.07 Leaves-EtOH: 2.83 ± 0.05 Flower-EO: 1.90 ± 0.04 Leaves-EO: 1.28 ± 0.09	
Aerva lanata L. Juss	Herb	**Solvent extraction**: 50% EtOH, 80% EtOH, 100% EtOH, H_2O	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-Kojic acid as positive control	**Antioxidant:**	27

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
		Temperature: 60 °C, 80 °C, 100 °C, 180 °C	**Antioxidant**: DPPH, ABTS, metal-chelating activity, oxygen radical absorbance (ORAC) assays		**-Tyrosinase inhibition EC_{50} (μg/mL)**:	**a) DPPH assay (mg TE/g)**:	
			Antielastase: Elastase inhibition assay		**100% EtOH**:	**100% EtOH**:	
			Anticollagenase activity: Collagenase inhibition assay		60 °C: 46.48 ± 2.93	60 °C: 10.07 ± 0.23	
					180 °C: 52.19 ± 2.84	80 °C: 9.17 ± 0.07	
					80% EtOH:	100 °C: 10.28 ± 0.46	
					60 °C: 43.32 ± 0.57	180 °C: 72.48 ± 0.91	
					180 °C: 60.10 ± 0.44	**80% EtOH**:	
					50% EtOH:	60 °C: 19.86 ± 0.01	
					60 °C: 46.08 ± 0.29	80 °C: 18.02 ± 0.09	
					180 °C: 58.56 ± 0.37	100 °C: 48.43 ± 1.60	
					H_2O:	180 °C: 119.85 ± 1.95	
					60 °C: 155.97 ± 1.34	**50% EtOH**:	
					180 °C: 124.62 ± 1.14	60 °C: 24.84 ± 0.52	
					Kojic acid: 28.42 ± 0.11	80 °C: 23.28 ± 0.00	
						100 °C: 24.28 ± 1.18	
						180 °C: 82.63 ± 0.90	
						H_2O:	
						60 °C: 15.22 ± 0.71	
						80 °C: 16.27 ± 0.67	
						100 °C: 21.71 ± 0.94	
						180 °C: 79.94 ± 1.12	
						b) ABTS assay (mg TE/g):	
						100% EtOH:	
						60 °C: 9.90 ± 0.01	
						80 °C: 12.77 ± 0.00	
						100 °C: 12.31 ± 0.21	
						180 °C: 98.94 ± 1.75	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						80% EtOH:	
						60 °C: 11.60 ± 0.10	
						80 °C: 14.37 ± 0.28	
						100 °C: 50.22 ± 0.36	
						180 °C: 107.58 ± 1.32	
						50% EtOH:	
						60 °C: 34.72 ± 0.80	
						80 °C: 36.11 ± 1.06	
						100 °C: 33.61 ± 0.83	
						180 °C: 81.16 ± 3.81	
						H_2O:	
						60 °C: 38.61 ± 0.48	
						80 °C: 42.16 ± 0.34	
						100 °C: 34.57 ± 1.88	
						180 °C: 88.12 ± 1.26	
						c) Metal chelating activity:	
						EC_{50} (mg/mL):	
						100% EtOH:	
						60 °C: 1.58 ± 0.17	
						180 °C: 5.30 ± 0.70	
						80% EtOH:	
						60 °C: 3.42 ± 0.06	
						180 °C: 5.10 ± 0.01	
						50% EtOH:	
						60 °C: 2.59 ± 0.18	
						180 °C: 3.70 ± 0.08	
						H_2O:	
						60 °C: na	
						180 °C: na	
						d) ORAC assay (mM TE/g):	
						100% EtOH:	
						60 °C: 0.36 ± 0.06	
						180 °C: 1.85 ± 0.19	
						80% EtOH:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						60 °C: 0.93 ± 0.20	
						180 °C: 2.35 ± 0.18	
						50% EtOH:	
						60 °C: 0.90 ± 0.30	
						180 °C: 3.84 ± 0.06	
						H_2O:	
						60 °C: 0.81 ± 0.09	
						180 °C: 2.32 ± 0.20	
						Antielastase:	
						-Epigallocatechin gallate as positive control	
						EC_{50} (mg/mL):	
						100% EtOH:	
						60 °C: na	
						180 °C: 57.26 ± 0.30	
						80% EtOH:	
						60 °C: 95.25 ± 1.26	
						180 °C: 22.54 ± 1.86	
						50% EtOH:	
						60 °C: 153.82 ± 2.88	
						180 °C: 35.81 ± 0.81	
						H_2O:	
						60 °C: na	
						180 °C: 166.23 ± 5.42	
						Anticollagenase:	
						-Epigallocatechin gallate as positive control	
						EC_{50} (mg/mL):	
						100% EtOH:	
						60 °C: 598.23 ± 2.65	
						180 °C: 78.47 ± 0.29	
						80% EtOH:	
						60 °C: 129.44 ± 0.49	
						180 °C: 59.73 ± 0.31	
						50% EtOH:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						60 °C: 158.08 ± 3.61 180 °C: 21.76 ± 1.27 **H_2O:** 60 °C: 63.07 ± 14.08 180 °C: 134.32 ± 3.20	
Allium ursinum	Leaves	**Solvent extraction**: H_2O, 70% EtOH, 100% EtOH	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	28
		Temperature: 40 °C	**Antioxidant**: DPPH assay		**- Tyrosinase inhibition IC_{50} (mg/mL)**: H_2O: 0.414 70% EtOH: 0.392 100% EtOH: 0.402 Kojic acid: 0.031	**A) DPPH assay**: -Ascorbic acid as standard SC_{50} (values of active DPPH scavengers): H_2O: 0.471 mg/mL 70% EtOH: 0.532 mg/mL 100% EtOH: 0.643 mg/mL Ascorbic acid: 0.008 μ/mL	
Aronia melanocarpa	Stems	**Solvent extraction**: H_2O	**Antityrosinase**: Dopachrome method using L-DOPA as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	29
		Temperature: 130 °C	**Antioxidant**: DPPH and reducing power assays		**-Tyrosinase inhibition of H_2O extract (mg KAE/g extract)**: 15.87 ± 3.82	**a) DPPH assay**:	
			Enzyme inhibitory activity: α-amylase and α-glucosidase were evaluated using Caraway-Somogyi iodine/potassium iodide (IKI) and 4-*N*-trophenyl-α-D-glucopyranoside method respectively			-IC_{50} of H_2O extract: 0.10 ± 0.02 mg/mL **b) Reducing power assay**:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						-IC_{50} of H_2O extract: 1.25 ± 0.03 mg/mL **Antidiabetic activity**: **a) α-amylase inhibition (mmol ACAE/g extract)**: 0.59 ± 0.01 -Acarbose as standard **b) α-glucosidase (mmol ACAE/g extract)**: 7.50 ± 0.32 -Acarbose as standard	
Artemisia asiatica	NR	**Preparation**: 95% EtOH extract was purchased	**Antimelanogenesis**: Melanin formation assays using B16F10, a melanoma cell line	-Arbutin as positive control	-Arbutin as positive control	NR	30
			Antityrosinase: Mushroom tyrosinase activity assay using L-DOPA as a substrate and cellular tyrosinase activity assay in B16F10 cells	-EtOH extract suppressed melanin secretion and decreased the melanin content in α-MSH -stimulated B16F10 cells in a dose-dependent manner	-EtOH extract inhibited the mushroom tyrosinase and cellular tyrosinase activity in a dose-dependent manner and had a stronger tyrosinase inhibitory effect than arbutin		
Artemisia capillaris	NR	**Solvent extraction**: 100% EtOH with concentrations of 0, 6.25, 12.5, 25, 50 μg/mL	**Antimelanogenesis**: Melanin content assay using B16F10 mouse melanoma cells	EtOH extract reduced the cellular melanin content in a dose-dependent manner in α-MSH-stimulated B16F10 cells, with a 40.24% inhibition at 50 μg/mL	EtOH extract significantly decreased cellular tyrosinase activity in a dose-dependent manner, with a 30.92% inhibition at 50 μg/mL	NR	31
		Temperature: 25 °C	**Antityrosinase**: Cellular tyrosinase activity assay in B16F10 cells				
Asparagus cochinchinen-sis	Roots	**Solvent extraction and preparation**: 25% EtOAc and fermentation	**Antimelanogenesis**: Melanin content assay using HEMs and A375.S2	Fermented and unfermented extracts inhibit melanogenesis in HEMs and A375.S2 in a	-Kojic acid and α-arbutin as positive controls	**Antioxidant**:	32

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
				dose-dependent manner			
		Temperature: 40 °C	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine as a substrate and cellular tyrosinase activity assay in HEMs and A375.S2		**a) Mushroom tyrosinase activity**:	**A) DPPH assay**:	
			Antioxidant: DPPH and reducing power assays		-IC_{50} (mg/L):	-BHT as standard	
					Fermented extracts: 50.6 ± 3.1	-IC_{50} (mg/L):	
					Unfermented extracts: 527.3 ± 23.6	Fermented extracts: 250.6 ± 32.5	
					Kojic acid: 18.6 ± 0.5	Unfermented extracts: 586.9 ± 86.1	
					α-arbutin: 261.4 ± 12.8	BHT: 105.3 ± 285.6 mg/L	
					b) Cellular tyrosinase activity (% of inhibition):	**B) Reducing power assay**:	
					Fermented extracts: 48.6% ± 1.8% − 55.8% ± 2.3%	-BHA, ascorbic acid, α-tocopherol as standards	
					Unfermented extracts: 3.6% ± 2.0% − 28.4% ± 1.3%	-IC_{50} (mg/L):	
						Fermented extracts: 25.7 ± 3.5	
						Unfermented extracts: 59.0 ± 6.2	
						BHA: 35.4 ± 2.6	
						Ascorbic acid: 76.8 ± 6.2	
						α-tocopherol: 53.2 ± 3.7	
Aurea helianthus	Stem	**Solvent extraction**: EtOH	**Antimelanogenesis**: Melanin content assay using B16 melanoma cells	The extract reduced the melanin content by 20% in α-MSH-stimulated B16 melanoma cells	The extract inhibited the tyrosinase activity in a dose-dependent manner	NR	4
		Temperature: 60 °C	**Antityrosinase**: Cellular				

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
			tyrosinase activity assay in B16 cells				
Beta vulgaris subsp. Maritime(L.) Arcang.	Aerial parts	**Preparation**: Aerial parts subjected to hydro distillation and essential oil was collected	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosinase as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	33
			Antioxidant: DPPH (2,2-Diphenyl-1-picrylhydrazyl) radical scavenging assay, ABTS (2,2′-azino-bis-3-azoline-6-sulfonic acid) radical-scavenging assay, reducing power assay, catalase activity, paraoxonase activity (*PON1*)		**-Tyrosinase Inhibition rate (%)**:	**a) DPPH assay**:	
			Anticholinesterase activity: Colorimetric method		Essential oil: 67	-BHT as standard	
					Kojic acid: 85	-IC_{50} (mg/mL): Essential oil: 0.055 ± 0.006 BHT: 0.018 ± 0.010	
						b) ABTS assay: -BHT as standard -IC_{50} (mg/mL): Essential oil: 0.079 ± 0.010 BHT: 0.050 ± 0.0	
						c) Reducing power assay: -BHT as standard -IC_{50} (mg/mL): Essential oil: 0.120 ± 0.002 BHT: 0.020 ± 0.010	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						d) Catalase activity (u/mg protein):	
						-Vitamin C as standard	
						- Essential oil: 524.447 ± 2.58	
						-Vitamin C: 757.575 ± 0.002	
						e) PON1 activity(μM/min/L)	
						-Ascorbic acid as standard	
						-Essential oil: 55.0 ± 1.5	
						-Ascorbic acid: 55.0 ± 0.2	
						Anticholinesterase activity:	
						-Galantamine as standard	
						-IC_{50} (μg/mL):	
						Essential oil: 36 ± 5	
						Galantamine: 0.38 ± 0.002	
Camellia oleifera Abel	Shell	**Solvent extraction**: MeOH, H_2O, 1,3-butanediol	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-Kojic acid as positive control	NR	34
		Temperature: 50 °C			**-Tyrosinase inhibition rate (%)**:		
					1,3-butanediol extract: 71.9		
					MeOH extract: 49.2		
					H_2O extract: 39.3		
Carapa procera	Leaves, stem, bark	**Extraction method (solvent extraction, temperature)**: Maceration (MeOH, 25 °C), infusion (boiling water, 100 °C)	**Antityrosinase**:	NR	-Kojic acid as positive control	**Antioxidant**:	35
			Tyrosinase inhibition assay		**-Tyrosinase inhibition (mg KAE/g extract)**:	-Trolox and EDTA as standard	
			Antioxidant: DPPH, ABTS, CUPRAC, FRAP, metal chelating, PM assays		Leaves: 73.43 ± 0.07	-In general, MeOH extract of stem bark had the highest antioxidant activity in all tested assays with 3.14 ± 0.01 mmol TE/g of ABTS assay, 4.47 ± 0.07 mmol TE/g of assay, and 2.15 ± 0.01 mmol TE/g of FRAP assay	
			α-glucosidase, α-amylase, and cholinesterase inhibition: α-amylase,		Stem barks: 75.25 ± 0.20	**Cholinesterase inhibition (mg GALAE/g)**:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
			α-glucosidase, and cholinesterase inhibition assays			-Catechin as positive control **AChE inhibition**: Leaves: 2.55 ± 0.02 Stem bark: 2.54 ± 0.01 **BChE inhibition**: Leaves: 4.16 ± 0.26 Stem bark: 4.58 ± 0.13 **α-glucosidase and α-amylase inhibition**: -Acarbose and galantamine as positive control for α-glucosidase and α-amylase inhibition assays, respectively -MeOH extract of both plant parts exhibits moderate inhibitory activity against α-glucosidase (0.95 ± 0.01 mmol ACAE/g) and high inhibitory activity against α-amylase (0.77 ± 0.01 mmol ACAE/g)	
Celastrus hindsii	Leaves	**Solvent extraction**: MeOH	**Antityrosinase**: Tyrosinase inhibition assay using L-tyrosine as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	36
		Extracted crude extract separated into: hexane, H_2O, EtOAc extract	**Antioxidant**: DPPH and ABTS assays		**-Tyrosinase inhibition IC_{50} (μg/mL)**:	**a) DPPH assay**:	
		Separated extracts were further fractionated, and the fractions were combined to run column chromatography a second time. α-Amyrin and β-Amyrin were identified through gas chromatography−mass spectrometry			α-Amyrin and β-amyrin: 178.85 ± 3.28	-BHT as positive control	
		Temperature: 25 °C			Kojic acid: 15.55 ± 2.28	-IC_{50} (μg/mL): α-Amyrin and β-Amyrin: 125.55 ± 0.98 BHT: 8.22 ± 0.89 **b) ABTS assay**: -BHT as standard	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						-IC_{50} (μg/mL):	
						α-Amyrin and β-Amyrin: 155.28 ± 1.01	
						BHT: 53.40 ± 1.52	
Cinnamomum camphora	Leaves, branches	**Solvent extraction**: First ultrasonically extracted with acetone aqueous solution and then extracted by PE and EtOAc	**Antityrosinase**: Monophenolase and diphenolase activity assay	NR	**-Tyrosinase monophenolase inhibition IC_{50} (μg/mL)**:	**Antioxidant**:	37
		Proanthocyanidins (PAs) were obtained after several steps of extraction	**Antioxidant**: DPPH, ABTS, and FRAP assays		Leaves: 167 ± 18	**a) DPPH assay**:	
					Branches: 268 ± 24	-Vitamin C as standard	
					-Tyrosinase diphenolase inhibition IC_{50} (μg/mL):	-IC_{50} (μg/mL):	
					Leaves: 70 ± 7	Leaves: 78 ± 13	
					Branches: 91 ± 8	Branches: 274 ± 28	
						Vitamin C: 72.9 ± 0.5	
						b) ABTS assay:	
						-Vitamin C as standard	
						-IC_{50} (μg/mL):	
						Leaves: 117 ± 16	
						Branches: 230 ± 30	
						Vitamin C: 74 ± 9	
						c) FRAP assay:	
						-IC_{50} (μg/mL):	
						Leaves: 4.7 ± 0.5	
						Branches: 3.6 ± 0.4	
Citrus junos	Leaves, flowers, seeds	**Preparation**: Transfer of explants into a medium to generate yellow callus extract with concentrations of 0, 50, 100, 500, 1000 μg/mL	**Antimelanogenesis**: Melanin content assay using B16F10, a melanoma cell line	-Arbutin as positive control	Callus extract showed inhibition of tyrosinase activity in a dose-dependent manner.	**Antioxidant**:	38
			Antityrosinase: Mushroom tyrosinase activity assay using L-DOPA as a substrate	-1000 μg/mL of callus extract showed a 59.3 ± 4.20% inhibition of melanogenesis, which was stronger than arbutin.		**a) DPPH assay**:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
			Antioxidant: DPPH assay			-Ascorbic acid as standard -1000 μg/mL of callus extract exhibited 68.5 ± 9.49% of DPPH free radical scavenging ability, which was comparable to 125 μM of ascorbic acid (62.3 ± 1.78%).	
Clausena indica	Roots	**Solvent extraction**: MeOH	**Antityrosinase**: Tyrosinase inhibitory assay using L-tyrosine as a substrate	NR	-Myricetin as positive control	**Antioxidant**:	39
		Extracted crude extract fractioned into: EtOAc, hexane	**Antioxidant**: DPPH, ABTS, and lipid peroxidation inhibitory (LPI) assays		**-Tyrosinase inhibition IC_{50} (μg/mL)**:	**a) DPPH assay**:	
		EtOAc extract was subjected to column chromatography to produce 5 fractions (Re1−Re5). Three compounds (dentatin, nordentatin, clausine K) were isolated from 5 fractions			Dentatin: NR	-BHT as standard	
					Nordentatin: NR	-IC_{50} (μg/mL):	
					Clausine K: 179.5	Dentatin: NR	
					Myricetin: 735.6	Nordentatin: 49.2 ± 0.5	
						Clausine K: 2197.8 ± 53.3	
						BHT: 16.0 ± 0.2	
						b) ABTS assay:	
						-BHT as standard	
						-IC_{50} (μg/mL):	
						Dentatin: NR	
						Nordentatin: 69.9 ± 1.1	
						Clausine K: 5264.0 ± 164.0	
						BHT: 82.8 ± 1.1	
						c) LPI assays:	
						-BHT as standard	
						-LPI (%):	
						Dentatin: 37.9 ± 0.8% Nordentatin: 69.8 ± 0.4%	
						Clausine K: 60.6 ± 1.1%	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						BHT: 82.7 ± 0.3%	
Cosmos caudatus Kunth	Leaves	**Solvent extraction**: H_2O	**Antityrosinase**: Antityrosinase assay using L-tyrosine as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	40
			Antioxidant: DPPH and ABTS assays		**-Tyrosinase inhibition IC_{50} (μg/mL)**:	**a) DPPH assay**:	
					H_2O extract: 693.2	-Trolox as standard	
					Kojic acid: 77.8	-IC_{50} (μg/mL):	
						H_2O extract: 163.6	
						Trolox: 3.32	
						b) ABTS assay:	
						-Trolox as standard	
						-IC_{50} (μg/mL):	
						H_2O extract: 57.2	
						Trolox: 6.51	
Cymbidium sp. (Orchidaceae)	Flowers, leaves, pseudobulbs, roots	**Solvent extraction**: CH_2Cl_2, EtOAc, EtOH/H_2O with concentrations of 75, 150, 300 μg/mL	**Antityrosinase**: Dopachrome method using L-DOPA as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	41
			Antioxidant: DPPH assay		**-Tyrosinase inhibition rate (%) at 300 μg/mL**:	**a) DPPH assay**:	
			Collagenase inhibitory activity: Collagenase assay		-CH_2Cl_2 extracts of any plant parts were not active	-Gallic acid as positive control	
					EtOAc:	-IC_{50}(μg/mL):	
					Pseudobulb: 54.19 ± 3.72	Flowers:	
					Roots: 37.50 ± 2.54	CH_2Cl_2: na	
					Flowers: 28.29 ± 2.93	EtOAc: na	
					EtOH/H_2O:	EtOH/H_2O: na	
					Pseudobulb: 64.11 ± 2.34	Leaves:	
					Roots and Flowers: na	CH_2Cl_2: na	
						EtOAc: na	
						EtOH/H_2O: na	
						Pseudobulbs:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						CH_2Cl_2: 165.78	
						EtOAc: 114.18	
						EtOH/H_2O: 233.32	
						Roots:	
						CH_2Cl_2: 174.61	
						EtOAc: 127.17	
						EtOH/H_2O: 304.02	
						Collagenase inhibitory activity: EtOAc extract of pseudobulbs and roots displayed 4.01 ± 1.32% and 82.79 ± 1.60% inhibition of collagenase at 75 μg/mL. It exhibited high inhibitory activity	
Cytinus hypocistis	Whole plant, petals, stalks, nectar	**Solvent extraction**: 80:20 EtOH/H_2O	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	42
			Antioxidant: OxHLIA (oxidative hemolysis inhibition), TBARS (Thiobarbituric acid reactive substance) assays		**-Tyrosinase inhibition IC_{50} (mg/mL)**:	**a) OxHLIA**	
			Antidiabetic: α-glycosidase inhibitory assay		Whole plant extract (CH): 0.20 ± 0.01	-Trolox as standard	
			Anti-inflammatory: Nitric acid production was assessed using LPS-stimulated RAW 264. Seven macrophages		Petals extract (PCH): 0.19 ± 0.01	-IC_{50} (ng/mL):	
					Stalks extract (SCH): 0.09 ± 0.02	CH: 285 ± 4	
					Nectar extract (NCH): 27.6 ± 0.7	PCH: 279 ± 5	
					Kojic acid: 0.078 ± 0.001	SCH: 306 ± 2	
						NCH: 672 ± 15	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						Trolox: 20384 ± 36 **b) TBARS** -Trolox as standard -IC_{50} (ng/mL): CH: 413 ± 9 PCH: 342 ± 2 SCH: 634 ± 12 NCH: 551 ± 13 Trolox: 5389 ± 320 **Antidiabetic activity**: -Acarbose as positive control -IC_{50} (mg/mL): CH: 0.040 ± 0.001 PCH: 0.046 ± 0.004 SCH: 0.039 ± 0.001 NCH: 0.214 ± 0.005 Acarbose: 0.83 ± 0.02 **Anti-inflammatory**: -Dexamethasone as positive control -IC_{50} (μg/mL): CH: 136 ± 11 PCH: 127 ± 8 SCH: 127 ± 12 NCH: 277 ± 14 Dexamethasone: 16 ± 1	
Dalea pazensis Rusby	Roots	**Solvent extraction**: Benzene **Extracted crude extract fractioned into**: *n*-hexane/EtOAc, chloroform/EtOH and benzene/EtOAc to yield 4 compounds which are pazentin A (1), pazentin B (2), 4′-hydroxy-2′-3-methoxy-5′-(1‴,1‴-dimethylallyl)-8-prenylpinocembrin (3) and 2′,4′-dihydroxy-4 5′-(1‴,1‴-dimethylallyl)-8-prenylpinocembrin (4)	**Antimelanogenesis**: Melanin content assay using B16 murine melanoma cells	-Kojic acid as positive control - **Melanin inhibition IC_{50}**:	-Kojic acid as positive control **Mushroom tyrosinase activity assay**:	NR	43

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
		Temperature: 25 °C	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosinase as a substrate and intracellular tyrosinase inhibition assay in B16 cells	Compound 1 (0.75 ± 0.2 μM) > Compound 4 (1.0 ± 0.4 μM) > Compound 2 and 3 (5.0 ± 1.0 μM and 5.0 ± 1.8 μM)	-IC_{50} (μM): Compound 1 and 2:0 Compound 3: 49.80 ± 0.09 Compound 4: 2.32 ± 0.06 Kojic acid: 4.93 ± 0.01 **Intracellular tyrosinase inhibition assay**: -% Intracellular tyrosinase inhibition: Compound 4: 34.2 ± 0.2% Compound 1, 2, and 3: 0% Kojic acid: 45.4 ± 0.1		
Dendropanax morbiferus H. Lev	Leaves	**Solvent extraction**: H_2O	**Antimelanogenesis**: Melanin content assay using B16F10 melanoma cells	-Arbutin as positive control	-Arbutin as positive control	NR	8
		Temperature: 100 °C	**Antityrosinase**: Intracellular tyrosinase activity assay in B16F10 cells	-H_2O extract effectively decreased the melanin content in α-MSH-stimulated B16F10 cells	-H_2O extract remarkably reduced the intracellular tyrosinase activity in α-MSH-stimulated B16F10 cells in a dose-dependent manner		
Dimocarpus longan Lour. (Longan)	Barks	**Sample preparation**: Powders of longan bark were obtained using a vacuum freeze-drying machine	**Antimelanogenesis**: Melanin content assay using B16 mouse melanoma cells	200 μg/mL of condensed tannins decreased the melanin content of B16 cells to 45.2 ± 1.3%	- **Monophenolase IC_{50}**:	NR	44
		Solvent extraction: 70% acetone/H_2O were first ultrasonic extracted the powder of longan bark and then further purified by petroleum ether (PE) and ethyl acetate to obtain the condensed tannins (CTs) of longan	**Antityrosinase**: Monophenolase and diphenolase activity assay and intracellular tyrosinase		CTs: 43.7 ± 0.3 μg/mL		

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
		bark with concentrations of 50, 100, 150, 200 μg/mL	activity assay using B16 mouse melanoma cells				
					-Diphenolase IC_{50}: CTs: 11.5 ± 0.8 μg/mL -In intracellular tyrosinase activity assay, 200 μg/mL of condensed tannins significantly reduced intracellular tyrosinase activity of B16 cells to 40.3 ± 1.5%.		
Erica arborea L.	Leaves	**Solvent extraction**: EtOH	**Antityrosinase**: Mushroom tyrosinase activity assay	NR	-Kojic acid as positive control	**Antioxidant**:	45
		Temperature: 120 °C	**Antioxidant**: DPPH, ABTS, FRAP, and CUPRAC assays, metal chelating, PM methods		**-Tyrosinase inhibition (mg KAE/g)**:	**a) DPPH assay (mg TE/g extract)**:	
		Extraction method: Accelerated solvent extraction (ASE), microwave-assisted extraction (MAE), maceration (MAC), Soxhlet (SOE), and ultrasound-assisted extraction (UAE)	**Enzyme inhibition activity**: Cholinesterase, α-amylase and α-glucosidase inhibition assays		ASE: 177.43 ± 2.30	ASE: 209.59 ± 4.37	
					MAE: 180.29 ± 1.87	MAE: 179.17 ± 2.93	
					MAC: 171.18 ± 3.45	MAC: 92.19 ± 1.46	
					SOE: 172.20 ± 1.82	SOE: 76.43 ± 0.90	
					UAE: 171.05 ± 1.14	UAE: 66.61 ± 3.41	
						b) ABTS assay (mg TE/g extract):	
						ASE: 359.45 ± 18.22	
						MAE: 325.87 ± 9.48	
						MAC: 176.27 ± 9.25	
						SOE: 185.15 ± 6.28	
						UAE: 148.06 ± 1.96	
						c) CUPRAC assay (mg TE/g extract):	
						ASE: 872.24 ± 9.87	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						MAE: 782.27 ± 10.12	
						MAC: 449.96 ± 11.72	
						SOE: 442.15 ± 7.75	
						UAE: 340.90 ± 6.89	
						d) FRAP assay (mg TE/g extract):	
						ASE: 590.53 ± 4.19	
						MAE: 532.11 ± 9.52	
						MAC: 328.78 ± 8.42	
						SOE: 324.48 ± 5.74	
						UAE: 227.36 ± 1.44	
						e) Metal chelating assay (mg EDTAE/g extract):	
						ASE: 4.74 ± 0.30	
						MAE: 3.49 ± 0.40	
						MAC: 3.80 ± 0.16	
						SOE: 1.43 ± 0.01	
						UAE: 5.13 ± 0.42	
						f) PM method (mmol TE/g extract):	
						ASE: 1.84 ± 0.03	
						MAE: 1.66 ± 0.04	
						MAC: 1.50 ± 0.05	
						SOE: 1.66 ± 0.05	
						UAE: 1.26 ± 0.03	
						Cholinesterase inhibition (mg GALAE/g extract):	
						AChE inhibition:	
						ASE: 3.71 ± 0.03	
						MAE: 4.33 ± 0.03	
						MAC: 4.91 ± 0.14	
						SOE: 4.67 ± 0.18	
						UAE: 4.91 ± 0.11	
						BChE inhibition:	
						ASE: 5.52 ± 0.05	
						MAE: 5.69 ± 0.06	
						MAC: 5.99 ± 0.06	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						SOE: 5.97 ± 0.13	
						UAE: 6.18 ± 0.01	
						α-amylase inhibition (mmol ACAE/g extract):	
						ASE: 0.52 ± 0.04	
						MAE: 0.39 ± 0.02	
						MAC: 0.48 ± 0.06	
						SOE: 0.38 ± 0.03	
						UAE: 0.39 ± 0.06	
						α-glucosidase inhibition (mmol ACAE/g extract):	
						ASE: 1.63 ± 0.02	
						MAE: 1.64 ± 0.01	
						MAC: 1.60 ± 0.01	
						SOE: 1.57 ± 0.01	
						UAE: 1.62 ± 0.01	
Fagus sylvatica L.	Bark	**Extraction method**: Microwave-assisted extraction	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	46
		Solvent extraction: H_2O, 50:50 EtOH-H_2O, 80:20 EtOH-H_2O	**Antioxidant**: DPPH and FRAP assays		**-Tyrosinase inhibition (%)**:	**a) DPPH assay (mg TE/g extract)**:	
			Antidiabetic: α-glucosidase inhibitory assay		H_2O: na	H_2O: 676.29 ± 19.80	
					50:50 EtOH/H_2O: 45.99 ± 5.26	50:50 EtOH/H_2O: 741.43 ± 59.44	
					80:20 EtOH/H_2O: na	80:20 EtOH/H_2O: 505.02 ± 42.02	
						b) FRAP assay (mg TE/g extract):	
						H_2O: 625.13 ± 9.62	
						50:50 EtOH/H_2O: 783.24 ± 31.24	
						80:20 EtOH/H_2O: 592.84 ± 44.02	
						Antidiabetic activity:	
						-Acarbose as positive control	
						-IC_{50} (μg/mL):	
						H_2O: 92	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						50:50 EtOH/H_2O: 168	
						80:20 EtOH/H_2O: 38	
						Acarbose: 838	
Feijoa sellowiana	Leaves	**Solvent extraction**: Methylene chloride	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-Kojic acid, quercetin as positive control	**Antioxidant**:	47
			Antioxidant: DPPH, ABTS, FRAP, CUPRAC, PM and metal chelating assays		**-Tyrosinase inhibition (mg KAE/g extract)**:	**a) DPPH assay (mg TE/g extract)**:	
			Enzyme inhibition activity: α-glucosidase, α-amylase, and cholinesterase inhibition assays		Extract: 115.85 ± 2.55	-Trolox as standard	
					Quercetin: 163.05 ± 5.19	Extract: 90.58 ± 0.89	
						b) ABTS assay (mg TE/g extract):	
						-Trolox as standard	
						Extract: 113.80 ± 0.02	
						c) FRAP assay (mg TE/g extract):	
						-Trolox as standard	
						Extract: 102.58 ± 0.41	
						d) CUPRAC assay (mg TE/g extract):	
						-Trolox as standard	
						Extract: 180.23 ± 0.44	
						e) Metal chelating assay (mg EDTAE/g extract):	
						-EDTA as standard	
						Extract: 21.21 ± 0.88	
						f) PM assay (mg TE/g extract):	
						-Trolox as standard	
						Extract: 5.31 ± 0.13	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						Cholinesterase inhibition (mg GALAE/g extract):	
						-Galantamine as positive control	
						AChE inhibition:	
						-Extract: 4.18 ± 0.37	
						BChE inhibition:	
						-Extract: 2.55 ± 0.16	
						α-glucosidase inhibition (mmol ACAE/g extract):	
						-Acarbose as positive control	
						-Extract: 1.52 ± 0.01	
						α-amylase inhibition (mmol ACAE/g extract):	
						-Acarbose as positive control	
						-Extract: 1.06 ± 0.01	
Galla rhois	NR	**Solvent extraction**: MeOH	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-Kojic acid, ascorbic acid, arbutin as positive controls	NR	48
					-Tyrosinase inhibition IC_{50} (mg/mL):		
					MeOH: 0.163		
					Kojic acid: 0.316		
					Ascorbic acid: 1.520		
					Arbutin: 2.511		
Garcinia atroviridis Griff. ex. T. Anderson	Fruit pericarps	**Solvent extraction**: H_2O with concentrations of 7.81, 15.63, 31.25, 62.50, 125, 250, 500, 1000 μg/mL	**Antimelanogenesis**: Melanin content assay using B16F10 mouse melanoma cells	-Kojic acid as positive control	**Mushroom tyrosinase activity**:	**Antioxidant**:	49
		Temperature: 105 °C	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate and cellular tyrosinase activity in B16F10 cells	-Kojic acid and 125 μg/mL of H_2O extract reduced the melanin content to 46.94% and 46.96%, respectively in α-MSH-stimulated B16F10 cells	-Kojic acid as positive control	**a) DPPH assay**:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			Antioxidant: DPPH and ABTS assays		- IC_{50}:	-Ascorbic acid as standard	
					H_2O extract: 40.72 ± 1.83 μg/mL	-IC_{50}:	
					Kojic acid: 8.00 ± 0.47 μg/mL	H_2O extract: 628.85 ± 32.67 μg/mL	
					Cellular tyrosinase activity:	Ascorbic acid: 62.22 ± 0.67 μg/mL	
					-Only concentration of 125 μg/mL of H_2O extract effectively inhibited the cellular tyrosinase activity in B16F10 cells.	**b) ABTS assay**:	
						-Ascorbic acid as standard	
						-IC_{50}:	
						H_2O extract: 321.41 ± 12.76 μg/mL	
						Ascorbic acid: 6.27 ± 0.19 μg/mL	
Gentiana veitchiorum	Flowers, roots	**Solvent extraction**: Milli-Qwater	**Antimelanogenesis**: Melanin content assay using B16F10 murine melanoma cells	-Ascorbic acid as positive control	Isoorientin inhibited the intracellular tyrosinase activity in a dose-dependent manner but did not have a significant inhibitory effect on mushroom tyrosinase activity.	**Antioxidant**: The flower extracts and isoorientin significantly reduced the cellular ROS level	50
		Temperature: 80 °C	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate and intracellular tyrosinase activity assay in B16F10 cells	-The flower extracts greatly reduced the melanin content on B16F10 cells, but the root extract did not show any effect.			
			Antioxidant: Cellular ROS levels measured using ROS-RODROS/RNS Detection Kit	-Identified flavonoids from flower extract, isoorientin decreased the melanin content in a dose-dependent manner.			
Granny Smith apple	Fruits	**Preparation**: Cells of Granny Smith apple were obtained and powdered. The dried cell powder was extracted	**Antityrosinase**: Mushroom tyrosinase activity assay	NR	-Kojic acid as positive control	NR	51

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
		with MeOH and 1% Butylated hydroxytoluene at 25 °C	using L-DOPA as a substrate				
					-Tyrosinase inhibition IC_{50} (mg/mL): Granny Smith culture cell extract: 1.21 Kojic acid: 0.0177		
Hippophae rhamnoides L.	Seed residues	**Solvent extraction**: 80% EtOH	**Antimelanogenesis**: Melanin content assay using B16F10 mouse melanoma cells	-Kojic acid as positive control	-Kojic acid as positive control	**Antioxidant**:	12
			Antityrosinase: Intracellular tyrosinase activity in B16F10 cells	-The seed residues extract (4.55 mg mL^{-1} and 45.45 mg mL^{-1}) effectively reduced the melanin content in B16F10 cells	The seed residues extract (concentration ranged from 0.10 mg mL^{-1} to 3.00 mg mL^{-1}) significantly reduced the tyrosinase activity in B16F10 cells, compared to the control	**a) DPPH assay**:	
			Antioxidant: DPPH assay, hydroxyl radical scavenging assay			-Ascorbic acid and trolox as standards	
						-EC_{50} (mg mL^{-1}): Seed residues extract: 0.09 ± 0.01 Ascorbic acid: 0.25 ± 0.02 Trolox: 0.10 ± 0.00	
						b) Hydroxyl radical scavenging assay	
						-The seed residues extract showed little hydroxyl scavenging ability	
Juglans mandshurica	Dried fruits	**Solvent extraction**: MeOH	**Antimelanogenesis**: Melanin content assay using B16F10, a melanoma cell line	-Fruit MeOH extract showed antimelanogenesis effects in B16F10 melanoma cells by significantly reduced expression of MITF	-Kojic acid as positive control	NR	52
		Extracted crude extract subsequently partitioned into: chloroform, EtOAc, H_2O (3 fractions)	**Antityrosinase**: Tyrosinase activity assay	-Compound 1 showed the strongest antimelanogene-	-Compound 1 showed strong tyrosinase inhibition activity by		

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			using L-DOPA as a substrate	sis effects by effectively decreasing expression of MITF and decreasing melanin contents in a dose-dependent manner	decreasing tyrosinase expression		
		Fractions were further isolated to obtain 3 phenolic compounds which are 2-[4-(3-hydroxypropyl)−2-methoxyphenoxy]−1,3-propanediol (1), (−)-evofolin B (2) and (2*S*)-schweinfurthinol (3)					
Kadsura coccinea	Roots, stems, leaves, fruits	**Solvent extraction**: ethyl alcohol	**Antimelanogenesis**: Melanin content assay using α-MSH-stimulated B16F10 murine melanoma cells	-Arbutin as positive control	-Arbutin as positive control	**Antioxidant**:	53
			Antityrosinase: Intracellular tyrosinase activity in α-MSH-stimulated B16F10 cells	-Leaves > roots > stems > fruits (highest to lowest)	-Leaves > roots > stems > fruits (highest to lowest)	**a) DPPH assay**:	
			Antioxidant: DPPH and ABTS assays			**DPPH radical scavenging activity (%)**: Leaves (99.9 ± 0.1%) >Roots (95.5 ± 3.6%) > Seeds (25.7 ± 2.1%) > Flowers (8.7 ± 1.1%) (highest to lowest) **b) ABTS assay**: **ABTS radical scavenging activity (%)**: Leaves (94.7 ± 2.9%) > Roots (82.8 ± 5.9%) > Seeds (29.7 ± 2.0 %) > Flowers (15.9 ± 2.0%) (highest to lowest)	
Kummerowia striata	Aerial parts	**Solvent extraction**: EtOH	**Antimelanogenesis**: Melanin content assay using B16F10,	-Arbutin as positive control	-Arbutin as positive control	**Antioxidant**:	54

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			a melanoma cell line				
		Extracted crude extract partitioned into: CH_2Cl_2, EtOAc, *n*-BuOH	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine as a substrate	-EtOH extract decreased the melanin content in α-MSH-stimulated B16F10 cells in a dose-dependent manner	-EtOH extract exerted a significant mushroom tyrosinase inhibitory activity in a dose-dependent manner	**a) DPPH assay**:	
		Temperature: 25 °C	**Antioxidant**: DPPH and ABTS assays			-BHA as standard -IC_{50} (μg/mL): EtOH extract: 98.71 BHA: 14.96 **b) ABTS assay**: -BHA as standard -IC_{50} (μg/mL): EtOH extract: 24.64 μg/mL BHA: 4.65	
Leonurus japonicus	Aerial parts	**Solvent extraction**: MeOH	**Antimelanogenesis**: Melanin content assay using B16F10 murine melanoma cells	Five diterpenes identified from the extracts could inhibit melanin production in α-MSH-stimulated B16F10 cells	Two diterpenes from the extracts had moderate antityrosinase activity	NR	55
		Extracted crude extract fractioned into: EtOAc, H_2O, hexane, 95% MeOH	**Antityrosinase**: Cellular tyrosinase activity assay in B16F10 cells				
		Fractions were further used to isolate 25 bioactive compounds					
		Temperature: 25 °C					
Lepechinia meyenii	NR	**Solvent extraction**: 96% EtOH	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine and L-DOPA as substrates	NR	-Kojic acid as positive control	NR	56

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
		Extracted crude extract was first fractioned and three compounds were further isolated which were p-coumaric acid, caffeic acid, and rosmarinic acid			**-Tyrosinase inhibition IC_{50} using L-tyrosine (μM):**		
					p-coumaric acid: 0.30		
					Caffeic acid: 1.50		
					Rosmarinic acid: 4.14		
					Kojic acid: 33.45		
					-Tyrosinase inhibition IC_{50} using L-DOPA (μM):		
					p-coumaric acid: 0.62		
					Caffeic acid: 2.30		
					Rosmarinic acid: 8.59		
					Kojic acid: 38.98		
Limonium delicatulum	Leaves, roots	**Solvent extraction**: MeOH, H_2O	**Antityrosinase**: Tyrosinase inhibition assay using L-DOPA as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	57
		Temperature: 25 °C	**Antioxidant**: DPPH, ABTS, CUPRAC assays, galvinoxyl radical (GOR) scavenging activity, reducing power, Phenanthroline assay, sliver nanoparticle assay (SNP), β-carotene-linoleic acid bleaching assay		**-Tyrosinase inhibition IC_{50} (μg/mL):**	**a) DPPH assay:**	
			Anti-inflammatory: Determined *in vitro* by the thermal denaturation of bovum serum albumin (BSA)		MeOH leaves: 24.77 ± 0.5	-IC_{50} (μg/mL):	
					MeOH roots: 9.87 ± 0.15	MeOH leaves: 10.58 ± 0.18	
					H_2O-leaves: na	MeOH roots: 5.79 ± 0.05	
					H_2O roots: na	H_2O leaves: 79.65 ± 0.23	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
					Kojic acid: 25.23 ± 0.21	H_2O roots: 69.34 ± 0.95 BHA: 6.68 ± 0.59 BHT: 16.02 ± 0.35 Ascorbic acid: 4.15 ± 0.03 Trolox: 5.25 ± 0.21 **b) ABTS assay**: -IC_{50} (μg/mL): MeOH leaves: 6.56 ± 0.25 MeOH roots: 7.29 ± 0.04 H_2O leaves: 26.01 ± 0.93 H_2O roots: 29.16 ± 0.16 BHA: 1.55 ± 0.26 BHT: 7.54 ± 0.69 Ascorbic acid: 3.21 ± 0.06 Trolox: 3.04 ± 0.05 **c) GOR**: -IC_{50} (μg/mL): MeOH leaves: 11.09 ± 0.16 MeOH roots: 10.31 ± 0.82 H_2O leaves: 84.07 ± 0.44 H_2O roots: 50.17 ± 2.09 BHA: 3.32 ± 0.18 BHT: 5.38 ± 0.06 Ascorbic acid: 5.02 ± 0.01 Trolox: 4.31 ± 0.05 **d) CUPRAC assay**: -$A_{0.5}$ (μg/mL): MeOH leaves: 13.5 ± 0.55 MeOH roots: 6.81 ± 0.07 H_2O leaves: 171.94 ± 0.83 H_2O roots: 80.1 6 ± 1.36 BHA: 4.81 ± 0.87 BHT: 1.82 ± 0.19 Ascorbic acid: 8.69 ± 0.14	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						Trolox: 8.31 ± 0.15 **e) Reducing power**: -$A_{0.5}$ (μg/mL): MeOH leaves: 11.2 ± 0.06 MeOH roots: 20.51 ± 0.3 H_2O leaves: 95.57 ± 2.02 H_2O roots: 46.54 ± 0.4 BHA: 9.29 ± 0.22 BHT: 8.41 ± 1.46 Ascorbic acid: 5.45 ± 0.15 Trolox: 3.62 ± 0.29 **f) Phenanthroline assay**: -$A_{0.5}$ (μg/mL): MeOH leaves: 7.34 ± 0.27 MeOH roots: 3.55 ± 0.02 H_2O leaves: 22.6 ± 1.36 H_2O roots: 11.82 ± 0.75 BHA: 2.24 ± 0.17 BHT: 0.93 ± 0.07 Ascorbic acid: 5.25 ± 0.20 Trolox: 3.11 ± 0.09 **g) SNP**: -$A_{0.5}$ (μg/mL): MeOH leaves: 9.45 ± 0.9 MeOH roots: 21.66 ± 0.08 H_2O leaves: 46.60 ± 0.46 H_2O roots: 96.24 ± 1.70e Ascorbic acid: 7.14 ± 0.05 Trolox: 34.17 ± 1.23 h) β-Carotene-linoleic acid bleaching assay: -IC_{50} (μg/mL): MeOH leaves: 98.6 ± 0.32 MeOH roots: >50 H_2O leaves: 293.17 ± 0.14	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						H_2O roots: >50	
						BHA: 1.24 ± 0.01	
						BHT: 1.26 ± 0.03	
						Anti-inflammatory:	
						-Diclofenac sodium as standard	
						-Inhibition (%) at 500 μg/mL:	
						MeOH leaves: 90.21 ± 1.69	
						MeOH roots: 89.74 ± 1.63	
						H_2O leaves: 43.32 ± 0.13	
						H_2O roots: 38.14 ± 0.81	
Lophira lanceolata Tiegh. ex Keay	Stem barks, leaves	**Extraction method**: Infusion, Soxhlet (SOX), maceration (MAC), homogenizer-assisted extraction (HAE) technique	**Antityrosinase**: Colorimetric enzyme inhibition assay	NR	-Kojic acid as positive control	**Antioxidant**:	58
		Solvent extraction: MeOH, H_2O	**Antioxidant**: DPPH, ABTS, CUPRAC, FRAP, and ferrous-ion chelating assays		**-Tyrosinase inhibition (mg KAE/g)**:	**A) DPPC assay (mgTE/g extract)**:	
			α-glucosidase, α-amylase, and cholinesterase inhibition: Colorimetric enzyme inhibition assays		Leaves:	Leaves:	
					HAE-MeOH: 126.03 ± 3.57	HAE-MeOH: 93.82 ± 0.23	
					HAE- H_2O: na	HAE- H_2O: 74.38 ± 1.49	
					MAC-MeOH: 122.21 ± 2.79	MAC-MeOH: 85.82 ± 0.15	
					MAC-H_2O: na	MAC-H_2O: 76.44 ± 0.71	
					Soxhlet: 131.17 ± 1.96	Soxhlet: 93.37 ± 0.18	
					Infusion: 4.65 ± 0.19	Infusion: 93.81 ± 0.43	
					Stem barks:	Stem barks:	
					HAE-MeOH: 151.65 ± 0.25	HAE-MeOH: 194.83 ± 0.21	
					HAE-H_2O: 94.58 ± 1.87	HAE-H_2O: 190.53 ± 0.24	
					MAC-MeOH: 153.21 ± 0.15	MAC-MeOH: 195.23 ± 0.24	
					MAC-H_2O: 100.46 ± 2.27	MAC-H_2O: 189.07 ± 0.48	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
					Soxhlet: 151.98 ± 0.66	Soxhlet: 195.18 ± 0.55	
					Infusion: 100.95 ± 2.37	Infusion: 187.70 ± 0.47	
						b) ABTS assay (mgTE/g extract):	
						Leaves:	
						HAE-MeOH: 132.25 ± 0.09	
						HAE-H_2O: 72.57 ± 0.09	
						MAC-MeOH: 129.28 ± 0.19	
						MAC-H_2O: 73.35 ± 1.25	
						Soxhlet: 132.09 ± 0.07	
						Infusion: 129.90 ± 1.13	
						Stem barks:	
						HAE-MeOH: 264.43 ± 0.13	
						HAE-H_2O: 263.35 ± 0.53	
						MAC-MeOH: 263.93 ± 0.07	
						MAC-H_2O: 263.90 ± 0.39	
						Soxhlet: 265.04 ± 0.99	
						Infusion: 261.52 ± 3.99	
						c) CUPRAC assay (mgTE/g extract):	
						Leaves:	
						HAE-MeOH: 287.73 ± 21.98	
						HAE-H_2O: 123.07 ± 1.57	
						MAC-MeOH: 239.54 ± 0.86	
						MAC-H_2O: 123.09 ± 0.46	
						Soxhlet: 284.72 ± 5.61	
						Infusion: 257.11 ± 0.16	
						Stem barks:	
						HAE-MeOH: 794.11 ± 13.71	
						HAE-H_2O: 849.09 ± 2.23	
						MAC-MeOH: 735.75 ± 16.98	
						MAC-H_2O: 853.99 ± 13.27	
						Soxhlet: 709.05 ± 1 1.31	
						Infusion: 581.83 ± 6.02	
						d) FRAP assay (mgTE/g extract):	
						Leaves:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						HAE-MeOH: 231.21 ± 0.57	
						HAE-H_2O: 97.97 ± 0.73	
						MAC-MeOH: 174.22 ± 2.71	
						MAC-H_2O: 106.90 ± 0.87	
						Soxhlet: 212.95 ± 2.25	
						Infusion: 213.92 ± 1.68	
						Stem barks:	
						HAE-MeOH: 569.02 ± 5.23	
						HAE-H_2O: 648.34 ± 3.86	
						MAC-MeOH: 501.74 ± 7.13	
						MAC-H_2O: 683.57 ± 11.09	
						Soxhlet: 515.99 ± 25.34	
						Infusion: 354.37 ± 3.87	
						e) PM assay (mmol TE/g extract):	
						Leaves:	
						HAE-MeOH: 2.58 ± 0.35	
						HAE-H_2O: 1.17 ± 0.05	
						MAC-MeOH: 2.43 ± 0.21	
						MAC-H_2O: 1.01 ± 0.09	
						Soxhlet: 2.05 ± 0.12	
						Infusion: 1.72 ± 0.05	
						Stem barks:	
						HAE-MeOH: 4.84 ± 0.08	
						HAE-H_2O: 4.79 ± 0.08	
						MAC-MeOH: 4.38 ± 0.13	
						MAC-H_2O: 4.41 ± 0.04	
						Soxhlet: 4.37 ± 0.27	
						Infusion: 3.47 ± 0.05	
						f) Chelating assays (mg EDTAE/g extract):	
						Leaves:	
						HAE-MeOH: 22.68 ± 0.74	
						HAE-H_2O: 6.76 ± 1.76	
						MAC-MeOH: 30.26 ± 0.57	
						MAC-H_2O: 7.13 ± 1.57	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						Soxhlet: 20.76 ± 0.81	
						Infusion: 8.35 ± 0.48	
						Stem barks:	
						HAE-MeOH: 2.42 ± 0.47	
						HAE-H_2O: 6.15 ± 1.12	
						MAC-MeOH: 2.09 ± 0.45	
						MAC-H_2O: 4.35 ± 0.14	
						Soxhlet: 3.38 ± 0.81	
						Infusion: 4.92 ± 0.53	
						Cholinesterase inhibition (mg GALAE/g):	
						AChE inhibition:	
						Leaves:	
						HAE-MeOH: 4.40 ± 0.10	
						HAE- H_2O:	
						MAC-MeOH: 4.01 ± 0.30	
						MAC-H_2O: 0.51 ± 0.04	
						Soxhlet: 4.22 ± 0.21	
						Infusion: 0.24 ± 0.01	
						Stem barks:	
						HAE-MeOH: 5.18 ± 0.03	
						HAE- H_2O: 3.44 ± 0.08	
						MAC-MeOH: 5.11 ± 0.04	
						MAC-H_2O: 2.97 ± 0.09	
						Soxhlet: 5.11 ± 0.03	
						Infusion: 1.93 ± 0.19	
						BChE inhibition:	
						Leaves:	
						HAE-MeOH: na	
						HAE-H_2O: na	
						MAC-MeOH: na	
						MAC-H_2O: na	
						Soxhlet: na	
						Infusion: na	
						Stem barks:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						HAE-MeOH: 7.87 ± 1.68	
						HAE-H_2O: na	
						MAC-MeOH: 7.31 ± 1.33	
						MAC-H_2O: na	
						Soxhlet: 8.66 ± 1.75	
						Infusion: na	
						α-glucosidase inhibition (mmol ACAE/g):	
						Leaves:	
						HAE-MeOH: 2.86 ± 0.16	
						HAE-H_2O:	
						MAC-MeOH: 2.74 ± 0.01	
						MAC-H_2O:	
						Soxhlet: 2.77 ± 0.01	
						Infusion:	
						Stem barks:	
						HAE-MeOH: 2.74 ± 0.01a	
						HAE-H_2O:	
						MAC-MeOH: 2.76 ± 0.01	
						MAC-H_2O:	
						Soxhlet: 2.75 ± 0.01	
						Infusion:	
						α-amylase inhibition (mmol ACAE/g):	
						Leaves:	
						HAE-MeOH: 0.60 ± 0.02	
						HAE-H_2O: 0.18 ± 0.01	
						MAC-MeOH: 0.66 ± 0.01	
						MAC-H_2O: 0.13 ± 0.01	
						Soxhlet: 0.61 ± 0.01	
						Infusion: 0.11 ± 0.01	
						Stem barks:	
						HAE-MeOH: 1.12 ± 0.02	
						HAE-H_2O: 0.78 ± 0.08	
						MAC-MeOH: 1.13 ± 0.02	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						MAC-H_2O: 0.65 ± 0.03 Soxhlet: 1.13 ± 0.03 Infusion: 0.33 ± 0.03	
Lotus	Seedpod	**Solvent extraction**: Hot H_2O (95 °C) with concentrations of 0, 5, 10, 15, 20 μg/mL	**Antimelanogenesis**: Melanin content assay using B16F10 melanoma cells	10, 15, and 20 μg/mL of the seedpod extract of lotus greatly reduced the melanin production in α-MSH-stimulated B16F10 cells	10, 15, and 20 μg/mL of the seedpod extract of lotus significantly decreased the 65%, 76%, and 112% of tyrosinase activity in α-MSH-stimulated B16F10 cells	NR	59
			Antityrosinase: Cellular tyrosinase activity assay in B16F10 cells				
Maclura tricuspidata	Leaves	**Solvent extraction**: MeOH	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	Two identified flavonols named kaempferol and quercetin had the most potent activity for tyrosinase inhibition	**Antioxidant**: Kaempferol and quercetin had good antioxidant activity	60
		Extracted crude extract partitioned into: *n*-hexane, EtOAc, *n*-BuOH, CH_2Cl_2 EtOAc and CH_2Cl_2 fractions were chromatographed over silica gel to give 21 active compounds.	**Antioxidant**: DPPH assay				
Manilkara kauki	Fruits, leaves, seeds, stem barks, woods	**Solvent extraction**: MeOH, H_2O	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine as a substrate	NR	-Kojic acid and α-arbutin as positive controls	**Antioxidant**:	15
		Temperature: 25 °C, 60 °C	**Antioxidant**: DPPH and FRAP assays		**-Tyrosinase inhibition IC_{50} (mg mL^{-1})**: MeOH extracts: Fruits: 0.63 ± 0.01 Leaves: 0.38 ± 0.01 Seeds: 5.56 ± 0.03 Stem barks: 0.25 ± 0.03 Woods: No activity	**a) DPPH assay**: **DPPH radical scavenging activity (%)**: MeOH extracts: Fruits: 8.80 ± 0.16 Leaves: 47.01 ± 0.14 Seeds: 2.21 ± 0.05 Stem barks: 57.87 ± 0.27	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
					H_2O extracts:	Woods: 43.51 ± 0.27	
					Fruits: 0.86 ± 0.03	H_2O extracts:	
					Leaves: 0.50 ± 0.01	Fruits: 1.03 ± 0.05	
					Seeds: 6.73 ± 0.03	Leaves: 55.49 ± 0.06	
					Stem barks: 0.41 ± 0.01	Seeds: 0.41 ± 0.03	
					Woods: No activity	Stem barks: 48.89 ± 0.14	
						Woods: 14.75 ± 0.06	
						b) FRAP assay:	
						FRAP activity (mg TE g^{-1} crude extract):	
						MeOH extracts:	
						Fruits: 11.96 ± 0.64	
						Leaves: 209.74 ± 1.28	
						Seeds: 16.41 ± 0.85	
						Stem barks: 211.59 ± 1.40	
						Woods: 72.70 ± 0.85	
						H_2O extracts:	
						Fruits: 5.48 ± 0.32	
						Leaves: 219.37 ± 0.32	
						Seeds: 4.19 ± 0.32	
						Stem barks: 107.33 ± 0.96	
						Woods: 41.59 ± 0.85	
Melaleuca quinquenervia	NR	**Preparation**: Steam-distilled essential oil was purchased with concentrations of 0, 5, 10, 20 μg/mL	**Antimelanogenesis**: Melanin content assay using B16 murine melanoma cells	-Arbutin as positive control	-Arbutin as positive control	NR	1
			Antityrosinase: Cellular tyrosinase activity assay in B16 cells	-20 μg/mL of essential oil exhibited a 40.7% melanin inhibitory effect, stronger than arbutin (16.1% at 100 μM)	-20 μg/mL of essential oil had a 20.4% tyrosinase inhibitory effect, which is stronger than arbutin (5.5% at 100 μM)		
Melastoma normale	Roots	**Solvent extraction**: 80% acetone	**Antityrosinase**: Mushroom tyrosinase activity assay	NR	-Kojic acid as positive control	NR	61

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			using L-DOPA as a substrate				
		Extracted crude extract partitioned into: PE, EtOAc. The EtOAc fraction was further divided into ten fractions. Fractions were further separated to obtain 12 compounds			-Quercetin, one of the compounds that was isolated, showed a significant antityrosinase activity with IC_{50} of 76.83 ± 2.02 μM -Kojic acid has an IC50 of 100.52 ± 2.63.		
Morus alba L.	Dried leaves	**Solvent extraction**: 70% EtOH	**Antimelanogenesis**: Melanin content assay using B16F10, mouse skin melanoma cells	-Arbutin as positive control	-Arbutin as positive control	NR	5
		Extracted crude extract fractioned into: *n*-hexane, EtOAc, *n*-BuOH, aqeuous	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate and intracellular tyrosinase activity assay in B16F10 cells	-Three compounds isolated from EtOH extracts named, norartocarpetin, moracin J and steppogenin decreased melanin production which exhibit antimelanogenesis effects in α-MSH-stimulated B16F10 cells.	-Norartocarpetin, moracin J, and steppogenin significantly inhibited mushroom tyrosinase activity and intracellular tyrosinase activity in a dose-dependent manner.		
		Fractions were further isolated to obtain 12 compounds.					
		Temperature: 25 °C					
Morus alba L.	Leaves obtained from Chiang Mai (CM), Sakon Nakon (SK), Buriram (BR), Thailand	**Extraction method**: Maceration method, pulsed electric field (PEF) extraction method	**Antityrosinase**: Tyrosinase inhibitory assay that used L-tyrosine and L-DOPA as substrates	NR	-Kojic acid as positive control	**Antioxidant**:	62
		Solvent extraction: 95% EtOH	**Antioxidant**: DPPH, ABTS and FRAP assays		-PEF extracts exhibited significant inhibitory	-Ascorbic acid as positive control	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
					effects compared to the maceration method		
					-PEF extract from BR demonstrated the highest antityrosinase activity, with IC_{50} of against L-tyrosine and L-DOPA of 54.1 ± 5.4 and 32.2 ± 3.4 μg/mL, respectively	-Extracts obtained by the PEF method had higher radical scavenging activity than the maceration method.	
					-Leaves from BR had a significantly high FRAP value which is comparable to kojic acid (IC_{50}: 28.0 ± 5.1 μg/mL with L-DOPA as substrate)	-PEF extract from BR had DPPH inhibition of 45.3 ± 0.8%, TEAC value of 115.1 ± 2.8 mg Trolox/g extract (ABTS assay), and EC_1 value of 52.4 ± 0.5 mg FeSO4/g extract (FRAB assay).	
Myrica rubra	Fruits	**Solvent extraction**: Pure H_2O, 50% H_2O, 50% ethyl alcohol, 5% pure H_2O, 95% ethyl alcohol with concentrations of 0.5, 1, 1.5, 2.0 g L^{-1}	**Antimelanogenesis**: Melanin quantification assay using A2058, human melanoma cells and B16F10, mouse melanoma cells	-Arbutin as positive control	-Pure H_2O extract has stronger inhibitory effects than 50% ethyl alcohol and 95% ethyl alcohol extracts	NR	6
			Antityrosinase: Mushroom tyrosinase activity assay using L-DOPA as a substrate and cellular tyrosinase activity assay in A2058 and B16F10 cells	-2.0 g L^{-1} of pure H_2O extract reduced the melanin content to 76.5% and 82.5% in A2058 and B16F10 cells, respectively	**Mushroom tyrosinase activity assay**:		
				-Pure H_2O extract has stronger inhibitory effects than 50% ethyl alcohol and 95% ethyl alcohol extracts	-2.0 g L^{-1} of pure H_2O extract reduced the mushroom tyrosinase activity to 61.7%.		
					Cellular tyrosinase activity assay:		
					-2.0 g L^{-1} of pure H_2O extract reduced the cellular tyrosinase activity to 65.78% and 74.9% in A2058 and B16F10 cells, respectively		

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
Nardostachys jatamansi	Leaves, rootstock	**Preparation**: *in vitro*-raised plants and wild plants were collected	**Antityrosinase**: Modified dopachrome method using L-DOPA as a substrate	NR	-Kojic acid as positive control	**Antioxidant**:	63
		Solvent extraction: MeOH, acetone, chloroform, acetonitrile, H_2O	**Antioxidant**: ABTS and PM assay, lipid peroxidation (LPO) inhibition method		-MeOH rootstock extracts of *in vitro*-cultured plants have the highest antityrosinase activity which is comparable to kojic acid	**a) ABTS assay**:	
			Cholinesterase inhibitory activity: Cholinesterase inhibition assay		**-Tyrosinase inhibition IC_{50} (μg/mL)**:	-Trolox as standard	
			Antihyperglycemic activity: α-amylase inhibition assay		MeOH rootstock extracts of *in vitro*-cultured plants: 168.12 ± 3.6	-IC_{50} (μg/mL):	
			Anti-inflammatory: Spectrophotometric measurement of linoleic acid oxidation by the enzyme 5-lipoxygenase (5-LOX)		Kojic acid: 54.44 ± 2.3	MeOH rootstock extracts of *in vitro*-cultured plants: 13.55 ± 0.8	
						Trolox: 7.5 ± 1.4	
						b) PM assay:	
						-MeOH rootstock extracts of *in vitro* cultured plants: 789 ± 8.7 μg ascorbic acid equivalents/g extract	
						c) LPO inhibition method:	
						-Rutin as standard	
						-IC_{50} (μg/mL):	
						MeOH rootstock extracts of *in vitro* cultured plants: 15.24 ± 0.8	
						Rutin: 3.82 ± 0.5	
						Cholinesterase inhibition:	
						AchE Inhibition:	
						-Galanthamine as standard	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						-IC_{50} (μg/mL): MeOH rootstock extracts of *in vitro* cultured plants: 31.18 ± 2.6 MeOH rootstock extracts of wild plants: 36.46 ± 2.1 Galantamine: 0.94 ± 0.03 **Antihyperglycemic activity**: -Acarbose as standard -IC_{50} (μg/mL): MeOH rootstock extract of *in vitro* cultured plants: 90.69 ± 2.1 Acarbose: 52.36 ± 3.1 **Anti-inflammatory**: -IC_{50} (μg/mL): MeOH rootstock of *in vitro* cultured plants: 14.58 ± 0.9 MeOH leaf extracts of *in vitro* cultured plants: 23.54 ± 1.6 Positive control: 2.56 ± 0.4	
Nepeta glomerulosa Boiss.	Aerial parts	**Solvent extraction**: Methanol (MeOH) (100 μg/mL)	**Antimelanogenesis**: Melanin content assay using B16F10 melanoma cells	-Kojic acid as positive control	-Kojic acid as positive control	**Antioxidant**: Only MeOH and *n*-BuOH extracts greatly suppressed the oxidative stress caused by hydrogen peroxide	3
		Extracted crude extract subjected to subsequent extraction with solvents (100 μg/mL): *n*-hexane, dichloromethane (CH_2Cl_2), ethyl acetate (EtOAc), *n*-butanol (*n*-BuOH), water (H_2O)	**Antityrosinase**: Mushroom tyrosinase activity assay and cellular tyrosinase activity assay in B16F10 cells	-100 μg/mL concentration of MeOH, EtOAc, and *n*-BuOH extracts had significant inhibitory effects on melanin synthesis	-Mushroom tyrosinase activity was inhibited only by 100 μg/mL of EtOAc extract		
		Temperature: 25 °C	**Antioxidant**: Hydrogen peroxide scavenging assay		-100 μg/mL of methanol extract significantly inhibited cellular tyrosinase activity in B16F10 cells		
Olea europeae	Leaves	**Solvent extraction**: MeOH	**Antimelanogenesis**: Melanin content assay using B16 melanoma cells	-Arbutin as positive control	NR	NR	64

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
		Seventeen compounds were isolated from MeOH extract		-Three compounds named oleuroepin, oleoside dimethyl ester and oleoside 11-methyl ester, presented good inhibition of melanogenesis **-Melanin content (%) at 12.5, 25, 50 μM, respectively**: Oleuroepin: 63.8 ± 3.3, 46.4 ± 3.3, 33.9 ± 15.4 Oleoside dimethyl ester: 33.9 ± 4.0, 28.1 ± 0.7, 5.3 ± 3.8 Oleoside 11-methyl ester: 25.8 ± 8.1, 22.3 ± 14.0, 16.0 ± 10.2 Arbutin at 20 μM: 91.3 ± 2.6			
Pelargonium graveolens	Aerial parts	**Solvent extraction**: *n*-hexane, CH_2Cl_2, MeOH **Temperature**: 25 °C	**Antityrosinase**: Tyrosinase inhibition assay using L-DOPA as a substrate **Antioxidant**: DPPH assay, ABTS assay, CUPRAC assay, reducing power, iron chelation	NR	-Kojic acid as positive control **-Tyrosinase inhibition IC_{50} (μg/mL)**: *n*-hexane: 37.60 ± 1.83 CH_2Cl_2: 37.63 ± 1.35 MeOH: 21.11 ± 0.38 Kojic acid: 25.23 ± 0.78	**Antioxidant**: **a) DPPH assay**: -BHT and BHA as standard -IC_{50} (μg/mL): *n*-hexane: 37.60 ± 1.83 CH_2Cl_2: 116.91 ± 6.50 MeOH: 12.96 ± 0.63 BHA: 5.73 ± 0.41	65

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						BHT: 22.32 ± 1.19 **b) ABTS assay**: -BHT and BHA as standard -IC_{50} (μg/mL): *n*-hexane: 44.46 ± 2.30 CH_2Cl_2: 10.46 ± 1.33 MeOH: 10.20 ± 0.63 BHA: 1.81 ± 0.10 BHT: 1.29 ± 0.30 **c) CUPRAC assay**: -BHT and BHA as standard -IC_{50} (μg/mL): *n*-hexane: 89.95 ± 3.00 CH_2Cl_2: 53.36 ± 0.88 MeOH: 20.29 ± 0.51 BHT: 5.35 ± 0.71 BHA: 8.97 ± 3.94 **d) Reducing power**: -BHA as standard -IC_{50} (μg/mL): *n*-hexane: 77.29 ± 0.87 CH_2Cl_2: 64.60 ± 0.15 MeOH: 43.48 ± 0.65 BHA: 9.29 ± 0.22 **e) Iron chelation**: -EDTA as standard -IC_{50} (μg/mL): *n*-hexane: 47.20 ± 2.85 CH_2Cl_2: 66.72 ± 2.96 MeOH: 31.74 ± 3.21 EDTA: 8.80 ± 0.47	
Persicaria orientalis	Roots	**Solvent extraction**: MeOH	**Antimelanogenesis**: Melanin content assay using B16 mouse melanoma cells	-Arbutin as positive control	-Kojic acid as positive control	NR	66

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
		Extracted crude extract subsequently partitioned into: *n*-hexane, EtOAc, and EtOH extracts. Then, EtOH extract was further used to isolate the nine bioactive compounds	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine and L-DOPA as substrates	-Vanicoside B isolated from EtOH extracts exhibited a significant high extracellular (71.9% and 72.0%) and intracellular (35.3 and 27.3%) melanin inhibitory activity at 50 and 25 μM, respectively	**-Tyrosinase inhibition IC_{50} using**L-**tyrosine (μg/mL)**:		
		Bioactive compounds were tested in the concentrations of 6.25, 12.5, 25, 50 μM		-It showed a better inhibitory activity than arbutin (58% at 730 μM)	*n*-hexane: >1000		
		Temperature: 50 °C			EtOAc: 80		
					EtOH: 22		
					Kojic acid: 2		
					-Tyrosinase inhibition IC_{50} using L-**DOPA (μg/mL)**:		
					n-hexane: >1000		
					EtOAc: 311		
					EtOH: 39		
					Kojic acid: 26		
Photinia × *fraseri*	Leaves	**Solvent extraction**: 70% acetone	**Antityrosinase**: Mushroom tyrosinase monophenolase and diphenolase activity assay	NR	PAs showed better inhibition of tyrosinase diphenolase activity than monophenolase activity	NR	67
		H_2O phase was then extracted to obtain a crude proanthocyanidins (PAs) extract					
Phyllanthus phillyreifolius	Leaves, branches, stems	**Extraction method**: Soxhlet extraction, maceration extraction, and decoction	**Antityrosinase**:	NR	**Tyrosinase inhibition (mg KAE/g extract)**:	**Antioxidant**:	68
		Solvent extraction: EtOAc, 70% MeOH	Tyrosinase inhibition assay		- Kojic acid as positive control	**a) DPPH assay (mmol TE/g extract)**:	
			Antioxidant: DPPH, ABTS, FRAP,		Decoction: 66.29 ± 1.51	- Trolox as standard	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
			CUPRAC, and PM assays, chelating effect				
			Enzyme inhibition activity: cholinesterase, α-amylase, and α-glucosidase inhibition assays		EtOAc maceration: 88.93 ± 0.53	Decoction: 1.91 ± 0.13	
					EtOAc-Soxhlet: 78.79 ± 1.52	EtOAc-Maceration: 2.73 ± 0.01	
					MeOH Maceration: 88.46 ± 1.35	EtOAc Soxhlet: 2.49 ± 0.04	
					MeOH Soxhlet: 87.19 ± 0.28	MeOH Maceration: 2.91 ± 0.01	
						MeOH Soxhlet: 2.85 ± 0.02	
						b) ABTS assay (mmol TE/g extract):	
						-Trolox as standard	
						Decoction: 4.11 ± 0.02	
						EtOAc Maceration: 3.21 ± 0.17	
						EtOAc Soxhlet: 2.65 ± 0.05	
						MeOH Maceration: 4.12 ± 0.09	
						MeOH Soxhlet: 3.68 ± 0.10	
						c) CUPRAC assay (mmol TE/g extract):	
						-Trolox as standard	
						Decoction: 4.80 ± 0.07	
						EtOAc Maceration: 4.78 ± 0.33	
						EtOAc Soxhlet: 3.75 ± 0.03	
						MeOH Maceration: 4.96 ± 0.12	
						MeOH Soxhlet: 5.04 ± 0.17	
						d) FRAP assay (mmol TE/g extract):	
						-Trolox as standard	
						Decoction: 3.01 ± 0.12	
						EtOAc Maceration: 2.31 ± 0.11	
						EtOAc Soxhlet: 2.02 ± 0.10	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						MeOH Maceration: 2.92 ± 0.36	
						MeOH Soxhlet: 3.17 ± 0.15	
						e) Metal chelating (mmol EDTAE/g extract):	
						-EDTA as standard	
						Decoction: 22.91 ± 0.39	
						EtOAc Maceration: 17.89 ± 0.70	
						EtOAc Soxhlet: 19.02 ± 0.42	
						MeOH Maceration: 24.23 ± 0.57	
						MeOH Soxhlet: 26.30 ± 0.10	
						Cholinesterase inhibition (mg GALAE/g extract):	
						AChE Inhibition:	
						Decoction: 2.11 ± 0.04	
						EtOAc Maceration: 2.68 ± 0.01	
						EtOAc Soxhlet: 2.56 ± 0.05	
						MeOH Maceration: 2.33 ± 0.02	
						MeOH Soxhlet: 2.13 ± 0.03	
						BChE Inhibition:	
						Decoction: 1.26 ± 0.12	
						EtOAc Maceration: 2.27 ± 0.19	
						EtOAc Soxhlet: 2.06 ± 0.11	
						MeOH Maceration: 2.73 ± 0.23	
						MeOH Soxhlet: 1.20 ± 0.20	
						α-amylase inhibition (mmol ACAE/g extract):	
						Decoction: 0.19 ± 0.02	
						EtOAc Maceration: 0.63 ± 0.04	
						EtOAc Soxhlet: 0.68 ± 0.06	
						MeOH Maceration: 0.60 ± 0.04	
						MeOH Soxhlet: 0.56 ± 0.01	
						α-glucosidase inhibition (mmol ACAE/g extract):	
						Decoction: NR	
						EtOAc Maceration: NR	
						EtOAc Soxhlet: 45.07 ± 0.39	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						MeOH Maceration: NR	
						MeOH Soxhlet: NR	
Phyllostachys nigravar. henosis	Bamboo stems	**Solvent extraction**: H_2O, 50% EtOH, 80% EtOH, 100% EtOH, boiling H_2O	**Antimelanogenesis**: Melanin content assay using B16F10, a melanoma cell line	-80% EtOH extracts decreased the melanin content in α-MSH-stimulated B16F10 cells in a dose-dependent manner	-Ascorbic acid as positive control	**Antioxidant**:	13
		Extracted crude extract were then partitioned with MeOH, EtOAc, *n*-hexane	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine as a substrate		**-Tyrosinase inhibition IC_{50} (μg/mL)**:	**a) DPPH assay**:	
		Temperature: 121 °C, 25 °C, 100 °C	**Antioxidant**: DPPH and ABTS assays, hydroxyl radical scavenging activity method		80% EtOH extracts: 243.7	-Ascorbic acid as positive control	
					Ascorbic acid: 38.5	-IC_{50} (μg/mL):	
						H_2O: 1064.48 ± 107.77	
						50% EtOH: 714.35 ± 39.54	
						80% EtOH: 565.63 ± 17.75	
						100% EtOH: 2019.67 ± 69.40	
						Boiling H_2O: 877.34 ± 63.75	
						Ascorbic acid: 23.02 ± 0.39	
						b) ABTS assay:	
						-Ascorbic acid as positive control	
						-IC_{50} (μg/mL):	
						H_2O: 704.99 ± 28.53	
						50% EtOH: 463.81 ± 13.93	
						80% EtOH: 414.61 ± 35.12	
						100% EtOH: 669.68 ± 35.62	
						Boiling H_2O: 2258.18 ± 125.06	
						Ascorbic acid: 51.86 ± 0.72	
						c) Hydroxyl radical assay:	
						-Ascorbic acid as positive control	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						-IC_{50} (μg/mL): H_2O: 698.68 ± 24.40 50% EtOH: 560.19 ± 21.85 80% EtOH: 509.17 ± 33.76 100% EtOH: 766.73 ± 22.23 Boiling H_2O: 1395.93 ± 222.72 Ascorbic acid: 90.57 ± 0.60	
Pistacia atlantica subsp. *mutica*	Unripe fruits	**Solvent extraction and preparation**: MeOH and hydrodistillation to obtain the essential oil	**Antimelanogenesis**: Melanin content assay using B16F10, a melanoma cell line	-Kojic acid as positive control	-Kojic acid as positive control	**Antioxidant**:	11
		Extracted crude extract fractioned into: MeOH, *n*-hexane, CH_2Cl_2, EtOAc, BuOH, H_2O	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate and cellular tyrosinase activity assay in B16F10 cells	-MeOH, CH_2Cl_2, and EtOAc extracts (0.2−200 μg/mL), *n*-hexane (2−200 μg/mL), and H_2O	**Mushroom tyrosinase activity assay**:	-All extracts except 0.2 μg/mL of CH_2Cl_2 extract were able to significantly suppress the oxidative stress caused by H_2O_2	
		Temperature: 25 °C	**Antioxidant**: Hydrogen peroxide scavenging assay using B16F10 melanoma cells	Extract (20 and 200 μg/mL) showed significant inhibitory effect on melanogenesis, but essential oil and BuOH had no significant inhibitory effect on melanogenesis	-All extracts were able to inhibit mushroom tyrosinase activity except for 1000 μg/mL of *n*-hexane extract		
					Cellular tyrosinase activity: MeOH, EtOAc, and BuOH extracts (0.2−200 μg/mL), *n*-hexane (0.2 μg/mL), and CH_2Cl_2 (20 and 200 μg/mL) effectively inhibited cellular tyrosinase activity except for H_2O extract.		
Pistacia lentiscus L.	Leaves	**Solvent extraction**: MeOH extract (ME)	**Antityrosinase**: Mushroom	NR	-Kojic acid as positive control	**Antioxidant activity**:	69

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			tyrosinase activity assay using L-DOPA as a substrate and cellular tyrosinase activity assay in B16 cells				
		Temperature: 50 °C	**Antioxidant**: DPPH and FRAP assays		**Mushroom tyrosinase activity assay**:	**a) DPPH assay**:	
		Extraction method:	**Antielastase**: Elastase inhibition assay		-IC_{50} (μg/mL):	-Ascorbic acid as standard	
		Pressurized solvent extraction to obtain the ethyl acetate (EAE) and aqueous (AE) phases			EAE: 123	-IC_{50} (μg/mL):	
					Kojic acid: 20	ME: 19.62	
					Cellular tyrosinase activity:	EAE: 18.07	
					-IC_{50} (μg/mL):	AE: 19.52	
					EAE: 27.85 ± 1.75	Ascorbic acid: 13.85	
					Kojic acid: 142.09 ± 2.72	**b) FRAP assay (mg AEAC/g extract)**:	
						ME: 467.29 ± 21.77	
						EAE: 522.7 6 ± 22.99	
						AE: 421.91 ± 15.48	
						Antielastase:	
						-Epigallocatechin gallate as positive control	
						-IC_{50} (μg/mL):	
						EAE: 19	
						Epigallocatechin gallate: 12	
Polygonum maritimum L.	Aerial parts (leaves and stems)	**Solvent extraction**: acetone	**Antimelanogenesis**: Melanin content assay using B16 4A5 melanoma cells	**-Melanin inhibition IC_{50}**:	-Arbutin as positive control	**Antioxidant**:	70
		Temperature: 25 °C	**Antityrosinase**: Mushroom tyrosinase activity assay	Acetone extract: 77.7 μg/mL	**-Tyrosinase inhibition IC_{50} (μg/mL)**:	**a) Radical scavenging activity on superoxide radicals**:	
			Antioxidant: Radical		Acetone extract: 64.1	-Catechin as positive control	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			scavenging activity on superoxide radical, ferric thiocyanate, and thiobarbituric acid tests, PM method				
			Anti-inflammatory: Nitric acid production was assessed using LPS (Lipopolysaccharide)-stimulated RAW 264. Seven macrophages		Arbutin: 137	IC_{50} (μg/mL):	
						Acetone extract: 40.4	
						Catechin: 61.6	
						b) Feric thiocyanate and thiobarbituric acid tests:	
						IC_{50} (μg/mL):	
						Acetone extract: 784	
						c) Total antioxidant capacity:	
						IC_{50}:	
						Acetone extract: 647 μg/mL	
						Anti-inflammatory:	
						IC_{50} (μg/mL):	
						Acetone extract: 22.0	
						Positive control: 27.6	
Potentilla anserina L.	Rhizomes	**Solvent extraction**: 70% EtOH	**Antityrosinase**: Tyrosinase inhibitory assay using L-tyrosine and L-DOPA as substrates	NR	-Kojic acid as positive control	**Antioxidant**:	71
		Extracted crude extract fractioned into: PE, EtOAc, butyl alcohol, aqueous	**Antioxidant**: DPPH, ABTS and FRAP assays		-Butyl alcohol fraction (IC_{50} = 45.22 μg/mL (L-tyrosine), IC_{50} = 15.47 μg/mL (L-DOPA) > EtOAc fraction > EtOH > aqueous fraction (highest to lowest)	**a) DPPH assay**:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
		EtOAc was subjected to a silica gel column and eluted with dichloromethane/methanol to produce 10 fractions. These fractions were then further used to isolate 30 active compounds.	**α-glucosidase inhibition**: α-glucosidase inhibitory assay			-Ascorbic acid as positive control -IC_{50} (μg/mL): PE fraction: NR EtOAc fraction: 0.11 Butyl alcohol fraction: 1.16 EtOH extract: 7.27 Aqueous fraction: 16.33 **b) ABTS assay**: -Ascorbic acid as positive control -IC_{50} (μg/mL): PE fraction: NR EtOAc fraction: 0.42 Butyl alcohol fraction: 4.58 EtOH extract: 25.91 Aqueous fraction: 60.71 **c) FRAP assay**: -Ascorbic acid as positive control -EtOAc fraction is presented with the highest FRAP value. **α-glucosidase inhibition**: -Acarbose as positive control -Butyl alcohol fraction had the highest inhibition of α-glucosidase with an IC_{50} value of 14.18 μg/mL	
Potentilla paradoxa Nutt.	Whole plant	**Solvent extraction**: 95% EtOH	**Antimelanogenesis**: Melanin content assay using B16F10 melanoma cells	-Arbutin as positive control	NR	**Antioxidant**: **a) DPPH assay**:	72
			Antioxidant: DPPH, ABTS, FRAP, and CUPRAC assays	-Melanin content of α-MSH-stimulated B16F10 cells were suppressed dose-dependently by			

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
				the 95% EtOH extract			
						-Ascorbic as positive control	
						-95% EtOH extract showed DPPH radical scavenging ability in a dose-dependent manner	
						b) ABTS assay:	
						-Ascorbic as positive control	
						-95% EtOH extract showed ABTS radical scavenging ability in a dose-dependent manner	
						c) FRAP assay:	
						-Trolox as standard	
						-95% EtOH extract displayed a ferric reducing antioxidative capacity in a dose-dependent manner.	
						d) CUPRAC assay:	
						-Trolox as standard	
						-Copper ions were reduced by 95% EtOH extract in a dose-dependent manner	
Prasiola japonica	NR	**Preparation**: Loliolide, a monoterpenoid hydroxylactone from *P. japonica* was purchased	**Antimelanogenesis**: Melanin content assay using B16F10 mouse melanoma cells	-Arbutin as positive control	NR	**Antioxidant**:	73
		Solvent extraction of *P. japonica*: 70% EtOH	**Antioxidant**: ABTS assay	-Loliolide remarkably reduced the melanin content and secretion in α-MSH-stimulated B16F10 cells.		**a) ABTS assay**:	
		Temperature: 25 °C				-Ascorbic acid as positive control	
						-IC_{50} of loliolide: 61.52 ± 2.12 μM	
Pterocarpus marsupium	Heartwood	**Solvent extraction**: EtOH	**Antimelanogenesis**: Melanin content assay using B16 cell line	-Kojic acid as positive control	-Kojic acid as positive control	**Antioxidant**:	74
			Antityrosinase: Mushroom	-5, 10, 20, and 50 μg/mL of	-12.5, 50, and 200 μg/mL of extracts exerted 23%, 53%,	**a) DPPH assay**:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			tyrosinase activity assay using L-DOPA as a substrate	extracts presented 24%, 45%, 53%, and 69% of inhibition of melanogenesis in B16 cells, respectively	and 71% mushroom tyrosinase activity, respectively		
			Antioxidant: DPPH assay			-Ascorbic acid as standard -10, 20, and 50 μg/mL of extracts demonstrated 16%, 33%, and 73% DPPH radical-scavenging activity -10, 20, and 50 μg/mL of ascorbic acid demonstrated 15%, 31%, and 84% DPPH radical-scavenging activity	
Red maple (*Acer rubrum*)	Leaves	**Solvent extraction**: EtOH	**Antimelanogenesis**: Melanin content assay using B16F10, a murine melanoma cell line	Compared to the control group, 25 and 50 μM of GA effectively reduced the melanin content in B16F10 cells to 79.1% and 56.7%, respectively.	-Kojic acid and arbutin as positive controls	**Antioxidant**: 50 μM of GA reduced ROS levels to 55.1% in B16F10 cells	75
		Glucitol-core-containing gallotannins (GCGs) including Ginnalin A (GA), Ginnalin B (GB), Ginnalin C (GC), Maplexin F (MF), Maplexin J (MJ) were generated in the laboratory with concentration of 3, 6, 13, 25, 50 μM for antimelanogenesis and antioxidant activities, while for antityrosinase activity, concentration ranged from 16 to 500 μM were generated	**Antityrosinase**: Mushroom tyrosinase activity assay using L-tyrosine as substrate		**-Tyrosinase inhibition IC_{50} (μM)**:		
			Antioxidant: Hydrogen peroxide scavenging assay using B16F10 melanoma cells		GA: 101.4 ± 6.5 GB: >500 GC: >500 MF: 208.9 ± 3.1 MJ: 173.8 Kojic acid: 23.7 ± 0.9		

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
					Arbutin: 61.6 ± 2.8		
Rosa chinensis cv. "JinBian"	Flower buds	**Solvent extraction**: 95% EtOH, 65% EtOH, PE	**Antityrosinase**: Mushroom tyrosinase activity assay using L-DOPA as a substrate	NR	-α-Arbutin as positive control	**Antioxidant**:	76
		Temperature: 25 °C	**Antioxidant**: DPPH assay		**-Tyrosinase inhibition (%)**:	**a) DPPH assay**:	
					95% EtOH: 66.95 ± 0.27	-Trolox as standard	
					65% EtOH: 60.21 ± 0.09	-DPPH radical scavenger (%):	
					PE: 6.27 ± 0.68	95% EtOH: 94.36 ± 0.12	
					α-Arbutin: 22.15 ± 0.42	65% EtOH: 94.11 ± 0	
						PE: 17.25 ± 1.45	
						Trolox: 95.12 ± 0.29	
Rubus caesius L.	Leaves	**Solvent extraction**: H_2O (RC1), 50% MeOH (RC2), pure MeOH (RC3)	**Antityrosinase**: Tyrosinase inhibition assay using L-DOPA as a substrate	NR	**Tyrosinase inhibition (mg KAE/g extract)**:	**Antioxidant**:	77
		Extracted crude extract partitioned into: diethyl ether (RC4), EtOAc (RC5), *n*-BuOH (RC6)	**Antioxidant**: DPPH, ABTS, CUPRAC (Cupric Reducing Antioxidant Capacity), FRAP (Ferric reducing ability of plasma), phosphomolyb-denum (PM) and metal-chelating assays		RC1: 60.59 ± 0.37	**a) DPPH assay (mmol TE/g extract)**:	
		Temperature: 40 °C	**Enzyme inhibitory activity**: Cholinesterase, α-amylase, and α-glucosidase inhibition assays		RC2: 61.82 ± 1.43	-Trolox as standard	
					RC3: 61.83 ± 0.26	RC1: 0.17 ± 0.01	
					RC4: 55.32 ± 0.67	RC2: 0.57 ± 0.04	
					RC5: 56.92 ± 0.70	RC3: 1.05 ± 0.02	
					RC6: 63.12 ± 0.26	RC4: 1.58 ± 0.01	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						RC5: 1.58 ± 0.01	
						RC6: 1.55 ± 0.02	
						b) ABTS assay (mmol TE/g extract):	
						-Trolox as standard	
						RC1: 0.25 ± 0.01	
						RC2: 1.22 ± 0.08	
						RC3: 1.28 ± 0.03	
						RC4: 2.45 ± 0.03	
						RC5: 2.92 ± 0.03	
						RC6: 2.02 ± 0.03	
						c) CUPRAC assay (mmol TE/g extract):	
						-Trolox as standard	
						RC1: 0.34 ± 0.01	
						RC2: 1.63 ± 0.02	
						RC3: 1.60 ± 0.05	
						RC4: 3.49 ± 0.02	
						RC5: 4.98 ± 0.05	
						RC6: 2.82 ± 0.18	
						d) FRAP assay (mmol TE/g extract):	
						-Trolox as standard	
						RC1: 0.22 ± 0.01	
						RC2: 1.05 ± 0.03	
						RC3: 0.92 ± 0.04	
						RC4: 2.15 ± 0.08	
						RC5: 2.78 ± 0.13	
						RC6: 1.71 ± 0.21	
						e) PM method (mmol TE/g extract):	
						-Trolox as standard	
						RC1: 0.59 ± 0.02	
						RC2: 1.61 ± 0.15	
						RC3: 2.09 ± 0.18	
						RC4: 2.58 ± 0.11	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						RC5: 3.92 ± 0.34	
						RC6: 3.10 ± 0.26	
						f) Metal chelating assays (mg EDTAE/g extract):	
						-EDTA as standard	
						RC1: 12.00 ± 0.38	
						RC2: 16.62 ± 1.71	
						RC3: 14.67 ± 1.13	
						RC4: 5.19 ± 0.20	
						RC5: 8.07 ± 0.82	
						RC6: 12.94 ± 0.87	
						Cholinesterase inhibition:	
						AchE inhibition (mg GALAE/g extract):	
						RC1: 1.99 ± 0.04	
						RC2: 2.06 ± 0.07	
						RC3: 2.26 ± 0.05	
						RC4: 2.46 ± 0.01	
						RC5: 2.17 ± 0.02	
						RC6: 2.13 ± 0.05	
						BchE inhibition (mg GALAE/g extract):	
						RC1: 1.01 ± 0.03	
						RC2: 1.00 ± 0.09	
						RC3: 1.10 ± 0.0	
						RC4: NR	
						RC5: NR	
						RC6: NR	
						α-amylase inhibition (mmol ACAE/g extract):	
						RC1: 0.39 ± 0.03	
						RC2: 0.50 ± 0.04	
						RC3: 0.60 ± 0.02	
						RC4: 0.70 ± 0.07	
						RC5: 0.59 ± 0.05	
						RC6: 0.52 ± 0.09	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						Glucosidase inhibition (mmol ACAE/g extract):	
						RC1: 1.44 ± 0.02	
						RC2: 1.90 ± 0.02	
						RC3: 1.95 ± 0.01	
						RC4: 1.97 ± 0.14	
						RC5: 2.03 ± 0.01	
						RC6: 1.94 ± 0.02	
Scabiosa columbaria	Leaves	**Solvent extraction**: MeOH with concentrations of 25, 50, 100, 200 μg/mL	**Antimelanogenesis**: Melanin content assay using B16F10 melanoma cells	-Kojic acid as positive control	-Kojic acid as positive control	**Antioxidant**:	78
			Antityrosinase: Mushroom tyrosinase inhibition assay using L-DOPA as a substrate	-The extracts inhibited melanogenesis in α-MSH-stimulated B16F10 cells with increasing concentrations	-The extract exhibited tyrosinase inhibitory activity in a dose-dependent manner	**a) FRAP assay**:	
			Antioxidant: FRAP assay	-At 100 μg/mL of extracts, cellular melanin content was decreased to around 40%		-Trolox as standard	
						-The extracts displayed a significant FRAP activity than control, especially at 200 μg/mL	
Schinus terebinthifolius	Fruits, leaves	**Solvent extraction**: Hexane, acetone, MeOH, oil	**Antioxidant**: DPPH and ABTS assays	NR	-Kojic acid as positive control	**Antioxidant**:	79
			Antityrosinase: Tyrosinase inhibition activity assay using L-tyrosine as a substrate		**-Tyrosinase inhibition of leaves extracts (%)**:	**a) DPPH assay**:	
					Hexane: 73.68 ± 1.56	-Trolox as standard:	
					Acetone: 92.10 ± 1.81	-IC_{50} of leaf extracts (mg mL^{-1}):	
					MeOH: 100 ± 0.0	Hexane: 1.84	
					-Tyrosinase inhibition of fruit extracts (%):	Acetone: 0.62	
					Oil: 5.26 ± 0.6	MeOH: 0.53	
					Acetone: 78.94 ± 1.2	-IC_{50} of fruit extracts (mg mL^{-1}):	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
					MeOH: 63.15 ± 1.43	Oil: 0.016	
					Kojic acid: 86.7 ± 1.75	Acetone: 1.02	
						MeOH: 0.41	
						Trolox: 0.136 mg mL^{-1}	
						b) ABTS assay:	
						-Trolox as standard:	
						-IC_{50} of leaf extracts (mg mL^{-1}):	
						Hexane: 1.29	
						Acetone: 0.87	
						MeOH: 0.76	
						-IC_{50} of fruit extracts (mg mL^{-1}):	
						oil: 0.017	
						Acetone: 0.98	
						MeOH: 0.61	
						Trolox: 0.145	
Schisandra chinensis (Turcz.) Baillon	Dried fruits	**Solvent extraction**: 95% ethanol (EtOH)	**Antimelanogenesis**: Melanin content assay using B16F10, melanoma cells	-Arbutin as positive control	NR	NR	2
		Extracted crude extract fractioned into: *n*-hexane, CH_2Cl_2, EtOAc, *n*-BuOH, H_2O		**-Melanin inhibition IC_{50} (μg/mL)**:			
		Temperature: 25 °C		95% EtOH: 98.37			
				n-hexane: 11.58			
				CH_2Cl_2: 27.89			
				EtOAc: >100			
				n-BuOH: >100			
				H_2O: >100			
Scorzonera tomentosa L.	Aerial parts, roots	**Solvent extraction**: hexane, EtOAc, CH_2Cl_2, MeOH, H_2O	**Antityrosinase**: Standard *in vitro* bioassays	NR	-Kojic acid as positive control	**Antioxidant**:	80
		Temperature: 25 °C	**Antioxidant**: DPPH, ABTS, CUPRAC, FRAP, metal chelating, PM assay		**-Tyrosinase inhibition (mg KAE/g extract)**:	**a) DPPH and ABTS assays**:	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
			α-glucosidase, α-amylase, and cholinesterase inhibition: Standard *in vitro* bioassays		Aerial parts:	-MeOH and H_2O extracts of both plant parts showed good free radical scavenging ability	
					CH_2Cl_2: 63.32 ± 0.22	**b) CUPRAC assay**:	
					EtOAc: 61.65 ± 0.45	-MeOH extracts of both plant parts showed the highest activity (aerial parts: 164.06 ± 1.26 and roots: 93.18 ± 1.58 mg TE/g)	
					Hexane: 57.54 ± 0.12	**c) FRAP assay**:	
					H_2O: 16.40 ± 1.30	-MeOH extracts of roots (79.78 ± 0.27 mgTE/g) and H_2O extracts (41.36 ± 0.10 mg TE/g) of aerial parts were excellent sources of reducing agents	
					MeOH: 64.83 ± 0.28	**d) Metal chelating assay**:	
					Roots:	-H_2O and CH_2Cl_2 extracts of aerial parts have a metal chelating activity ranged from 2.13 ± 0.10 to 13.92 ± 0.86 mg EDTAE/g	
					CH_2Cl_2: 60.28 ± 0.23	-MeOH and CH_2Cl_2 extracts of roots have a metal chelating activity ranging from 0.53 ± 0.07 to 6.24 ± 0.17 mg EDTAE/g	
					EtOAc: 59.99 ± 0.19	-H_2O and hexane roots extracts showed no activity	
					Hexane: 63.54 ± 0.56	**e) PM assay**:	
					H_2O: 6.29 ± 0.50	-All plant parts extracts were found to have moderate activity	
					MeOH: 65.46 ± 0.31	**Cholinesterase inhibition (mg GALAE/g):**	
						AChE inhibition:	
						Aerial parts:	
						CH_2Cl_2: 2.57 ± 0.07	
						EtOAc: 2.15 ± 0.24	
						Hexane: 1.98 ± 0.24	
						H_2O: 2.13 ± 0.09	
						MeOH: 1.96 ± 0.10	
						Roots:	
						CH_2Cl_2: 2.41 ± 0.01	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						EtOAc: 2.17 ± 0.23	
						Hexane: 2.40 ± 0.27	
						H_2O: 1.83 ± 0.06	
						MeOH: 1.91 ± 0.04	
						BChE inhibition:	
						Aerial parts:	
						CH_2Cl_2: na	
						EtOAc: na	
						Hexane: na	
						H_2O: na	
						MeOH: na	
						Roots:	
						CH_2Cl_2: 1.92 ± 0.17	
						EtOAc: 3.80 ± 0.24	
						Hexane: 3.96 ± 0.57	
						H_2O: na	
						MeOH: 4.78 ± 0.23	
						α-glucosidase inhibition (mmol ACAE/g):	
						Aerial parts:	
						CH_2Cl_2: 0.65 ± 0.04	
						EtOAc: 0.70 ± 0.02	
						Hexane: 0.75 ± 0.01	
						H_2O: 0.18 ± 0.01	
						MeOH: 0.14 ± 0.01	
						Roots:	
						CH_2Cl_2: 0.68 ± 0.01	
						EtOAc: 0.67 ± 0.01	
						Hexane: 0.83 ± 0.01	
						H_2O: 0.09 ± 0.01	
						MeOH: 0.67 ± 0.07	
						α-amylase inhibition (mmol ACAE/g):	
						Aerial parts:	
						CH_2Cl_2: 0.57 ± 0.02	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						EtOAc: 0.60 ± 0.02	
						Hexane: 0.46 ± 0.02	
						H_2O: 0.08 ± 0.01	
						MeOH: 0.40 ± 0.01	
						Roots:	
						CH_2Cl_2: 0.55 ± 0.02	
						EtOAc: 0.57 ± 0.01	
						Hexane: 0.61 ± 0.02	
						H_2O: 0.09 ± 0.01	
						MeOH: 0.26 ± 0.05	
Sorghum bicolor	NR	**Solvent extraction**: 0, 20, 40, 60, 80, 95% EtOH	**Antimelanogenesis**: Melanin content assay using B16F10 melanoma cells	-Arbutin as positive control	-Arbutin as positive control	**Antioxidant**:	81
		Temperature: 40 °C	**Antityrosinase**: Tyrosinase inhibitory assay using L-tyrosine and L-DOPA as substrate	-60% EtOH extract effectively decreased melanin contents at 10 μg/mL concentration from 316.85% to 108.60% compared with arbutin (101.79%)	**-Tyrosinase inhibition IC_{50} using L-tyrosine (μg/mL)**:	**a) DPPH assay**:	
			Antioxidant: DPPH, ABTS, and malondialdehyde (MDA) assays		60% EtOH extract: 89.25	-Vitamin C as standard	
			α-glucosidase inhibition: α-glucosidase inhibitory assay		Arbutin: 74.35	-IC_{50} of 60% EtOH extract: 612.53 μg/mL	
					-Tyrosinase inhibition IC_{50} using L-DOPA of 60% EtOH extract (μg/mL): na	**b) ABTS assay**:	
						-Vitamin C as standard	
						-IC_{50} of 60% EtOH extract: 409.71 μg/mL	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						c) MDA assay: -Catechin as standard -IC_{50} of 60% EtOH extract: 16.56 μg/mL **α-glucosidase inhibition**: -Acarbose as positive control -IC_{50}: 60% EtOH extract: 46.29 μg/mL Acarbose: 216.05 μg/mL	
Stenocarpus sinuatus	Leaves	**Solvent extraction**: MeOH Extracted crude extract was defatted with hexane to produce a hexane soluble fraction	**Antityrosinase**: Antityrosinase assay using L-DOPA as a substrate		-Kojic acid as standard **- Tyrosinase inhibition IC_{50} (μg/mL)**: Hexane soluble fraction: 67.5 Kojic acid: 13.8		82
Tricholosporum goniospermum	Fruiting bodies	**Preparation**: Mycelium was isolated and cultured **Solvent extraction for fruiting bodies and mycelia**: *n*-hexane, EtOAc, MeOH **Temperature**: 20 °C	**Antityrosinase**: Colorimetric enzyme inhibition assays **Antioxidant**: DPPH, CUPRAC, and FRAP assays **α-amylase and cholinesterase inhibition**: Colorimetric enzyme inhibition assays	NR	-Kojic acid as positive control **-Tyrosinase inhibition (mg KAE/g extract)**: Fruiting bodies extracts: *n*-hexane: 83.80 ± 1.45 EtOAc: 554.30 ± 9.41 MeOH: 48.48 ± 0.07 Mycelia extracts: *n*-hexane: 127.76 ± 0.73 EtOAc: 412.81 ± 1.39 MeOH: 28.17 ± 0.39	**Antioxidant**: **a) DPPH assay (mg TE/g extract)**: -Trolox as standard Fruiting bodies extracts: *n*-hexane: 9.35 ± 0.16 EtOAc: 88.82 ± 1.47 MeOH: 17.69 ± 0.95 Mycelia extracts: *n*-hexane: 7.53 ± 0.70 EtOAc: 29.93 ± 3.54	83

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						MeOH: 7.74 ± 0.69	
						b) CUPRAC assay (mg TE/g extract):	
						-Trolox as standard	
						Fruiting bodies extracts:	
						n-hexane: 53.92 ± 1.31	
						EtOAc: 307.71 ± 3.83	
						MeOH: 131.52 ± 0.67	
						Mycelia extracts:	
						n-hexane: 54.35 ± 0.92	
						EtOAc: 155.31 ± 1.85	
						MeOH: 129.60 ± 0.56	
						c) FRAP assay (mg TE/g extract):	
						-Trolox as standard	
						Fruiting bodies extracts:	
						n-hexane: 14.86 ± 1.21	
						EtOAc: 134.06 ± 1.50	
						MeOH: 20.54 ± 0.77	
						Mycelia extracts:	
						n-hexane: 15.15 ± 1.62	
						EtOAc: 74.26 ± 1.79	
						MeOH: 12.94 ± 1.33	
						Cholinesterase inhibition:	
						AChE Inhibition (mg GALAE/g extract):	
						No activity for all extracts	
						BChE Inhibition (mg GALAE/g extract):	
						-Galantamine as standard	
						Fruiting bodies extracts:	
						n-hexane: 5.48 ± 0.03	
						EtOAc: 26.78 ± 0.21	
						MeOH: 5.07 ± 0.02	
						Mycelia extracts:	
						n-hexane: 9.14 ± 0.07	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						EtOAc: 25.21 ± 0.24	
						MeOH: 2.61 ± 0.01	
						α-amylase inhibition (mmol ACAE/g extract):	
						-Acarbose as standard	
						Fruiting bodies extracts:	
						n-hexane: 0.55 ± 0.01	
						EtOAc: 2.97 ± 0.10	
						MeOH: 0.21 ± 0.01	
						Mycelia extracts:	
						n-hexane: 0.73 ± 0.02	
						EtOAc: 2.25 ± 0.07	
						MeOH: 0.17 ± 0.01	
Vigna subterranea (bambara groundnut (BG))	Hulls (H), seeds (S)	**Extraction method (solvent extraction, temperature)**: Soxhlet extraction (95% EtOH, 60 °C), maceration extraction (95% EtOH, 37 °C), boiling (distilled water, 90 °C)	**Antimelanogenesis**: Melanin content assay using B16F10 murine melanoma cells	-Kojic acid as positive control	-Kojic acid as positive control	**Antioxidant**:	84
		BG-HS: Hull extracts prepared by Soxhlet	**Antityrosinase**: Modified dopachrome method using L-tyrosine as a substrate	**-Melanin inhibition rate (%)**:	**-Tyrosinase inhibition IC_{50} (mg/mL)**:	**a) DPPH assay**:	
		BG-HM: Hull extracts prepared by maceration	**Antioxidant**: DPPH assay, metal chelating activity, modified Ferric-thiocyanate method to assess the lipid peroxidation activity	BG-HS: 22.69	BG-HS: 0.07 ± 0.07	-Ascorbic acid as standard	
		BG-HB: Hull extracts prepared by boiling		BG-HM: 72.90	BG-HM: 0.45 ± 0.23	-SC_{50} (mg/mL):	
		BG-SS: Seed extracts prepared by Soxhlet		BG-HB: 32.15	BG-HB: 1.46 ± 0.30	BG-HS: 1.83 ± 0.16	
		BG-SM: Seed extracts prepared by maceration		BG-SS: na	BG-SS: 0.84 ± 0.27	BG-HM: 0.87 ± 0.02	
		BG-SB: Seed extracts prepared by boiling		BG-SM: 40.24	BG-SM: 0.64 ± 0.27	BG-HB: 1.18 ± 0.08	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
				BG-SB: 45.41 Kojic acid: 45.35	BG-SB: 2.86 ± 0.69 Kojic acid: 0.05 ± 0.03	BG-SS: 1.41 ± 0.09 BG-SM: 2.09 ± 0.06 BG-SB: 0.92 ± 0.15 Ascorbic acid: 0.04 ± 0.00 **b) Metal chelating activity**: -EDTA as standard -MC_{50} (mg/mL): BG-HS: 7.21 ± 0.76 BG-HM: 1.83 ± 0.09 BG-HB: 0.88 ± 0.16 BG-SS: 3.39 ± 0.53 BG-SM: 7.23 ± 0.32 BG-SB: 0.63 ± 0.04 EDTA: 0.73 ± 0.08 **c) Modified ferric-thiocyanate method**: -a-tocopherol as standard -LC_{50} (mg/mL): BG-HS: 3.79 ± 0.38 BG-HM: 0.70 ± 0.06 BG-HB: 0.83 ± 0.20 BG-SS: 4.68 ± 0.36 BG-SM: 3.56 ± 0.94 BG-SB: 6.93 ± 1.05 a-Tocopherol: 0.61 ± 0.06	
Vitis vinifera L. (white grape pomace)	NR	**Preparation**: White pomace was either frozen (wet pomace, WP) or dried at 60 °C (dried pomace, DP) **Solvent extraction**: H_2O, EtOH	**Antityrosinase**: Optimized tyrosinase enzyme inhibition assay using L-DOPA as a substrate **Antioxidant**: ABTS assay	NR	EtOH extracts of both WP and DP showed stronger antityrosinase activity (inhibition rate of 63% to 79%) than H_2O extracts (inhibition rate of 43% to 71%). DP samples have good inhibition of tyrosinase compared to WP	**Antioxidant**: H_2O and EtOH extracts of WP had higher antioxidant activity than DP samples. However, EtOH extracts of both WP and DP showed stronger antioxidant activity than H_2O extracts **Anti-inflammatory**: H_2O extract of DP has a higher anti-inflammatory activity than DP while there was no activity reported for ethanol extracts	85

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
			Anti-inflammatory activity: Bioluminescent cell-based assay performed using HEK293 cells				
Ziziphora taurica subsp. *cleonioides*	Aerial parts	**Solvent extraction**: EtOAc, MeOH, H_2O	**Antityrosinase**: Mushroom tyrosinase activity assay	NR	-Kojic acid as positive control	**Antioxidant**:	86
			Antioxidant: DPPH, ABTS, CUPRAC, FRAP, PM, ferrous chelating assays		**-Tyrosinase inhibition IC_{50} (mg/mL)**:	**a) DPPH assay**:	
			Enzyme inhibition activity: α-amylase inhibition evaluated by Caraway IKI method		EtOAc: 1.40 ± 0.06 MeOH: 1.25 ± 0.01	-BHA as standard	
					H_2O: 2.71 ± 0.42	-IC_{50} (mg/mL):	
					Kojic acid: 0.37 ± 0.02	EtOAc: 10.60 ± 0.79	
						MeOH: 4.75 ± 0.12	
						H_2O: 4.98 ± 0.15	
						BHA: 0.32 ± 0.01	
						b) ABTS assay:	
						-BHA as standard	
						-IC_{50} (mg/mL):	
						EtOAc: 4.11 ± 0.09	
						MeOH: 2.66 ± 0.02	
						H_2O: 2.61 ± 0.26	
						BHA: 0.25 ± 0.01	
						c) CUPRAC assay:	
						-BHA as standard	
						-IC_{50} (mg/mL):	
						EtOAc: 1.80 ± 0.03	
						MeOH: 1.97 ± 0.02	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						H_2O: 2.49 ± 0.06 BHA: 0.30 ± 0.01 **d) FRAP assay**: -BHA as standard -IC_{50} (mg/mL): EtOAc: 2.99 ± 0.26 MeOH: 1.14 ± 0.06 H_2O: 1.54 ± 0.15 BHA: 0.25 ± 0.01 **e) PM assay**: -BHA as standard -IC_{50} (mg/mL): EtOAc: 1.52 ± 0.02 MeOH: 1.82 ± 0.15 H_2O: 2.71 ± 0.26 BHA: 0.35 ± 0.01 **f) Ferrous chelating assay**: -EDTA as standard -IC_{50} (mg/mL): EtOAc: 6.47 ± 0.67 MeOH: 1.66 ± 0.02 H_2O: 1.04 ± 0.01 EDTA: 0.034 ± 0.001 **α-amylase inhibition**: -Acarbose as positive control -IC_{50} (mg/mL): EtOAc: 1.95 ± 0.04 MeOH: 3.97 ± 0.08 H_2O: 36.99 ± 0.13 Acarbose: 1.21 ± 0.07	
Ziziphus jujuba	Seeds	**Preparation**: Flavonoid glycosides were isolated from the seeds which were jujuboside A (JUA), jujuboside B (JUB), epiceanothicacid (EPA), betulin (BTL), and 6‴-feruloylspinosin (FRS),	**Antimelanogenesis**: Quantification of extracellular and intracellular melanin content	-Phenylthiourea (PTU) as positive control	-PTU as positive control	NR	7

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results: Antimelanogenesis	Results: Antityrosinase	Results: Others	References
			assay using B16F10 melanoma cells				
			Antityrosinase: *in vitro* mushroom tyrosinase activity assay	**-Extracellular melanin content was inhibited from**147.7 ± 5.2 **% to**:	**-Inhibitory rate of mushroom tyrosinase activity** (%):		
				JUB: 117.4 ± 0.5%	JUA: 7.4 ± 5.3		
				EPA: 119.9 ± 2.0 %	JUB: 33.9 ± 4.5		
				FRS: 106.8 ± 1.9 %	EPA: 38.4 ± 3.1		
				PTU: 92.4 ± 2.4%	BTL: 11.2 ± 5.1		
				-Intracellular melanin content was inhibited from153.5 ± 3.3 **% to**:	FRS: 45.7 ± 2.7		
				JUB: 114.7 ± 1.5%	PTU: 58.4 ± 1.0		
				EPA: 113.8 ± 2.1 %,			
				FRS: 101.4 ± 2.9 %			
				PTU: 95.3 ± 30.2 %			
Zizyphus lotus	Leaves, fruits	**Solvent extraction**: H_2O	**Antityrosinase**: Tyrosinase inhibition assay using L-DOPA as a substrate	NR	-Quercetin as positive control	**Antioxidant**:	87
			Antioxidant: DPPH, ABTS, and FRAP assays		**-Tyrosinase inhibition IC_{50} (μg/mL)**:	**a) DPPH assay (mg TE/g extract)**:	
			Antidiabetics: α-amylase and α-glucosidase inhibitory assays		Fruits: 70.23 ± 5.94	-Trolox as standard	
					Leaves: 129.11 ± 9.40	-IC_{50}:	
					Quercetin: 246.90 ± 1.90	Fruits: 74.87 ± 16.74	
						Leaves: 241.75 ± 17.37	
						b) FRAP assay (mg AAE/g extract):	
						-Ascorbic acid as standard	

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Table 1. continued

Plant name	Parts	Sample preparation and extraction methods	Biology assays	Results			References
				Antimelanogenesis	Antityrosinase	Others	
						-IC_{50}: Fruits: 55.30 ± 2.30 Leaves: 160.10 ± 2.30 **c) ABTS assay (mg TE/g extract)**: -Trolox as standard -IC_{50}: Fruits: 46.31 ± 11.02 Leaves: 301.34 ± 8.26 **Antidiabetic activity: α-amylase inhibition**: -Acarbose as positive control -IC_{50} (μg/mL): Fruits: 31.91 ± 1.53 Leaves: 20.40 ± 1.30 Acarbose: 396.42 ± 3.54 **α-glucosidase inhibition**: -Acarbose as positive control -IC_{50} (μg/mL): Fruits: 27.95 ± 2.45 Leaves: 8.66 ± 0.62 Acarbose: 199.53 ± 2.45	

[a]NR: Not reported. NA: No activity. BHA: Butylated hydroxyanisole. BHT: Butylated hydroxytoluene. AChE: Acetylcholinesterase. BChE: Butyrylcholinesterase. ACAE: Acarbose equivalent. TE: Trolox equivalent. EDTAE: Ethylenediaminetetraacetic acid equivalent. GALAE: Galantamine equivalent. KAE: Kojic acid equivalent. AEAC: Ascorbic acid equivalent. PM: Phosphomolybdenum assay. DPPH: 2,2-diphenyl-1-picrylhydrazyl. ABTS: 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic) acid. CUPRAC: cupric-reducing antioxidant capacity. FRAP: Ferric reducing antioxidant power assay.

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

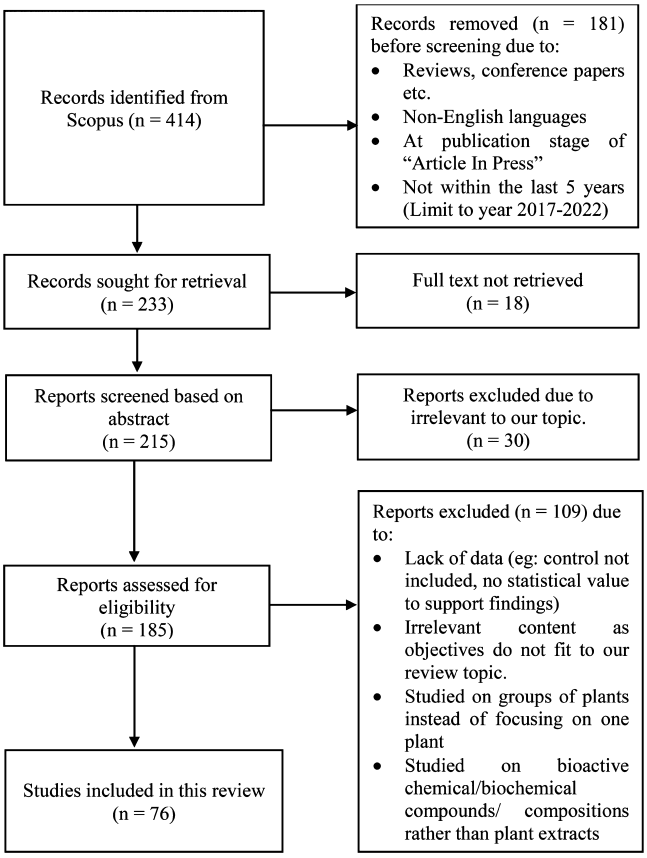


Figure 1. PRISMA flow diagram of the systematic review.

alcohol is much more effective than water for phytochemical extraction due to its ability to extract polar compounds and some nonpolar compounds.

Ethanol is one of the most suitable solvent extractions that can extract both polar compounds and nonpolar compounds. Ethanol was being used to extract the bioactive compounds from *Acer rubrum, Achillea biebersteinii, Achillea filipendulina, Aerva lanata* (L.) *Juss., Allium ursinum, Artemisia asiatica, Artemisia capillaris, Aurea helianthus, Cymbidium sp.* (Orchidaceae), *Cytinus hypocistis, Dalea pazensis Rusby, Erica arborea* L., *Fagus sylvatica* L., *Hippophae rhamnoides* L., *Kadsura coccinea, Kummerowia striata, Lepechinia meyenii, Morus alba* L., *Myrica rubra, Persicaria orientalis, Phyllostachys nigravar henosis, Potentilla anserina* L., *Potentilla paradoxa Nutt., Prasiola japonica, Pterocarpus marsupium, Rosa chinensis cv. "JinBian", Schisandra chinensis (Turcz.) baillon, Sorghum bicolor, Vigna subterranea,* and *Vitis vinifera* L. The ethanol used in these extractions of plants was from 25% ethanol in water up to 100%. By mixing ethanol with water, this can extract bioactive compounds with a wider polarity due to the ethanol solvent polarity being influenced by the high concentration of water contained in ethanol.

Water is widely utilized as solvent for extraction because it is the most polar and greenest solvent. It is nontoxic to human health and the environment, cost-effective, and safe to use.[19] Among the included articles, water was used to extract the bioactive compounds from *Achillea biebersteinii* and *Aerva lanata* (L.) *Juss., Allium ursinum, Aronia melanocarpa, Camellia oleifera Abel, Celastrus hindsii, Cosmos caudatus Kunth, Cymbidium sp. (Orchidaceae), Cytinus hypocistis, Dendropanax morbiferus H. Lev, Dimocarpus longan Lour., Fagus sylvatica* L., *Garcinia atroviridis Griff. ex. T. Anderson, Juglans mandshurica, Leonurus japonicus, Limonium delicatulum, Lophira lanceolata Tiegh. ex Keay, Manilkara kauki, Myrica rubra, Nardostachys jatamansi, Nepeta glomerulosa Boiss., Pistacia atlantica subsp. Mutica, Rubus cesius* L., *Schisandra chinensis (Turcz.) baillon, Scorzonera tomentosa* L., *Vitis vinifera* L., and *Ziziphora taurica subsp. Cleonioides* and *Zizyphus lotus*. It was used as a single solvent or commonly mixed with ethanol, methanol, or acetone. Further, properties of water extracts can be improved by increasing the temperature.[19] Boiling water has been used as an extract solvent for *Carapa procera, Phyllostachys nigravar. Henosis, Vigna subterranea,* and lotus.

Methanol generally produces higher extraction yields and extracts more phytochemical constituents due to its higher polarity than ethanol. Based on the study review, methanol extracts produce better results in terms of the biological activities. Methanol was used to extract the following plants: *Camellia oleifera Abel, Carapa procera, Celastrus hindsii, Clausena indica, Galla rhois, Granny Smith apple, Juglans mandshurica, Leonurus japonicus, Limonium delicatulum, Lophira lanceolata Tiegh. ex Keay, Maclura tricuspidata, Manilkara kauki, Nardostachys jatamansi, Nepeta glomerulosa* Boiss., *Olea europeae, Pelargonium graveolens, Persicaria orientalis, Phyllanthus phillyreifolius, Phyllostachys nigravar. Henosis, Pistacia atlantica subsp. mutica, Pistacia lentiscus* L., *Rubus cesius* L., *Scabiosa columbaria, Schinus terebinthifolius, Scorzonera tomentosa* L., *Stenocarpus sinuatus, Tricholosporum goniospermum,* and *Ziziphora taurica subsp. Cleonioides*. The methanol used in the extractions of plants was from 50% in water up to 100%.

Acetone, butanol, ethyl acetate, and dichloromethane are also regarded as polar solvents but much less polar than ethanol, methanol, and water. Hence, they can extract a mixture of both polar and nonpolar components. From the studies reviewed, acetone has been used to extract *Acanthus ilicifolius, Cinnamomum camphora, Dimocarpus longan Lour., Melastoma normale, Nardostachys jatamansi, Photinia fraseri, Polygonum maritimum* L., and *Schinus terebinthifolius*, whereas butanol had extracted *Kummerowia striata, Maclura tricuspidata, Morus alba* L., *Nepeta glomerulosa Boiss., Pistacia atlantica subsp. Mutica, Rubus cesius* L., and *Schisandra chinensis (Turcz.) Baillon*. The acetone used for extraction was from 70% in water up to 100%. Moreover, ethyl acetate was used to extract the following plants: *Asparagus cochinchinensis, Celastrus hindsii, Cinnamomum camphora, Clausena indica, Cymbidium sp.* (Orchidaceae), *Dalea pazensis Rusby, Juglans mandshurica, Kummerowia striata, Leonurus japonicus, Maclura tricuspidata, Melastoma normale, Morus alba* L., *Nepeta glomerulosa Boiss, Persicaria orientalis, Phyllanthus phillyreifolius, Phyllostachys nigravar. Henosis, Pistacia atlantica subsp. Mutica, Potentilla anserina* L., *Rubus cesius* L., *Schisandra chinensis (Turcz.) Baillon, Scorzonera tomentosa* L., *Tricholosporum goniospermum, Ziziphora taurica subsp. Cleonioides,* dichloromethane-extracted *Cymbidium sp. (Orchidaceae), Kummerowia striata, Maclura tricuspidata, Nepeta glomerulosa* Boiss, *Pelargonium graveolens, Pistacia atlantica subsp. Mutica, Schisandra chinensis (Turcz.) Baillon,* and *Scorzonera tomentosa* L.

Compared with polar solvents, there were fewer studies using nonpolar solvents. Based on the studies reviewed, nonpolar solvents used by the studies are chloroform, acetonitrile, *n*-hexane, benzene, 1,3-butanediol, oil, and petroleum ether. Chloroform was used as a single solvent or combined in use with ethanol to extract *Dalea pazensis Rusby, Juglans*

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

mandshurica, and *Nardostachys jatamansi*. Hexane has been used to extract the following plants: *Celastrus hindsii*, *Clausena indica*, *Dalea pazensis Rusby*, *Leonurus japonicus*, *Maclura tricuspidata*, *Morus alba* L., *Nepeta glomerulosa Boiss.*, *Pelargonium graveolens*, *Persicaria orientalis*, *Phyllostachys nigravar. Henosis*, *Pistacia atlantica subsp. mutica*, *Schinus terebinthifolius*, *Schisandra chinensis (Turcz.) Baillon*, *Scorzonera tomentosa* L., *Stenocarpus sinuatus*, and *Tricholosporum goniospermum*. There was only one study each for acetonitrile, 1,3-butanediol, and benzene solvents for extraction, which are *Nardostachys jatamansi*, *Camellia oleifera Abel*, and *Dalea pazensis Rusby*, respectively. Essential oils were isolated from *Achillea filipendulina* and *Beta vulgaris subsp. Maritime* (L.) *Arcang.*, *Melaleuca quinquenervia*, *Pistacia atlantica subsp. Mutica*, and *Schinus terebinthifolius* by subjecting to hydrodistillation. Essential oils are known for having numerous amounts of bioactive compounds. Petroleum ether was also utilized to extract *Cinnamomum camphora*, *Dimocarpus longan Lour.*, *Melastoma normale*, *Potentilla anserina* L., and *Rosa chinensis cv. "JinBian"*.

Other than solvent extraction, bioactive compounds also can be extracted using various conventional (classical) and nonconventional (innovative) methods. The methods that were used to extract bioactive compounds according to the studies reviewed included fractionation, accelerated solvent extraction (ASE) or pressurized solvent extraction (PLE), maceration (M), ultrasonic-assisted extraction (UAE), shaking extraction (SE), infusion, microwave-assisted extraction (MAE), Soxhlet (SOE), homogenizer-assisted extraction (HAE), pulsed electric field (PEF), and decoction. Among the methods described above, fractionation is most frequently used by separating plant extracts into various fractions. The fractions are then used to further isolate the bioactive compounds.[20] Extracts that were subjected to fractionation from the following plants were *Achillea biebersteinii*, *Celastrus hindsii*, *Clausena indica*, *Dalea pazensis Rusby*, *Juglans mandshurica*, *Leonurus japonicus*, *Lepechinia meyenii*, *Maclura tricuspidata*, *Melastoma normale*, *Morus alba* L., *Pistacia atlantica subsp. Mutica*, *Potentilla anserina* L., *Schisandra chinensis (Turcz.) Baillon*, and *Stenocarpus sinuatus*.

In the Soxhlet extraction method, the plant sample was first placed in the thimble chamber of the Soxhlet apparatus. The extraction solvent was heated in a round-bottom flask, vaporized into a sample timber, condensed in the condenser, and dripped back into the extract sample. A siphon was then used to aspirate the mixtures of solvent and extracts and emptied into the round-bottom flask to mix with the clean solvents.[21] In the included articles, the following plants are mentioned: *Erica arborea* L., *Lophira lanceolata Tiegh. ex Keay*, *Phyllanthus phillyreifolius*, and *Vigna subterranea* were extracted by this technique. The Soxhlet has several advantages including required smaller volume of solvents, simple to use, low-cost equipment, lack of filtration, and continuous contact between the solvent and the sample.[21] In addition, maceration is a method that immerses the plant materials in extracting solvent in a stoppered container. The mixture was then incubated for 2 to 3 days at room temperature with constant stirring to obtain the plant extracts.[20] Plant parts of *Achillea biebersteinii*, *Achillea filipendulina*, *Carapa procera*, *Erica arborea* L., *Lophira lanceolata Tiegh. ex Keay*, *Morus alba* L., *Phyllanthus phillyreifolius*, and *Vigna subterranea* were extracted by this method. Although this method is time consuming, it is still widely used because it is an easy to use and inexpensive method.

ASE and PLE are nonconventional methods introduced as an alternative to maceration and Soxhlet extraction. They are automated methods using liquid solvents to extract under elevated pressures and temperatures.[22] ASE or PLE was used to extract *Achillea biebersteinii*, *Erica arborea* L., and *Pistacia lentiscus* L. Furthermore, infusion applied a principle similar to maceration and decoction by soaking the plant material in solvents. *Carapa procera* and *L. lanceolata Tiegh. ex Keay* used infusion as an extraction method. Moreover, MAE uses microwave energy that results in rapid heating extraction of *Erica arborea* L. and *Fagus sylvatica* L..[23] UAE was used to extract *Achillea biebersteinii* and *Erica arborea* L. Other methods that have been mentioned, which are SE, HAE, PEF, and decoction, had only been used by one study each, respectively, to extract *Achillea biebersteinii*, *Lophira lanceolata Tiegh. ex Keay*, *Morus alba* L., and *Phyllanthus phillyreifolius*, respectively.

4. BIOLOGICAL ACTIVITIES

Biological activities such as antimelanogenesis, antityrosinase, antioxidant, and anti-inflammatory various natural plant species are summarized and tabulated in Table 1.

In order to pursue natural novel melanin inhibitors with fewer side effects, the investigation of various natural plant species has prompted the identification of numerous plant extracts or bioactive compounds that have the potential to be used as skin-whitening agents. Based on the studies we reviewed, the antimelanogenesis of natural plants was evaluated using melanin content assay in B16 melanoma cell lines, A375.S2 melanoma cells, and A2058 human melanoma cells. The effectiveness of melanogenesis inhibition was expressed as IC_{50} values, percentage of the control, and percentage of melanin inhibitory effects. IC_{50} values represent the concentration of extract required to inhibit melanin synthesis by 50%. Kojic acid and arbutin were commonly used as a positive control.

Tyrosinase is a multifunctional copper-containing enzyme that is commonly found in microorganisms, animals, and plants.[88] It is an essential enzyme in the melanin biosynthesis pathway and has always been a popular target to be used as melanogenesis inhibitors. Based on the studies we reviewed, the antityrosinases of natural plants were evaluated using the tyrosinase activity assay or mushroom tyrosinase activity assay using L-tyrosine and/or L-DOPA as substrates, the dopachrome method using L-DOPA as a substrate, and cellular tyrosinase activity assay using B16 melanoma cell lines. The effectiveness of tyrosinase inhibition was expressed as IC_{50} values, EC_{50} values, milligrams of kojic acid equivalent per gram of dry extract, and percentage of tyrosinase inhibitory effects. IC_{50} values represent the concentration of extract required to inhibit tyrosinase activity by 50%, while EC_{50} values represent the concentration of extract required to produce a half-maximal response. Kojic acid, arbutin, and ascorbic acid were commonly used as a positive control.

Antioxidants are molecules that neutralize free radicals by donating electrons to them. These can help to prevent cellular damage through their free radical scavenging ability.[89] Plants are found to comprise a variety of natural antioxidants that may have the potential to protect humans from UV-induced disorders. Based on the studies we reviewed, the antioxidant activities of natural plants were evaluated using a number of assays with six commonly used assays including 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic) acid

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

(ABTS), cupric-reducing antioxidant capacity (CUPRAC), ferric-reducing antioxidant power assay (FRAP), metal chelating, and a phosphomolybdenum assay (PM). The effectiveness of antioxidant activity was generally expressed as IC_{50} values, EC_{50} values, percentage of free radical scavenging ability, millimoles of Trolox equivalent per gram of dry extract, and milligrams of ethylenediaminetetraacetic acid equivalent per gram of dry extract. BHT, ascorbic acid, BHA, Trolox, and Vitamin C were commonly used as standards for DPPH, ABTS, FRAP, CUPRAC, and PM assays, whereas EDTA was used as a standard for the metal-chelating assay.

Other than depigmentation effects, anti-inflammatory and enzyme inhibitory activities such as cholinesterase, α-amylase, α-glucosidase, elastase, and collagenase inhibition were also commonly evaluated by researchers. Inflammation occurs in the body in response to tissue injury, cell death, and cancer or when infectious microorganisms such as bacteria, viruses, or fungi enter our body.[90] Inflammation can result in common symptoms including redness, swelling, heat, and pain; thus, anti-inflammatory activity plays a significant function in alleviating these symptoms. The anti-inflammatory activities of natural plant species were performed using several types of assays, but the assay commonly used to examine the anti-inflammatory activity is the assessment of nitric acid production using LPS-stimulated RAW 264.7 macrophages.

4.1. *Acanthus ilicifolius*. The antityrosinase and antioxidant activities of the condensed tannins (CT_S) of *A. ilicifolius* leaves were explored by Gong et al.[24] The tyrosinase inhibitory activity of *A. ilicifolius* leaves of CT_S was found to be comparable to the positive control, arbutin, with IC_{50} values of 19.7 ± 0.13 μg/mL and 10.89 mg/mL, respectively, on mushroom tyrosinase activity assay. This result indicated the high potential of *A. ilicifolius* CT_S in tyrosinase inhibition activity. The antioxidant effects of CT_S from *A. ilicifolius* were reflected in the DPPH, ABTS, and FRAP assays, compared with ascorbic acid as a standard antioxidant. The EC_{50} values of DPPH and ABTS scavenging activities were 104 ± 0.894 μg/mL and 86 ± 0.616 μg/mL, respectively, which were higher than that of ascorbic acid equivalent under the same conditions,[24] and the FRAP value was 758.28 ± 2.42 mg of AAE/g, indicating the high antioxidant activities of the CT_S from *A. ilicifolius*.[24]

4.2. *Achillea biebersteinii*. Strzepek-Gomolka et al. were the first to report the antimelanogenesis activity of *A. biebersteinii* flower extracts in mammalian cells. The results showed that fractions 25 and 27 obtained from the extracts using the ASE method reduced the release of melanin from B16F10 murine melanoma cells stimulated with α-melanocyte-stimulating hormone (α-MSH), without affecting the viability and morphology of the cells.[25] In view of the tyrosinase inhibitory activity of *A. biebersteinii* flower extracts, the most significant mushroom tyrosinase inhibitory activity was found in fractions 5, 6, and 7, displaying 34.9, 24.3, and 31.5% inhibitory activity, respectively.[25] While fractions 25 and 27 showed the most significant murine tyrosinase inhibition of about 80% murine tyrosinase inhibitory activity, which was higher than kojic acid, the control tyrosinase inhibitor at the same conditions was about 100 μg/mL. However, the extracts obtained by UAE and SE had better antioxidant activity than extracts obtained by ACE and maceration.[25]

4.3. *Achillea filipendulina*. Asghari and co-workers investigated the cholinesterase, α-amylase, and α-glucosidase inhibition activity of ethanol extracts and essential oils of *Achillea filipendulina* flowers and leaves using enzyme inhibition assays. Overall, ethanol extracts were found to be able to inhibit cholinesterase, α-amylase, and α-glucosidase more efficiently compared to essential oil. Ethanol flowers and leaf extracts presented the highest inhibitory effects against α-amylase (1.91 ± 0.05 mmol ACE/g extract) and α-glucosidase (2.97 ± 0.06 mmol ACE/g extract), respectively.[26] Ethanol flower extract demonstrated strong inhibitory effects against acetylcholinesterase and butyrylcholinesterase (AChE: 2.46 ± 0.06 mmol GALAE/g extract; BChE: 3.65 ± 0.07 mmol GALAE/g extract). Lastly, antielastase and anticollagenase activities can contribute to antiaging activity. The inhibition of cholinesterase including acetylcholinesterase and butyrylcholinesterase is able to effectively treat Alzheimer's disease since cholinesterase inhibitors were commonly prescribed to treat Alzheimer's disease. Also, α-amylase inhibition and α-glucosidase inhibition can be used as a therapeutic approach to treat diabetic patients by reducing the rate of glucose absorption.[26,68] Enzyme inhibitory activities were commonly evaluated using the colorimetric method or enzyme inhibition assays. Galantamine was used as a positive control for cholinesterase inhibition, while acarbose was used as a positive control for α-amylase and α-glucosidase inhibition. Furthermore, ethanol extracts of *A. filipendulina* flowers and leaves were reported with promising tyrosinase inhibitory effects with values of 23.97 and 24.41 mg KAEs/g extract, respectively.[26] On the other hand, the antioxidant activities of ethanol extracts and essential oils of *Achillea filipendulina* flowers and leaves were evaluated by DPPH, ABTS, PM, and metal chelating assays. Ethanol extracts of *A. filipendulina* flowers and leaves exhibited strong antiradical effects with values of 53.93 and 51.70 mg TEs/g sample for DPPH assays and 43.47 and 35.03 mg TEs/g sample for ABTS assays, respectively. The radical scavenging activity of flowers and leaves of essential oils against DPPH were moderate with values of 25.87 and 22.13 mg TEs/g sample, respectively. This trend was also observed in the abilities of essential oils of flowers (18.23 mg TEs/g sample) and leaves (15.40 mg TEs/g sample) in scavenging ABTS radicals. The ethanol extracts of *A. filipendulina* flowers and leaves exhibited stronger antioxidant effects in total antioxidant (84.03 and 70.17 mg AAEs/g sample) and metal chelating assays (37.13 and 30.47 mg EDTAEs/g sample) than the essential oils. In all types of antioxidant assays, flower extract showed higher activity than those of leaves.[26]

4.4. *Aerva lanata* (L). Juss. Pieczykolan et al. evaluated the antiaging activity of *Aerva lanata* (L). Juss extracts using elastase and collagenase inhibition assays.[27] The researchers found that 50% ethanol extract at 180 °C exhibited the highest antielastase and anticollagenase activities with EC_{50} values of 35.81 ± 0.81 and 21.76 ± 1.27 mg/mL, respectively. The highest antityrosinase activity was found in 80% ethanol extract at 60 °C with the EC_{50} of 43.32 ± 0.57 μg/mL, which is comparable with the positive control, kojic acid with an EC_{50} of 28.42 ± 0.11 μg/mL. Notably, water extract at 60 °C showed the highest EC_{50} value of tyrosinase inhibition with 155.97 ± 1.34 μg/mL. The 80% ethanol extract (180 °C) exhibited the highest DPPH (119.85 mg of Trolox/g DE) and ABTS (107.58 mg of Trolox/g DE) scavenging activity. The lowest antioxidant properties in both tests were obtained when 100% ethanol was used as a solvent: 9.17 mg of Trolox/g of DE at 80 °C (DPPH) and 9.90 mg of Trolox/g of DE at 60 °C (ABTS). The 100% ethanol extract at 60 °C showed the greatest metal chelating activity with an EC_{50} value of 1.58 ± 0.17 mg/mL. The highest value of oxygen radical absorbance

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

capacity was determined in the extract obtained in 50% ethanol at 180 °C with a value of 3.84 ± 0.06 mM TE/g.[27]

4.5. *Allium ursinum*. Nikkhahi et al. explored the antioxidant and tyrosinase inhibitory activities of *A. ursinum* extracts by using DPPH and mushroom tyrosinase assays.[28] From the results obtained, the water extract showed the highest DPPH radical scavenging activity with a SC_{50} (values of active DPPH scavengers) of 0.471 mg/mL, compared to 70% ethanol extract (0.532 mg/mL) and 100% ethanol extract (0.643 mg/mL). The SC_{50} of ascorbic acid (positive standard) was 0.008 μ/mL. On the other hand, the 70% ethanol extract exhibited the highest antityrosinase activity compared to water extract and 100% ethanol extract, with IC_{50} values of 0.392, 0.414, and 0.402 mg/mL, respectively. The positive control, kojic acid, indicated an IC_{50} value of 0.031 mg/mL in this study.[28]

4.6. *Aronia melanocarpa*. Based on Svarc-Gajic et al., the antityrosinase activity of the subcritical water extracts of chokeberry (*A. melanocarpa*) stems was calculated to be 15.87 ± 3.82 mg KAE/g extract by using the dopachrome method, while kojic acid was used as the positive control.[29] In the same study, the antioxidant activity of the chokeberry stem extracts was determined using the DPPH assay and reducing power tests. The IC_{50} values of chokeberry stem extracts in the DPPH assay and reducing power assay were reported as 0.10 ± 0.02 mg/mL and 1.25 ± 0.03 mg/mL, respectively.[29]

4.7. *Artemisia asiatica*. The antimelanogenesis and antityrosinase activities of 95% ethanol extract of *Artemisia asiatica* were reported by Jeong et al.[30] The studies found that the ethanol extract significantly suppressed melanin secretion and decreased the melanin content in α-MSH-stimulated B16F10 cells in a dose-dependent manner; the suppressive effect was comparable to the arbutin, the positive control in this study. Furthermore, the ethanol extract was found to inhibit both the mushroom and B16F10 cellular tyrosinase activity in a dose-dependent manner, and a stronger tyrosinase inhibitory effect than arbutin was reported.[30]

4.8. *Artemisia capillaris*. Woo et al. explored the *in vitro* antimelanogenesis and antityrosinase effects of *Artemisia capillaris* (100% ethanol extract) in different concentrations on B16F10 melanoma cells.[31] The results obtained showed that the extract reduced the cellular melanin content in a dose-dependent manner in α-MSH-stimulated B16F10 cells, with a 40.24% inhibition at 50 μg/mL. Besides, the ethanol extract also significantly decreased cellular tyrosinase activity in a dose-dependent manner, with a 30.92% inhibition at 50 μg/mL reported.[31]

4.9. *Asparagus cochinchinensis*. Wang et al. examined the fermented and unfermented *Asparagus cochinchinensis* root extracts in antimelanogenesis, antityrosinase, and antioxidant activities. The published results show that both fermented and unfermented extracts inhibited melanogenesis in human epidermal melanocytes (HEMs) and the human malignant melanoma cell line A375.S2 in a dose-dependent manner.[32] In the mushroom tyrosinase activity assay, fermented extracts were significantly higher than the unfermented extracts, with IC_{50} values of 50.6 ± 3.1 and 527.3 ± 23.6 mg/L, respectively. By contrast, the IC_{50} values of the antityrosinase activity for the positive controls kojic acid and a-arbutin were 18.6 ± 0.5 and 261.4 ± 12.8 mg/L, respectively.[32] Similarly, the results of cellular antityrosinase activity were 48.6% ± 1.8%−55.8% ± 2.3% and 3.6% ± 2.0%−28.4% ± 1.3% for the fermented and unfermented extracts, respectively, at a 1000 mg/L concentration. The fermented extract exhibited stronger radical scavenging activity with IC_{50} values of 250.6 ± 32.5 mg/L for the DPPH assay and 25.7 ± 3.5 mg/L for the reducing power assay compared to the unfermented extract (DPPH assay: 586.9 ± 86.1 mg/L; reducing power assay: 59.0 ± 6.2 mg/L). The butylated hydroxytoluene (BHT) was used as a positive control (IC_{50}: 105.3 ± 285.6 mg/L) in the DPPH assay, while beta hydroxy acid (BHA) (IC_{50}: 35.4 ± 2.6 mg/L), ascorbic acid (IC_{50}: 76.8 ± 6.2 mg/L), and α-tocopherol (IC_{50}: 53.2 ± 3.7 mg/L) were the standards for reducing the power assay.[32]

4.10. *Aurea helianthus*. According to Kim et al., the *Aurea helianthus* stem extract was found to exhibit an antimelanogenesis effect by reducing the melanin content by 20% in α-MSH-stimulated B16 melanoma cells. The extract was reported to inhibit the cellular tyrosinase activity in a dose-dependent manner in B16 cells.[4]

4.11. *Beta vulgaris* subsp. *Maritime* (L.) Arcang. Zardi-Bergaoui et al. reported the antityrosinase activity of hydrodistilled essential oil of the aerial parts of *B. vulgaris*, with an inhibition rate of 67% (cc = 100 μg/mL) compared to the positive standard, kojic acid (85%, 50 μg/mL).[33] The essential oil exhibited a significantly higher antioxidant activity according to the DPPH radical scavenging assay with an IC_{50} of 0.055 ± 0.006 mg/mL when compared to the BHT reference value of 0.018 ± 0.010 mg/mL. Similarly, in the ABTS and reducing power assays, the essential oil had reported IC_{50} values of 0.079 ± 0.010 and 0.120 ± 0.002 mg/mL, comparable to the BHT reference value of 0.050 ± 0.0 and 0.020 ± 0.010 mg/mL, respectively.[33] On the other hand, the study demonstrated significant activity of the enzyme catalase in the oil (524.447 ± 2.58 μ/mg protein) as compared to vitamin C (747.384 ± 016). In view of the paraoxonase test, the essential oil exhibited an interesting activity (55.0 ± 1.5 μM/min/L) comparable to that of ascorbic acid (55 ± 0.2 μM/min/L).[33]

4.12. *Camellia oleifera Abel*. Liu et al. evaluated the antityrosinase activity of *Camellia oleifera Abel* shell extracts by different solvent extraction. The results showed that the 1,3-butanediol extract has the highest tyrosinase inhibition rate of 71.9%, compared to those of the methanol extract (49.2%) and water extract (39.3%). Kojic acid was used as the positive control in this study.[34]

4.13. *Carapa procera*. According to Sinan et al., the tyrosinase inhibition activity of *Carapa procera* leaf extract was found as 73.43 ± 0.07 mg KAE/g extract, while the stem barks were reported to be 75.25 ± 0.20 mg KAE/g extract.[35] In general, methanol extract of stem bark had the highest antioxidant activity in all tested assays with 3.14 ± 0.01 mmol of TE/g of the ABTS assay, 4.47 ± 0.07 mmol of TE/g of the CUPRAC assay, and 2.15 ± 0.01 mmol of TE/g of the FRAP assay. Methanol extracts of both plant parts exhibited moderate inhibitory activity against α-glucosidase (0.95 ± 0.01 mmol ACAE/g) and high inhibitory activity against α-amylase (0.77 ± 0.01 mmol ACAE/g). As for anticholinesterase assays, the methanolic extracts of the two parts gave the highest inhibitory effects on acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), respectively (leaves: 2.55 ± 0.02 and 4.16 ± 0.26; stem bark: 2.54 ± 0.01 and 4.58 ± 0.13 mg GALAE/g).[35]

4.14. *Celastrus hindsii*. Viet et al. reported the antityrosinase and antioxidant activities of *Celastrus hindsii* leaf extracts (α-amyrin and β-amyrin).[36] The tyrosinase inhibition IC_{50} of α-amyrin and β-amyrin was 178.85 ± 3.28 μg/mL, while the IC_{50} for positive control of kojic acid was 15.55 ±

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

2.28 μg/mL. The DPPH radical scavenging activity of α-amyrin and β-amyrin was 125.55 ± 0.98 μg/mL, and a value of 155.28 ± 1.01 μg/mL for the ABTS assay was reported.[36] Both antioxidant assays were used BHT as a positive control, with the IC_{50} value of 8.22 ± 0.89 μg/mL for the DPPH assay and 53.40 ± 1.52 μg/mL for the ABTS assay, respectively.[36]

4.15. *Cinnamomum camphora*. Yang et al. investigated the antityrosinase and antioxidant activities of *Cinnamomum camphora* leaf and branch extracts.[37] The results found that the leaves exhibited higher antityrosinase activities in both monophenolase and diphenolase assays with an inhibition IC_{50} of 167 ± 18 and 70 ± 7 μg/mL, respectively, compared to the branches with tyrosinase monophenolase inhibition IC_{50} of 268 ± 24 and 91 ± 8 μg/mL in a tyrosinase diphenolase assay. Similar results were found in the antioxidant assays, as leaves exhibited great DPPH and ABTS radical scavenging activities with IC_{50} values of 78 ± 13 and 117 ± 16 μg/mL, respectively. Branch extracts showed relatively high IC_{50} values in the DPPH assay (274 ± 28 μg/mL) and ABTS assay (230 ± 30 μg/mL). In contrast, the IC_{50} values of the positive control, Vitamin C, were 72.9 ± 0.5 and 74 ± 9 μg/mL in DPPH and ABTS assays, respectively. Interestingly, the branch extract showed a lower IC_{50} value in the FRAP assay (3.6 ± 0.4 μg/mL) compared to leaves with an IC_{50} value of 4.7 ± 0.5 μg/mL.[37]

4.16. *Citrus junos*. Based on the studies by Adhikari et al., 1000 μg/mL of *Citrus junos* callus extract showed a 59.3 ± 4.20% inhibition of melanogenesis in B16F10 melanoma cells, which was stronger than the positive control, arbutin.[38] The callus extract was also reported to inhibit mushroom tyrosinase activity in a dose-dependent manner. In view of the DPPH assay, 1000 μg/mL of callus extract exhibited 68.5 ± 9.49% of DPPH free radical scavenging ability, which was comparable to 125 μM of ascorbic acid (62.3 ± 1.78%).[38]

4.17. *Clausena indica*. Quan et al. explored the antityrosinase and antioxidant activities of *Clausena indica* root extract by using tyrosinase inhibitory assay and DPPH, ABTS, and lipid peroxidation inhibitory (LPI) assays.[39] Among the isolated active components, the *C. indica* roots, clausine K and fraction Re4, performed the most remarkable tyrosinase inhibition, with IC_{50} values of 179.5 and 243.8 μg/mL, respectively, stronger than the positive control, myricetin (735.6 μg/mL). For the antiradical activities against DPPH and ABTS, nordentatin showed the lowest IC_{50} values of 49.2 ± 0.5 and 69.9 ± 1.1 μg/mL, respectively, among other isolates and comparable to the BHT standard (DPPH: 16.0 ± 0.2 μg/mL; ABTS: 82.8 ± 1.1 μg/mL). Markedly, relatively high IC_{50} values were found in clausine K against DPPH and ABTS, with values of 2197.8 ± 53.3 and 5264.0 ± 164.0 μg/mL, respectively. Similarly, in the LPI assay, nordentatin also showed the highest LPI value with 69.8 ± 0.4%, compared to dentatin (37.9 ± 0.8%) and clausine K (60.6 ± 1.1%). The BHT showed 82.7 ± 0.3% inhibition as standard in the LPI assay.[39]

4.18. *Cosmos caudatus Kunth*. Azwanida et al. reported the antityrosinase and antioxidant activities of *Cosmos caudatus Kunth* leaf extract by using an antityrosinase assay and DPPH and ABTS assays.[40] The extract showed an IC_{50} value of 693.2 μg/mL for tyrosinase inhibition, while the positive control, kojic acid, showed a value of 77.8 μg/mL. In the DPPH and ABTS assays, the extract was reported with IC_{50} values of 163.6 and 57.2 μg/mL, respectively. By contrast, the IC_{50} values of the antioxidant activity for the standard used, Trolox, were 3.32 and 6.51 μg/mL, respectively.[40]

4.19. *Cymbidium* sp. (Orchidaceae). Axiotis et al. studied the antityrosinase, antioxidant, and collagenase inhibitory activities of all the *Cymbidium* sp. byproduct extracts.[41] From the results obtained, the pseudobulbs' ethanol/water extract presented the highest antityrosinase activity among other extracts, showing 64.11 ± 2.34% inhibition at 300 μg/mL. For the ethyl acetate extracts, flowers, pseudobulbs, and roots exhibited a dose-dependent inhibition of 28.29 ± 2.93%, 37.50 ± 2.54%, and 54.19 ± 3.72% at 300 μg/mL, respectively. In the DPPH assay, ethyl acetate extracts of pseudobulbs and roots exhibited moderate antiradical activity with IC_{50} values of 114.18 and 127.17 μg/mL, respectively. However, the dichloromethane (DCM) and ethanol/water extracts of pseudobulbs (IC_{50} = 165.78 and 233.32 μg/mL, respectively) and roots (IC_{50} = 174.61 and 304.02 μg/mL, respectively) showed weak antioxidant activity. Regarding the collagenase inhibitory test, ethyl acetate extracts of pseudobulbs and roots exhibited high inhibitory activity by displaying 4.01 ± 1.32% and 82.79 ± 1.60% inhibition of collagenase at 75 μg/mL.[41]

4.20. *Cytinus hypocistis*. According to Silva et al., the antityrosinase, antioxidant, and anti-inflammatory activities of *Cytinus hypocistis* whole plants, petals, stalks, and nectar extracts were evaluated.[42] The highest tyrosinase inhibitory activity was found in *Cytinus hypocistis* stalk extracts, with an IC_{50} value of 0.09 ± 0.02 mg/mL, followed by a petal extract (0.19 ± 0.01 mg/mL), whole plant extract (0.20 ± 0.01 mg/mL), and nectar extract (27.6 ± 0.7 mg/mL), comparable to the positive control, kojic acid (0.078 ± 0.001 mg/mL). Interestingly, in the oxidative hemolysis inhibition assay and thiobarbituric acid reactive substance assay, petal extract exhibited the highest antioxidant activity among other tested extracts, with the IC_{50} value of 279 ± 5 and 342 ± 2 ng/mL, respectively. In the anti-inflammatory studies, petals and stalk extracts showed similar nitric oxide production inhibitory effects, with IC_{50} values of 127 ± 8 and 127 ± 12 μg/mL, respectively. While the IC_{50} values of the whole plant extract and nectar extract were 136 ± 11 and 277 ± 14 μg/mL, respectively. The positive control in this assay, dexamethasone, was reported with an IC_{50} of 16 ± 1 μg/mL.[42]

4.21. *Dalea pazensis Rusby*. Santi et al. reported the antimelanogenesis and antityrosinase activities of *Dalea pazensis Rusby* root extract by using the melanin content assay of B16 murine melanoma cells and mushroom tyrosinase assay and intracellular tyrosinase inhibition assay in B16 cells.[43] The isolated compound 1 from *Dalea pazensis Rusby* root extracts showed the lowest melanin inhibition IC_{50} of 0.75 ± 0.2 μM, followed by compounds 4 (1.0 ± 0.4 μM), 2 (5.0 ± 1.0 μM), and 3 (5.0 ± 1.8 μM). In the mushroom tyrosinase activity assay, the lowest IC_{50} was reported in compound 4 (2.32 ± 0.06 μM), comparable to kojic acid (4.93 ± 0.01 μM), while the highest IC_{50} was found in compound 3 (49.80 ± 0.09 μM). The IC_{50} values of both compounds 1 and 2 were not determined in this assay. However, in the intracellular tyrosinase inhibitory assay, compounds 1, 2, and 3 were found to have 0% inhibition, while compound 4 was reported with 34.2 ± 0.2% tyrosinase inhibition in B16 cells. The positive control used was kojic acid, with 45.4 ± 0.1% inhibitory activity reported.[43]

4.22. *Dendropanax morbiferus* H. Lev. Park et al. revealed the antimelanogenesis and antityrosinase activities of *Dendropanax morbiferus* H. Lev leaf extracts by using melanin content assay and intracellular tyrosinase activity assay in B16F10 melanoma cells.[8] Water extract of *Dendropanax morbiferus* H. Lev leaves was reported to effectively decrease

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

the melanin content in α-MSH-stimulated B16F10 cells. Furthermore, the extract also remarkably reduced the intracellular tyrosinase activity in α-MSH-stimulated B16F10 cells in a dose-dependent manner.[8]

4.23. *Dimocarpus longan Lour.* (Longan). Based on Chai et al., the antimelanogenesis and antityrosinase activities of longan bark extract were studied by using the melanin content assay, monophenolase and diphenolase activity assay, and intracellular tyrosinase activity assay using B16 mouse melanoma cells.[44] The 200 μg/mL of condensed tannins from longan bark extract reportedly decreased the melanin content of B16 cells to 45.2 ± 1.3%. The IC_{50} values of the condensed tannins reported in the monophenolase activity assay were 43.7 ± 0.3 and 11.5 ± 0.8 μg/mL in the diphenolase activity assay. Besides, 200 μg/mL of condensed tannins significantly reduced the intracellular tyrosinase activity of B16 cells to 40.3 ± 1.5%.[44]

4.24. *Erica arborea* L. Zengin et al. explored the antityrosinase and antioxidant activities of *Erica arborea* L. leaf extracts from different extraction methods.[45] From the mushroom tyrosinase assay, the microwave-assisted extraction (MAE) extract showed the strongest inhibitory activity against the tyrosinase enzyme at 180.29 ± 1.87 mg KAE/g, followed by accelerated solvent extraction (ASE) extract (177.43 ± 2.30 mg KAE/g), Soxhlet (SOE) extract (172.20 ± 1.82 mg KAE/g), maceration (MAC) extract (171.18 ± 3.45 mg KAE/g), and ultrasound-assisted extraction (UAE) extract (171.05 ± 1.14 mg KAE/g). The DPPH scavenging activities of the extracts were in the order of ASE (209.59 ± 4.37 mg TE/g extract) > MAE (179.17 ± 2.93 mg TE/g extract) > MAC (92.19 ± 1.46 mg TE/g extract) > SOE (76.43 ± 0.90 mg TE/g extract) > UAE (66.61 ± 3.41 mg TE/g extract). The same order was also found in the CUPRAC and FRAP assays. A slightly different trend was obtained from the results of the ABTS assay (mg TE/g extract) and phosphomolybdenum (PM) method (mmol TE/g extract), as the extracts were in the order of ASE (ABTS = 359.45 ± 18.22; PM = 148.06 ± 1.96) > MAE (325.87 ± 9.48; PM = 1.66 ± 0.04) > SOE (185.15 ± 6.28; PM = 1.66 ± 0.05) > MAC (176.27 ± 9.25; PM = 1.50 ± 0.05) > UAE (148.06 ± 1.96; PM = 1.26 ± 0.03). In contrast to the other antioxidant assays, the chelating activity of the extracts was in the order of UAE (5.13 ± 0.42 mg EDTAE/g extract) > ASE (4.74 ± 0.30 mg EDTAE/g extract) > MAC (3.80 ± 0.16 mg EDTAE/g extract) > MAE (3.49 ± 0.40 mg EDTAE/g extract) > SOE (1.43 ± 0.01 mg EDTAE/g extract).[45]

4.25. *Fagus sylvatica* L. Tanase et al. reported that the 50:50 ethanol−water extract of *Fagus sylvatica* L. has the strongest antioxidant activity in DPPH (741.43 ± 59.44 mg TE/g extract) and FRAP (783.24 ± 31.24 mg TE/g extract) assays, where this extract was recorded with the highest total phenolic contents.[46] The authors stated that antioxidant activity was also strongly associated with the amount of phenolic compounds. Besides, water extract showed higher antioxidant activities in both DPPH and FRAP assays (DPPH = 676.29 ± 19.80; FRAP = 783.24 ± 31.24 mg TE/g extract), as compared to the 80:20 ethanol−water extract (DPPH = 505.02 ± 42.02; FRAP = 592.84 ± 44.02 mg TE/g extract). On the other hand, the 50:50 ethanol−water extract of *Fagus sylvatica* L. bark was reported with 45.99 ± 5.26% tyrosinase inhibitory activity in mushroom tyrosinase activity assay using L-DOPA as a substrate, while water extract and 80:20 ethanol−water extract did not show any tyrosinase inhibitory activity.[46]

4.26. *Feijoa sellowiana*. The antityrosinase and antioxidant activities of *Feijoa sellowiana* leaf extract were reported by Saber et al.[47] The mushroom tyrosinase inhibition of the methylene chloride extract was 115.85 ± 2.55 mg of KAE/g of extract, while the quercetin (positive control) was 163.05 ± 5.19 mg of KAE/g extract. To evaluate the antioxidant activity of the extract, a total of 6 assays were done, which were DPPH (90.58 ± 0.89 mg TE/g extract), ABTS (113.80 ± 0.02 mg TE/g extract), FRAP (102.58 ± 0.41 mg TE/g extract), CUPRAC (180.23 ± 0.44 mg TE/g extract), metal chelating (21.21 ± 0.88 mg EDTAE/g extract), and PM (5.31 ± 0.13 mg TE/g extract) assays.[47]

4.27. *Galla rhois*. According to Parvez et al., the tyrosinase inhibition IC_{50} of *Galla rhois* methanol extract was reported at 0.163 mg/mL, lower than that for kojic acid (0.316 mg/mL), ascorbic acid (1.520 mg/mL), and arbutin (2.511 mg/mL) in the mushroom tyrosinase activity assay using L-DOPA as a substrate.[48]

4.28. *Garcinia atroviridis*. According to a study done by Chatatikun et al. that investigated the antimelanogenesis properties of various concentrations of water extracts of *Garcinia atroviridis*, the melanin content of α-MSH-stimulated B16F10 cells was decreased in a concentration-dependent manner.[49] At 125 μg/mL (maximum concentration tested) of water extract, it reduced the melanin content to 46.96% which was comparable to that of kojic acid (46.94%). In mushroom tyrosinase activity assay, water extract showed IC_{50} of 40.72 ± 1.83 μg/mL, while kojic acid was 8.00 ± 0.47 μg/mL. Nevertheless, only a concentration of 125 μg/mL of water extract was found to effectively inhibit the cellular tyrosinase activity in B16F10 cells. The DPPH and ABTS radical scavenging activities of water extract were reported with IC_{50} values of 628.85 ± 32.67 μg/mL and 321.41 ± 12.76 μg/mL, respectively, while ascorbic acid was used as the positive control (DPPH = 62.22 ± 0.67; ABTS = 6.27 ± 0.19 μg/mL).[49]

4.29. *Gentiana veitchiorum*. Based on Wu et al., the flower extracts of *Gentiana veitchiorum* reported greatly reduced the melanin content on B16F10 cells, but the root extract did not show any antimelanogenesis effect.[50] Isoorientin was identified from the flower extract, which decreased the melanin content in a dose-dependent manner. Isoorientin was also found to inhibit intracellular tyrosinase activity in a dose-dependent manner but did not have a significant inhibitory effect on mushroom tyrosinase activity. As for antioxidant assay, the flower extracts and isoorientin showed significantly reduced cellular reactive oxygen species (ROS) levels.[50]

4.30. Granny Smith Apple. Menbari et al. reported the antityrosinase activity of Granny Smith culture cell extract in a mushroom tyrosinase activity assay using L-DOPA as a substrate. The IC_{50} of the extract was 1.21 mg/mL, while that for kojic acid was reported to be 0.0177 mg/mL.[51]

4.31. *Hippophae rhamnoides* L. Zhang et al. explored the antimelanogenesis, antityrosinase, and antioxidant activities of *Hippophae rhamnoides* L. seed residues extracted by 80% ethanol.[12] The results showed that the seed residue extract (4.55 and 45.45 mg mL^{-1}) effectively reduced the melanin content in B16F10 mouse melanoma cells. Besides, the seed residue extract (concentration ranging from 0.10 to 3.00 mg mL^{-1}) significantly reduced the tyrosinase activity in B16F10 cells compared to the control, kojic acid. In the DPPH assay, an EC_{50} of 0.09 ± 0.01 mg mL^{-1} was reported in seed residue extract, comparable to the positive standards of ascorbic acid (0.25 ± 0.02 mg mL^{-1}) and Trolox (0.10 ± 0.00 mg mL^{-1}).

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

Nevertheless, the seed residue extract showed little hydroxyl scavenging ability.[12]

4.32. *Juglans mandshurica*. Based on Kim et al., *Juglans mandshurica* fruit methanol extract showed antimelanogenesis effects in B16F10 melanoma cells by significantly reducing the expression of the melanocyte-inducing transcription factor (MITF). The isolated compound 1 showed the strongest antimelanogenesis effects by effectively decreasing the expression of MITF and decreasing melanin content in a dose-dependent manner. On the other hand, compound 1 showed strong tyrosinase inhibition activity by decreasing tyrosinase expression in the tyrosinase activity assay using L-DOPA as a substrate.[52]

4.33. *Kadsura coccinea*. Jeon et al. explored the antioxidant activity of different plant parts of *Kadsura coccinea* extract and showed that leaves had the highest DPPH and ABTS radical scavenging activity (DPPH = 99.9 ± 0.1%; ABTS = 94.7 ± 2.9%) followed by roots (DPPH = 95.5 ± 3.6%; ABTS = 82.8 ± 5.9%), seeds (DPPH = 25.7 ± 2.1%; ABTS = 29.7 ± 2.0%), and flowers (DPPH = 8.7 ± 1.1%; ABTS = 15.9 ± 2.0%).[53] The authors highlighted that the leaves and root extracts had high polyphenol contents. In view of the melanin content assay using α-MSH-stimulated B16F10 murine melanoma cells, the antimelanogenesis activities of the extracts were in the order of leaves > roots > stems > fruits. A similar trend was observed in the antityrosinase assay, and the extracts also followed the order of leaves > roots > stems > fruits in terms of the extracts' antityrosinase properties.[53]

4.34. *Kummerowia striata*. Lee et al. reported the antimelanogenesis, antityrosinase, and antioxidant activities of *Kummerowia striata* aerial parts of ethanol extract. The extract was found to decrease the melanin content in α-MSH-stimulated B16F10 cells in a dose-dependent manner in the melanin content assay.[54] Similar to the mushroom tyrosinase activity assay, the extract also exerted significant tyrosinase inhibitory activity in a dose-dependent manner. The DPPH and ABTS assays revealed that the radical scavenging activities of the extract, IC_{50} values of 98.71 μg/mL and 24.64 μg/mL, respectively, were reported. The beta hydroxyl acid (BHA) was used as the standard control in both antioxidant assays, with the IC_{50} of 14.96 μg/mL (DPPH) and 4.65 μg/mL (ABTS).[54]

4.35. *Leonurus japonicus*. Lai et al. studied the methanol extract of *Leonurus japonicus* aerial parts in a melanin content assay and cellular tyrosinase activity assay using B16F10 murine melanoma cells. Five diterpenes identified from the extracts were reported to inhibit melanin production in α-MSH-stimulated B16F10 cells, while two diterpenes from the extracts had moderate antityrosinase activity.[55]

4.36. *Lepechinia meyenii*. Crespo et al. examined the antityrosinase activity of *Lepechinia meyenii* by subjecting the extracts to bioguided fractionation to isolate three bioactive compounds (*p*-coumaric acid, caffeic acid, and rosmarinic acid).[56] These three compounds were shown to be highly effective in inhibiting tyrosinase activity and to be more powerful than kojic acid. *p*-Coumaric acid had the strongest antityrosinase effects among the three compounds (IC_{50} using L-tyrosine as a substrate: 0.30 μM; IC_{50} using L-DOPA as a substrate: 0.62 μM. Based on previous research, *p*-coumaric acid was shown to have an efficient antimelanogenesis activity and strong free radical scavenging ability. It was also known as an effective tyrosinase inhibitor due to having a similar structure to the tyrosinase substrate and competing for the active sites with the substrate on tyrosinase.[91] The authors concluded that the fractions and isolated compounds, especially *p*-coumaric acid, could be used as a depigmenting agent.

4.37. *Limonium delicatulum*. Bakhouche et al. examined the antityrosinase, antioxidant, and anti-inflammatory activities of *Limonium delicatulum* leaves and root extracts by using methanol and water.[57] The results showed that methanol extract from roots strongly inhibited the enzyme with an IC_{50} value of 9.87 ± 0.15 μg/mL and was more potent than methanol extract from leaves (24.77 ± 0.5 μg/mL) and kojic acid (25.23 ± 0.21 μg/mL). All of the water extracts did not show any effects in the tyrosinase inhibition assay. The DPPH assay was used to measure the scavenging activity of the extracts, and the results showed that methanol root extract (IC_{50} = 5.79 ± 0.05 μg/mL) was the most powerful followed by methanol leaf extract (IC_{50} = 10.58 ± 0.18 μg/mL). Furthermore, methanol leaves and roots extracts of *L. delicatulum* exhibited higher antioxidant activity than BHT (IC_{50} = 16.02 ± 0.35 μg/mL). The aqueous extracts also exerted good antiradical activity, as the IC_{50} values obtained for aqueous roots and leaf extracts were 69.34 ± 0.95 and 79.65 ± 0.23 μg/mL, respectively. In a galvinoxyl radical (GOR) assay, results showed that methanol root extract exhibited a slightly higher antioxidant activity than methanol leaf extract (IC_{50} = 10.31 ± 0.82 and 11.09 ± 0.16 μg/mL, respectively), while methanol extracts from leaves and roots exhibited a close trapping effect on the ABTS radical (IC_{50} = 6.56 ± 0.25 and 7.29 ± 0.04 μg/mL, respectively), which is better than BHT (7.54 ± 0.69 μg/mL) and aqueous roots and leaf extracts (IC_{50} = 29.16 ± 0.16 and 26.01 ± 0.93 μg/mL, respectively). The IC_{50} values of aqueous root and leaf extracts against galvinoxyl radicals were 50.17 ± 2.09 and 84.07 ± 0.44 μg/mL, respectively. In the CUPRAC assay, methanol roots extract presented an $A_{0.5}$ of 6.81 ± 0.07 μg/mL and were stronger than ascorbic acid and Trolox ($A_{0.5}$ = 8.69 ± 0.14 and 8.31 ± 0.15 μg/mL, respectively). Similarly, methanol extract from leaves gave a promising effect to reduce copper ions with an $A_{0.5}$ of 13.5 ± 0.55 μg/mL, while aqueous extracts exhibited the weakest reducing capacity. Methanol leaf extract displayed higher reducing power when compared to methanol roots extract ($A_{0.5}$ = 11.2 ± 0.06 and 20.51 ± 0.3 μg/mL, respectively), whereas aqueous roots extract exhibited a higher effect than leaf extract with $A_{0.5}$ values of 46.54 ± 0.4 and 95.57 ± 2.02 μg/mL, respectively. Methanol leaf extract presented an $A_{0.5}$ of 9.45 ± 0.9 μg/mL and showed a better antioxidant capacity than methanolic roots extract and Trolox (21.66 ± 0.08 and 34.17 ± 1.23 μg/mL, respectively). Besides, in phenanthroline metal iron-reduction analysis, the lowest value of $A_{0.5}$ was obtained with methanol roots extract (3.55 ± 0.02 μg/mL), followed by methanol leaf extract (7.34 ± 0.27 μg/mL), aqueous roots extract (11.82 ± 0.75 μg/mL), and aqueous leaf extract (22.6 ± 1.36 μg/mL), respectively. In silver nanoparticle assay (SNP), methanol leaf extract showed the highest potential to reduce silver ions (Ag^+) than other extracts, with the $A_{0.5}$ of 9.45 ± 0.9 μg/mL which was comparable to the ascorbic acid (7.14 ± 0.05 μg/mL) and Trolox (34.17 ± 1.23 μg/mL). Lastly, methanol leaf extract exhibited slight activity with an IC_{50} value of 98.6 ± 0.32 μg/mL, while aqueous leaf extract showed a very weak effect with an IC_{50} of 293.17 ± 0.14 μg/mL in the β-Carotene-linoleic acid bleaching assay. The anti-inflammatory analysis showed that methanol leaf extract exhibited the highest inhibition activity of 90.21 ± 1.69% at 500 μg/mL, followed by methanol roots extract (89.74 ± 1.63%), aqueous leaf

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

extract (43.32 ± 0.13%), and last aqueous roots extract (38.14 ± 0.81%).[57]

4.38. *Lophira lanceolata* Tiegh. ex Keay. Sinan et al. reported the antityrosinase and antioxidant activities of *lanceolata* leaf and stem bark extracts by using colorimetric enzyme inhibition assay and DPPH, ABTS, CUPRAC, FRAP, and ferrous-ion chelating assays.[58] The antityrosinase effects were exhibited for the methanol leaf extracts, with the highest activity reported for extract obtained using the Soxhlet extraction method (131.17 ± 1.96 mg KAE/g), followed by HAE-MeOH (126.03 ± 3.57 mg KAE/g) and MAC-MeOH (122.21 ± 2.79 mg KAE/g). No inhibitory activity against tyrosinase was displayed by the HAE-Water and MAC-Water extracts. All stem bark extracts showed significant inhibitory potency against tyrosinase in the following order: MAC-MeOH (153.21 ± 0.15 mg KAE/g) > SOX-MeOH (151.98 ± 0.66 mg KAE/g) > HAE-MeOH (151.65 ± 0.25 mg KAE/g) > infusion (100.95 ± 2.37 mg KAE/g) > MAC-water (100.46 ± 2.27 mg KAE/g) > HAE-Water (94.58 ± 1.87 mg KAE/g).[58] For the leaf extracts, the highest free scavenging activity was observed in the HAE-MeOH (DPPH = 93.82 ± 0.23; ABTS = 132.25 ± 0.09 mg TE/g), followed by infused (DPPH = 93.81 ± 0.43 mg TE/g) and SOX-MeOH (ABTS = 132.09 ± 0.07 mg TE/g) extracts (58). The HAE-MeOH extract has shown the highest cupric and ferric reducing power, with values of 287.73 ± 21.98 and 231.21 ± 0.57 mg TE/g, respectively. Among the stem bark extracts, the highest free radical quenching activity was exhibited by the SOX-MeOH (DPPH = 195.18 ± 0.55; ABTS = 265.04 ± 0.99 mg TE/g), followed by HAE-MeOH (DPPH: 194.83 ± 0.21; ABTS = 264.43 ± 0.13 mg TE/g) extracts. Furthermore, reducing capacity was exhibited by all the tested stem bark extracts, with the aqueous extracts obtained using maceration (CUPRAC= 853.99 ± 13.27; FRAP= 853.99 ± 13.27 mg TE/g) and homogenizer assisted (CUPRAC = 683.57 ± 11.09; FRAP = 648.34 ± 3.86 mg TE/g) methods being superior sources of reducing agents in both CUPRAC and FRAP assay. With respect to metal chelating properties, the activity varied between 6.76 ± 1.76 (HAE-Water) and 22.68 ± 0.74 (HAE-MeOH) mg EDTAE/g and 2.09 ± 0.45 (MAC-MeOH) and 6.15 ± 1.12 mg EDTAE/g for the leaf and stem bark extracts, respectively.[58]

4.39. Lotus. The lotus seedpod was extracted with hot water (95 °C) with concentrations of 0, 5, 10, 15, and 20 μg/mL, and the antimelanogenesis and antityrosinase activities were studied by Hsu et al.. The concentrations of 10, 15, and 20 μg/mL of the seedpod extract of lotus greatly reduced the melanin production in α-MSH-stimulated B16F10 cells, showing the promising antimelanogenesis properties of the extracts. Similarly, the concentrations of 10, 15, and 20 μg/mL of the seedpod extract of lotus significantly decreased the 65%, 76%, and 112% of tyrosinase activity in α-MSH-stimulated B16F10 cells.[59]

4.40. *Maclura tricuspidate*. Jo et al. examined the antityrosinase and antioxidant activities of the leaf extract of *Maclura tricuspidate* by using the mushroom tyrosinase activity assay and DPPH assay. Results showed that the two identified flavanols named kaempferol and quercetin had the most potent activity for tyrosinase inhibition and also exhibited good antioxidant activity.[60]

4.41. *Manilkara kauki*. Based on Srisupap and Chaicharoenpong, the methanol extract of *Manilkara kauki* stem barks showed the lowest IC_{50} value of tyrosinase inhibition, 0.25 ± 0.03 mg/mL, followed by water extract of *Manilkara kauki* stem barks, 0.41 ± 0.01 mg/mL.[15] Overall, methanol extracts showed a lower IC_{50} of tyrosinase inhibition compared with the water extracts. The same tyrosinase inhibitory trend was found in both extraction methods, which followed the order of stem barks > leaves > fruits > seeds, while woods showed no inhibitory activity at all. In the DPPH assay, methanol extract of stem barks showed the highest radical scavenging activity of 57.87 ± 0.27%, followed by water extract of leaves (55.49 ± 0.06%), methanol extract of leaves (47.01 ± 0.14%), and methanol extract of woods (43.51 ± 0.27%) (15). On the other hand, the methanol extract of stem barks also exhibited the strongest FRAP activity with 211.59 ± 1.40 mg TE g^{-1} crude extract, followed by water extract of leaves, with 219.37 ± 0.32 mg TE g^{-1} crude extract.[15]

4.42. *Melaleuca quinquenervia*. Chao et al. revealed that the 20 μg/mL of *Melaleuca quinquenervia* essential oil exhibited a 40.7% melanin inhibitory effect, stronger than the positive control, arbutin (16.1% at 100 μM), in the melanin content assay using B16 murine melanoma cells.[1] Furthermore, the 20 μg/mL of essential oil had a 20.4% tyrosinase inhibitory effect, which is stronger than arbutin (5.5% at 100 μM).[1]

4.43. *Melastoma normale*. Quercetin, one of the compounds that was isolated from *Melastoma normale* roots' 80% acetone extract, showed significant antityrosinase activity with IC_{50} of 76.83 ± 2.02 μM, while kojic acid has an IC_{50} of 100.52 ± 2.63 μM, reported by He et al.[61]

4.44. *Morus alba* L. Li et al. were the first to report the antimelanogenesis and antityrosinase activity of *Morus alba* L. leaf extract. The three compounds isolated from ethanol extracts named, norartocarpetin, moracin J and steppogenin decreased melanin production which exhibited antimelanogenesis effects in α-MSH-stimulated B16F10 cells.[5] The antityrosinase activity of *Morus alba* L. leaf extract was shown in norartocarpetin, moracin J and steppogenin significantly inhibited mushroom tyrosinase activity and intracellular tyrosinase activity in a dose-dependent manner in B16F10 cells.[5] Another study by Chaiyana et al. explored the antityrosinase and antioxidant activities of the maceration method and pulsed electric field (PEF) extraction method of *Morus alba* L. leaves obtained from Chiang Mai (CM), Sakon Nakon (SK), Buriram (BR), Thailand. Results showed that PEF extracts exhibited significant inhibitory effects compared to the maceration method, while PEF extract from BR demonstrated the highest antityrosinase activity, with IC_{50} against L-tyrosine and L-DOPA of 54.1 ± 5.4 and 32.2 ± 3.4 μg/mL, respectively. These results were comparable to kojic acid (IC_{50} = 28.0 ± 5.1 μg/mL with L-DOPA as substrate), the positive control. Expectedly, extracts obtained by the PEF method had higher radical scavenging activity than the maceration method, and leaves from BR had a significantly high FRAP value. To be specific, PEF extract from BR had DPPH inhibition of 45.3 ± 0.8%, TEAC value of 115.1 ± 2.8 mg Trolox/g extract (ABTS assay), and EC_1 value of 52.4 ± 0.5 mg $FeSO_4$/g extract (FRAB assay).[62]

4.45. *Myrica rubra*. Juang et al. examined the antimelanogenesis and antityrosinase properties of *Myrica rubra* fruit extract with different solvent extraction.[6] Results published suggested that pure water extract has stronger melanogenesis inhibitory effects than 50% ethyl alcohol and 95% ethyl alcohol extracts, as 2.0 g L^{-1} of pure water extract reduced the melanin content to 76.5% and 82.5% in A2058 and B16F10 mouse melanoma cells, respectively. Interestingly, pure water extract

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

also has stronger tyrosinase inhibitory effects than 50% ethyl alcohol and 95% ethyl alcohol extracts. The 2.0 g L^{-1} of pure water extract successfully reduced the mushroom tyrosinase activity to 61.7% and reduced the cellular tyrosinase activity to 65.78% and 74.9% in A2058 and B16F10 cells, respectively.[6]

4.46. *Nardostachys jatamansi*. Bose et al. found that methanol rootstock extracts of *in vitro*-cultured *Nardostachys jatamansi* plants have the highest antityrosinase activity with IC_{50} of 168.12 ± 3.6 μg/mL, which is comparable to kojic acid 54.44 ± 2.3 μg/mL.[63] The antioxidant potential of methanol rootstock extracts of *in vitro*-cultured plants was demonstrated in ABTS and PM assays, as well as the lipid peroxidation (LPO) inhibition method. The IC_{50} of methanol rootstock extracts was 13.55 ± 0.8 μg/mL in the ABTS assay and 789 ± 8.7 μg ascorbic acid equivalents/g extract in the PM assay. While the result obtained from the LPO inhibition method was 15.24 ± 0.8 μg/mL for the methanol rootstock extracts of *in vitro*-cultured plants and 3.82 ± 0.5 μg/mL reference value of rutin. Lastly, the methanol rootstock extracts of *in vitro*-cultured plants showed 14.58 ± 0.9 μg/mL anti-inflammatory activity, which was stronger than the methanol leaf extracts of in vitro-cultured plants with IC_{50} of 23.54 ± 1.6 μg/mL.[63]

4.47. *Nepeta glomerulosa* Boiss. Emami et al. evaluated the antimelanogenesis inhibitory activity of methanol (MeOH), *n*-hexane, ethyl acetate (EtOAc), dichloromethane (CH_2Cl_2), *n*-butanol (BuOH), and water extracts isolated from *N. glomerulosa* in B16 melanoma cell line.[3] From the results obtained, a 100 μg/mL concentration of MeOH, EtOAc and n-BuOH extracts showed significant inhibitory effects on melanin synthesis. However, mushroom tyrosinase activity was inhibited only by 100 μg/mL of EtOAc extract, while 100 μg/mL of methanol extract significantly inhibited cellular tyrosinase activity in B16F10 cells. Only MeOH and *n*-BuOH extracts greatly suppressed the oxidative stress caused by hydrogen peroxide in the B16F10 melanoma cells.[3]

4.48. *Olea europeae*. Elkattan et al. explored the anti-melanogenesis activity of *Olea europeae* leaf extract, and three compounds named oleuroepin, oleoside dimethyl ester, and oleoside 11-methyl ester presented good inhibition of melanogenesis in B16 melanoma cells.[64] In particular, the melanin content of oleuropein at 12.5, 25, and 50 μM was 63.8 ± 3.3%, 46.4 ± 3.3%, and 33.9 ± 15.4%, respectively, while those of oleoside dimethyl ester were 33.9 ± 4.0% (12.5 μM), 28.1 ± 0.7% (25 μM), and 5.3 ± 3.8% (50 μM). Those of oleoside 11-methyl ester were 25.8 ± 8.1% (12.5 μM), 22.3 ± 14.0% (25 μM), and 16.0 ± 10.2% (50 μM).[64] For reference, the melanin content of arbutin at 20 μM was 91.3 ± 2.6%.[64]

4.49. *Pelargonium graveolens*. Aanachi et al. explored the antityrosinase activity of *Pelargonium graveolens* using *n*-hexane, dichloromethane, and methanol as solvent extraction.[65] The result demonstrated that methanol extract exhibited the strongest antityrosinase activity among the 3 extracts with IC_{50} of 21.11 ± 0.38 μg/mL. The tyrosinase inhibition IC_{50} of *n*-hexane was 37.60 ± 1.83 μg/mL, while dichloromethane was 37.63 ± 1.35 μg/mL. For reference, kojic acid was reported with an IC_{50} value of 25.23 ± 0.78 μg/mL in the tyrosinase inhibition assay. The antioxidant capacity of the extracts of *P. graveolens* was evaluated, and the methanol extract was reported to be the strongest in all five assays including the DPPH (IC_{50} of 12.96 ± 0.63 μg/mL), ABTS (IC_{50} of 10.20 ± 0.63 μg/mL), CUPRAC ($A_{0.5}$ of 20.29 ± 0.51 μg/mL), iron chelation (IC_{50} of 31.74 ± 3.21 μg/mL), and reducing power ($A_{0.5}$ of 43.38 ± 0.65 μg/mL). In contrast, the antioxidant activity of dichloromethane extract was moderate, with IC_{50} values of 116.91 ± 6.50 μg/mL (DPPH), 10.46 ± 1.33 μg/mL (ABTS), and 66.72 ± 2.96 μg/mL (iron chelation) and $A_{0.5}$ values of 53.36 ± 0.88 and 64.60 ± 0.15 μg/mL for CUPRAC and reducing power, respectively. Generally, the lowest capacity was observed with the hexane extract, with the IC_{50} of 37.60 ± 1.83, 44.46 ± 2.30, and 47.20 ± 2.85 μg/mL for the DPPH, ABTS, and iron chelation assays and $A_{0.5}$ of 89.95 ± 3.00 and 77.29 ± 0.87 μg/mL in CUPRAC and reducing power.[65]

4.50. *Persicaria orientalis*. Based on Masum et al., vanicoside B isolated from ethanolic extracts of *Persicaria orientalis* roots exhibited a significant high extracellular (71.9% and 72.0%) and intracellular (35.3 and 27.3%) melanin inhibitory activity at 50 and 25 μM, respectively, in the B16 mouse melanoma cells.[66] It showed better inhibitory activity than the positive control, arbutin (58% at 730 μM).[66] Furthermore, the ethanolic extract also demonstrated the highest tyrosinase inhibition with IC_{50} of 22 μg/mL (L-tyrosine) and 39 μg/mL (L-DOPA), compared to the ethyl acetate extract (L-tyrosine = 80 μg/mL; L-DOPA = 311 μg/mL) and *n*-hexane (L-tyrosine = >1000 μg/mL; L-DOPA = >1000 μg/mL).[66] The kojic acid was used as the positive control in the mushroom tyrosinase assay, with the IC_{50} of 2 μg/mL (L-tyrosine) and 26 μg/mL (L-DOPA assay) reported.[66]

4.51. *Photinia* × *fraseri*. Song et al. reported that crude proanthocyanidin (PA) extract of *Photinia* × *fraseri* leaves demonstrated better inhibition of tyrosinase diphenolase activity than monophenolase activity in the mushroom tyrosinase activity assay.[67]

4.52. *Phyllanthus phillyreifolius*. Mahomoodally et al. revealed that the macerated ethyl acetate extract of the aerial parts of *P. phillyreifolius* exhibited the highest tyrosinase inhibitory properties with 88.93 ± 0.53 mg KAE/g followed by macerated methanolic extract (88.46 ± 1.35 mg KAE/g), Soxhlet methanolic extract (87.19 ± 0.28 mg KAE/g), Soxhlet ethyl acetate extract (78.79 ± 1.52 mg KAE/g), and decoction extract (66.29 ± 1.51 mg KAE/g).[68] Besides, the macerated methanol extract of *P. phillyreifolius* possessed the highest DPPH and ABTS scavenging properties (2.91 ± 0.01 and 4.12 ± 0.09 mmol TE/g, respectively), while the decoction extract was also equally effective in scavenging the ABTS radical (4.11 ± 0.02 mmol TE/g). The decoction extract was the weakest DPPH scavenger (1.91 ± 0.13 mmol TE/g) (68). In the CUPRA assay, Soxhlet methanolic extract showed the highest activity at 5.04 ± 0.17 mmol TE/g, followed by macerated methanol extract (4.96 ± 0.12 mmol TE/g), decoction extract (4.80 ± 0.07 mmol TE/g), macerated ethyl acetate extract (4.78 ± 0.33 mmol TE/g), and last the Soxhlet ethyl acetate extract (3.75 ± 0.03 mmol TE/g). A similar trend was reported in the metal chelating assay, with the order of Soxhlet methanolic extract > macerated methanol extract > decoction extract > Soxhlet ethyl acetate extract > macerated ethyl acetate extract. Similarly, the Soxhlet methanolic extract also exhibited the highest FRAP activity at 3.17 ± 0.15 mmol TE/g, followed by decoction extract (3.01 ± 0.12 mmol TE/g), macerated methanol extract (2.92 ± 0.36 mmol TE/g), macerated ethyl acetate extract (2.31 ± 0.11 mmol TE/g), and Soxhlet ethyl acetate extract (2.02 ± 0.10 mmol TE/g).[68]

4.53. *Phyllostachys nigravar Henosis*. Choi et al. discovered that the 80% ethanol extracts from the *P. nigravar* bamboo stem decreased the melanin contents in α-MSH-stimulated B16F10 cells in a dose-dependent manner.[13] The

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

tyrosinase inhibitory potential of the 80% ethanol extracts was moderate, with an IC_{50} of 243.7 μg/mL, compared to the ascorbic acid of 38.5 μg/mL.[13] Furthermore, the highest DPPH and ABTS scavenging effects were found in the 80% ethanol extracts, with the IC_{50} of 565.63 ± 17.75 and 414.61 ± 35.12 μg/mL, respectively, followed by the 50% ethanol extracts (DPPH: 714.35 ± 39.54; ABTS: 463.81 ± 13.93 μg/mL). The 100% ethanol extracts showed the least DPPH activity, with an IC_{50} of 2019.67 ± 69.40 μg/mL, while boiling water extracts showed the least ABTS scavenging effects (2258.18 ± 125.06 μg/mL). In the hydroxyl radical assay, similar results were reported in 50% and 80% ethanol extracts, with an IC_{50} of 560.19 ± 21.85 and 509.17 ± 33.76 μg/mL, respectively.[13] Generally, the antioxidant activity of the extracts followed the order of 80% ethanol extracts > 50% ethanol extracts > 100% ethanol extracts > water > boiling water.

4.54. *Pistacia atlantica* Subsp. *Mutica*. Eghbali-Feriz et al. discovered the *P. atlantica* MeOH, CH_2Cl_2, and EtOAc extracts (0.2 to 200 μg/mL), and *n*-hexane (2 to 200 μg/mL) and H_2O extract (20 and 200 μg/mL) showed significant inhibitory effect on melanogenesis; however, essential oil and BuOH had no significant inhibitory effect on melanogenesis.[11] Besides, all extracts of the *P. atlantica* were reported to inhibit mushroom tyrosinase activity except for 1000 μg/mL of *n*-hexane extract. In cellular tyrosinase activity assay, MeOH, EtOAc, and BuOH extracts (0.2−200 μg/mL), *n*-hexane (0.2 μg/mL), and CH_2Cl_2 (20 and 200 μg/mL) were found to effectively inhibit B16F10 cells' tyrosinase activity except for H_2O extract. Lastly, all extracts except 0.2 μg/mL of CH_2Cl_2 extract were able to significantly suppress the oxidative stress caused by hydrogen peroxide.[11]

4.55. *Pistacia lentiscus L.* Elloumi et al. examined the antityrosinase potential of PDL leaf extract in both mushroom tyrosinase activity assay and cellular tyrosinase activity assay in B16 cells.[69] The ethyl acetate (EAE) extract exhibited a great cellular tyrosinase activity with IC_{50} of 27.85 ± 1.75 μg/mL, compared to the kojic acid with IC_{50} of 142.09 ± 2.72 μg/mL. However, the EAE extract only showed moderate mushroom tyrosinase activity with IC_{50} of 123 μg/mL, compared to the kojic acid (20 μg/mL). Besides, the EAE extract exhibited the strongest antioxidant activity among the 3 extracts with IC_{50} of 18.07 μg/mL in the DPPH assay and 522.7 6 ± 22.99 mg AEAC/g extract in the FRAP assay. Methanolic extract and aqueous extract showed similar antioxidant activity with IC_{50} of 19.62 and 19.52 μg/mL in the DPPH assay, respectively, while 467.29 ± 21.77 and 421.91 ± 15.48 mg AEAC/g extract were in the FRAP assay, respectively. The reference value from ascorbic acid in the DPPH assay was 13.85 μg/mL. The antielastase potential of EAE extract was reported with IC_{50} of 19 μg/mL, which is comparable to the epigallocatechin gallate of 12 μg/mL.[69]

4.56. *Polygonum maritimum* L. Rodrigues et al. reported that an acetone extract of *P. maritimum* L. was able to effectively reduce nitric acid production on LPS-stimulated RAW 264. Seven macrophages with IC_{50} of 22.0 μg/mL were compared to positive control (27.6 μg/mL).[70] The antioxidant activity of acetone extract was evaluated by determining radical scavenging activity on superoxide radicals, ferric thiocyanate, and thiobarbituric acid tests and total antioxidant capacity; results obtained were presented with IC_{50} values of 40.4 μg/mL, 784 μg/mL, and 647 μg/mL, respectively. Nevertheless, the acetone extract tyrosinase inhibitory effect was reported with an IC_{50} of 64.1 μg/mL, much lower than the positive control, arbutin, with 137 μg/mL.[70]

4.57. *Potentilla anserina* L. Based on Yang et al., in the tyrosinase inhibitory assay, the most active fraction from *P. anserina* extract was the butyl alcohol fraction [IC_{50} = 45.22 μg/mL (L-tyrosine), IC_{50} = 15.47 μg/mL (L-DOPA)], which was followed by the ethyl acetate fraction, the total extract, and the aqueous fraction with IC50 from 81.40 to 250.95 μg/mL (L-tyrosine) and IC_{50} from 33.37 to 128.56 μg/mL (L-DOPA), respectively.[71] With regard to the DPPH and ABTS assays, the most active fraction was the ethyl acetate fraction [IC_{50} = 0.11 μg/mL (for DPPH), IC_{50} = 0.42 μg/mL (for ABTS)] followed by the butyl alcohol fraction [IC_{50} = 1.16 μg/mL (for DPPH), IC_{50} = 4.58 μg/mL (for ABTS)], total extract [IC_{50} = 7.27 μg/mL (for DPPH), IC_{50} = 25.91 μg/mL (for ABTS)] and aqueous fraction [IC_{50} = 16.33 μg/mL (for DPPH), IC_{50} = 60.71 μg/mL (for ABTS)]. Notably, the ethyl acetate fraction is presented with the highest FRAP value.[71]

4.58. *Potentilla paradoxa* Nutt. Lee et al. revealed that the melanin content of α-MSH-stimulated B16F10 cells was suppressed dose dependently by 95% ethanol extract of *P. paradoxa*.[72] With regard to the antioxidant assays, the 95% ethanol extract showed DPPH and ABTS radical scavenging ability as well as ferric reducing antioxidative capacity in a dose-dependent manner. In the CUPRAC assay, copper ions were reduced by 95% ethanol extract in a dose-dependent manner.[72]

4.59. *Prasiola japonica*. According to Park et al., loliolide, a monoterpenoid hydroxylactone from *P. japonica*, was found to remarkably reduce the melanin content and secretion in α-MSH-stimulated B16F10 cells. In the ABTS antioxidant assay, the IC_{50} value of loliolide was 61.52 ± 2.12 μM.[73]

4.60. *Pterocarpus marsupium*. Deguchi et al. studied the antimelanogenesis, antityrosinase, and antioxidant properties of *Pterocarpus marsupium* heartwood extract by using B16 cells, mushroom tyrosinase activity assay, and DPPH assay.[74] In the melanin content assay, the concentrations of 5, 10, 20, and 50 μg/mL of extracts presented 24%, 45%, 53%, and 69% inhibition of melanogenesis in B16 cells, respectively, while in the mushroom tyrosinase activity assay, the concentrations of 12.5, 50, and 200 μg/mL of extracts exerted 23%, 53%, and 71% mushroom tyrosinase activity, respectively. The concentration of 10, 20, and 50 μg/mL of extracts demonstrated 16%, 33%, and 73% DPPH radical-scavenging activity, which were comparable to 10, 20, and 50 μg/mL of ascorbic acid of 15%, 31%, and 84% DPPH radical-scavenging activity.[74]

4.61. Red maple (*Acer rubrum*). Ma et al. reported that the antimelanogenesis activity of Ginnalin A from red maple leaves at 25 and 50 μM effectively reduced the melanin content in B16F10 cells to 79.1% and 56.7%, respectively.[75] Ginnalin A also exhibited the strongest tyrosinase inhibitory effect in the mushroom tyrosinase activity assay, with an IC_{50} of 101.4 ± 6.5 μM, followed by Maplexin J (173.8 μM) and Maplexin F (208.9 ± 3.1 μM). However, Ginnalin B and Ginnalin C showed poor tyrosinase inhibition with IC_{50} > 500 μM reported. For reference, the tyrosinase inhibition IC_{50} of kojic acid was 23.7 ± 0.9 μM, while arbutin was 61.6 ± 2.8 μM. Lastly, 50 μM of Ginnalin A was reported to reduce ROS levels to 55.1% in B16F10 cells.[75]

4.62. *Rosa chinensis cv. "JinBian"*. Li et al. investigated the antioxidant activity of *Rosa chinensis cv. "JinBian"* with different types of solvent extraction including 95% ethanol, 65% ethanol, and petroleum ether. The results presented that

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

95% ethanol has the highest DPPH free radical scavenging ability of 94.36 ± 0.12%, followed by 65% ethanol (94.11 ± 0%), both comparable to the standard Trolox with 95.12 ± 0.29% DPPH activity. Besides, 95% ethanol also exhibited the highest tyrosinase inhibitory activity of 66.95 ± 0.27%, while α-arbutin was only reported to be 22.15 ± 0.42%. Nonetheless, petroleum ether showed limited antioxidant and antityrosinase activities, with 17.25 ± 1.45% DPPH activity and 6.27 ± 0.68% tyrosinase inhibition reported.[76]

4.63. *Rubus caesius* L. Grochowski et al. examined the antityrosinase and antioxidant activities of *Rubus caesius* L. leaf extract with various solvent extraction methods and partitioned.[77] The tyrosinase inhibitory effect of all extracts was arrange in the order of *n*-BuOH (RC6) > pure MeOH (RC3) > 50% MeOH (RC2) > water (RC1) > EtOAc (RC5) > diethyl ether (RC4), with the values of 63.12 ± 0.26, 61.83 ± 0.26, 61.82 ± 1.43, 60.59 ± 0.37, 56.92 ± 0.70, and 55.32 ± 0.67 mg KAE/g extract, respectively. In view of the DPPH and ABTS radical scavenging properties, RC4, RC5, and RC6 exhibited similar scavenging activity which was more powerful than the other extracts, with the values of 1.58 ± 0.01, 1.58 ± 0.01, and 1.55 ± 0.02 mmol TE/g extract (DPPH) and 2.45 ± 0.03, 2.92 ± 0.03, and 2.02 ± 0.03 mmol TE/g extract (ABTS), respectively. The RC5 showed the highest CUPRAC at 4.98 ± 0.05 mmol TE/g extract, followed by RC4 (3.49 ± 0.02 mmol TE/g), RC6 (2.82 ± 0.18 mmol TE/g), RC2 (1.63 ± 0.02 mmol TE/g), RC3 (1.60 ± 0.05 mmol TE/g), and RC1(0.34 ± 0.01 mmol TE/g). The same trend was reported in the FRAP assay, as RC5 (2.78 ± 0.1305 mmol TE/g) > RC4 (2.15 ± 0.08 mmol TE/g) > RC6 (1.71 ± 0.21 mmol TE/g) > RC2 (1.05 ± 0.03 mmol TE/g) > RC3 (0.92 ± 0.04 mmol TE/g) > RC1(0.22 ± 0.01 mmol TE/g). In the phosphomolybdenum (PM) assay, RC5 (3.92 ± 0.34 mmol TE/g) was the highest, followed by RC6 (3.10 ± 0.26 mmol TE/g) and RC4 (2.58 ± 0.11 mmol TE/g), while RC1 showed the least effect at 0.59 ± 0.02 mmol TE/g. Notably, RC2 showed the strongest metal chelating effects with 16.62 ± 1.71 mg EDTAE/g, followed by RC3 (14.67 ± 1.13 mg EDTAE/g) and RC6 (12.94 ± 0.87 mg EDTAE/g).[77]

4.64. *Scabiosa columbaria*. Otang-Mbeng and Sagbo explored the antimelanogenesis property of *Scabiosa columbaria* leaf extract in melanin content assay using B16F10 melanoma cells.[78] Results showed that the extracts inhibited melanogenesis in α-MSH-stimulated B16F10 cells with increasing concentrations, and the cellular melanin content was decreased to around 40% at 100 μg/mL of extract concentration. The antityrosinase activity of the extracts was also reported in a dose-dependent manner. In the antioxidant assay, the extracts displayed a more significant FRAP activity than Trolox, especially at 200 μg/mL.[78]

4.65. *Schinus terebinthifolius*. Sassi et al. reported that *Schinus terebinthifolius* leaf extracts by using methanol showed 100 ± 0.0% of tyrosinase inhibitory effect, while acetone and hexane extracts showed 92.10 ± 1.81 and 73.68 ± 1.56% inhibition, respectively. All of the leaf extract was found to be comparable to the positive control, kojic acid, with 86.7 ± 1.75% inhibition reported. Interestingly, acetone fruit extract showed the highest tyrosinase inhibition (78.94 ± 1.2%) among other fruit extracts, as methanol fruit extract was found with 63.15 ± 1.43% and oil extracts with only 5.26 ± 0.6% tyrosinase inhibition. The DPPH and ABTS assays revealed that oil extract of *Schinus terebinthifolius* fruit has the highest radical scavenging activity, with an IC_{50} value of 0.016 and 0.017 mg/mL, respectively, stronger than the Trolox (DPPH = 0.136 mg/mL; ABTS = 0.145 mg/mL). Other than that, both leaf and fruit methanol extract also exhibited promising radical scavenging activity, with IC_{50} values of 0.53 and 0.41 mg/mL in the DPPH assay, as well as 0.76 and 0.61 mg/mL in the ABTS assay.[79]

4.66. *Schisandra chinensis* (*Turcz.*) *Baillon*. According to Lee et al., the melanin inhibitory values (IC_{50}) of *Schisandra chinensis (Turcz.) Baillon* dried fruit extracts with *n*-hexane were the strongest (11.58 μg/mL), followed by CH_2Cl_2 (27.89 μg/mL) and 95% ethanol (98.37 μg/mL), while IC_{50} values for EtOAc, *n*-BuOH, and water extracts were all higher than 100 μg/mL.[2]

4.67. *Scorzonera tomentosa* L. Dall'Acqua et al. examined the tyrosinase inhibitory potential and antioxidant properties of the extracts of *Scorzonera tomentosa* L. aerial parts and roots by using different solvents.[80] Remarkable tyrosinase activities were reported in all extracts of both plant parts, with methanolic extracts (aerial parts = 64.83 ± 0.28; roots = 65.46 ± 0.31 mg KAE/g) being the most potent, while water extracts (aerial parts = 16.40 ± 1.30; roots = 6.29 ± 0.50 mg KAE/g) were the least effective. Dichloromethane, ethyl acetate, and hexane extracts showed moderate tyrosinase inhibition activities with values from 57.54 ± 0.12 to 63.32 ± 0.22 mg of KAE/g (aerial parts) and values from 59.99 ± 0.19 to 63.54 ± 0.56 mg of KAE/g (roots), respectively. From the DPPH and ABTS assays, methanolic and aqueous extracts of both plant parts showed good free radical scavenging ability, while no activity was displayed by the hexane aerial part extract in the DPPH assay. For the CUPRAC assay, methanolic extracts of both plant parts showed the highest activity (aerial parts: 164.06 ± 1.26 and roots: 93.18 ± 1.58 mgTE/g), while for the FRAP assay, methanolic extracts of roots (79.78 ± 0.27 mgTE/g) and aqueous extracts (41.36 ± 0.10 mgTE/g) of aerial parts were excellent sources of reducing agents. The metal chelating activity for the tested extracts of aerial parts ranged from 2.13 ± 0.10 mg (aqueous) to 13.92 ± 0.86 mg (dichloromethane) EDTAE/g, while extracts of roots reported a metal chelating activity ranging from 0.53 ± 0.07 mg (methanol) to 6.24 ± 0.17 mg (dichloromethane) EDTAE/g. Aqueous and hexane root extracts showed no metal chelating activity.[80] Lastly, moderate activity was reported for all plant part extracts in the PM assay.[80]

4.68. *Sorghum bicolor*. Han et al. evaluated the antimelanogenesis activity of various concentrations of ethanol extracts of *Sorghum bicolor*, and 60% ethanol extract significantly decreased the melanin contents from 316.85% to 108.60%, which was comparable to that for kojic acid (101.79%).[81] The 60% ethanol extract has been found to have the highest total phenolic content compared with other concentrations of ethanol extracts. The above two findings revealed that the total phenolic and flavonoid contents were positively correlated with free radical scavenging ability and tyrosinase inhibition, which contributed to their strong antimelanogenesis properties. Besides, the tyrosinase inhibition IC_{50} of 60% ethanol extract was 89.25 μg/mL (L-tyrosine), comparable to the arbutin of 74.35 μg/mL; however, no results were reported for L-DOPA.[81] With regard to the DPPH and ABTS assays, the IC_{50} values of 60% ethanol extract were 612.53 and 409.71 μg/mL, respectively. In the MDA assay, the 60% ethanol extract was reported with an IC_{50} value of 16.56 μg/mL.[81]

4.69. *Stenocarpus sinuatus*. According to Younis et al., the tyrosinase inhibitory effect (IC_{50}) of hexane soluble

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

fraction from *Stenocarpus sinuatus* leaf extract was 67.5 μg/mL, while 13.8 μg/mL was reported in kojic acid.[82]

4.70. *Tricholosporum goniospermum*. Angelini et al. examined the antityrosinase and antioxidant activities of *n*-hexane, ethyl acetate, and methanol extracts from fruiting bodies and liquid-cultured mycelia of *T. goniospermum*.[83] From the results obtained, the ethyl acetate extracts displayed the most effective tyrosinase inhibition with fruiting body extracts of 554.30 ± 9.41 mg KAE/g and mycelia extracts of 412.81 ± 1.39 mg KAE/g. Besides, *n*-hexane extracts showed a better tyrosinase inhibition than methanol, with 83.80 ± 1.45 and 48.48 ± 0.07 mg KAE/g (fruiting bodies extracts) and 127.76 ± 0.73 and 28.17 ± 0.39 mg KAE/g (mycelia extracts), respectively. The results from the colorimetric enzyme inhibition assay were consistent with the antioxidant assays, as ethyl acetate extracts exhibited the strongest antioxidant capacity [DPPH = 88.82 ± 1.47 (fruiting bodies) and 29.93 ± 3.54 (mycelia) mg TE/g; CUPRAC = 307.71 ± 3.83 (fruiting bodies) and 155.31 ± 1.85 (mycelia) mg TE/g; FRAP = 134.06 ± 1.50 (fruiting bodies) and 74.26 ± 1.79 (mycelia) mg TE/g], followed by methanol and *n*-hexane extracts. In general, fruiting body extracts displayed better antioxidant activity than mycelia extract, while methanol extracts showed stronger antioxidant capacity than *n*-hexane extracts, except for the mycelia extracts in FRAP assay (methanol = 12.94 ± 1.33; *n*-hexane = 15.15 ± 1.62 mg TE/g).[83]

4.71. *Vigna subterranea* (Bambara Groundnut (BG)). Chutoprapat et al. reported that hull extracts of *Vigna subterranea* obtained by maceration extraction presented the highest antimelanogenesis activity with an inhibition rate of 72.90 ± 0.08%, compared to hull extracts obtained by Soxhlet extraction and boiling and seed extracts obtained by maceration extraction, Soxhlet extraction, and boiling.[84] It was also superior to kojic acid, with an inhibition rate of only 45.35 ± 0.28%. Further, it also has good antityrosinase and antioxidant activities that contribute to its high antimelanogenesis activity. To be specific, the hull extracts prepared by Soxhlet exhibited the most effective tyrosinase inhibition (0.07 ± 0.07 mg/mL), followed by hull extracts prepared by maceration (0.45 ± 0.23 mg/mL), comparable to the positive control, kojic acid, of 0.05 ± 0.03 mg/mL. Hull extracts prepared by maceration also displayed the strongest DPPH scavenging activity and the highest capacity in the modified Ferric-thiocyanate method, with SC_{50} of 0.87 ± 0.02 mg/mL and LC_{50} of 0.70 ± 0.06 mg/mL, respectively. Also, the seed extracts prepared by boiling exhibited the strongest metal chelating activity as an MC_{50} of 0.63 ± 0.04 mg/mL, lower than the EDTA standard of 0.73 ± 0.08 mg/mL. This study revealed that the antimelanogenesis activity was shown to be influenced by the plant parts and extraction method as the authors stated that different extraction methods may exhibit different biological activities by successful isolation of valuable phytochemical constituents.[84]

4.72. *Vitis vinifera* L. (White Grape Pomace). Ferri et al. reported that ethanol extracts of both white grape wet and dried pomace had stronger antityrosinase activity (inhibition rate of 63% to 79%) than aqueous extracts (inhibition rate of 43% to 71%). To be specific, the dried pomace samples showed better tyrosinase inhibition than wet pomace.[85] On the other hand, aqueous and ethanol extracts of wet pomace were reported to have a higher antioxidant activity than dried pomace samples. Nevertheless, ethanol extracts of both wet and dried pomace showed antioxidant activity stronger than that of aqueous extracts. In terms of anti-inflammatory activity, the results showed that aqueous extract of dried pomace exhibited better effects than dried pomace extract, while there was no activity reported for ethanol extracts.[85]

4.73. *Ziziphora taurica*. Sarikurkeu et al. and coresearchers reported that the methanol extract of *Ziziphora taurica* possessed the strongest tyrosinase inhibition activity with the lowest IC_{50} of 1.25 ± 0.01 mg/mL, followed by ethyl acetate with an IC_{50} of 1.40 ± 0.06 mg/mL.[86] Methanol extract also possessed the strongest DPPH scavenging potential (IC_{50} = 4.75 ± 0.12 mg/mL) and the lowest IC_{50} = 1.14 ± 0.06 mg/mL in the FRAP assay. Notably, the aqueous extract showed the strongest ABTS scavenging and ferrous chelating activities with IC_{50} values of 2.61 ± 0.26 and 1.04 ± 0.01 mg/mL, respectively. Ethyl acetate was reported to have the lowest IC_{50} value of 1.80 ± 0.03 mg/mL in the CUPRAC assay. The authors further explained that the amount of phenolic content was strongly determined by the polarity of the solvent used. Methanol is a highly polar solvent and very effective in extracting phenolic compounds.[86]

4.74. *Ziziphus jujuba*. Molagoda et al. reported the antimelanogenesis of seed extracts of *Ziziphus jujuba* by using quantification of extracellular and intracellular melanin content assays using B16F10 melanoma cells.[7] The extracellular melanin content was inhibited from 147.7 ± 5.2% to 106.8 ± 1.9% by 6‴-feruloylspinosin (FRS), 117.4 ± 0.5% by jujuboside B (JUB), and 119.9 ± 2.0% by epiceanothicacid (EPA). Similarly, intracellular melanin content was inhibited from 153.5 ± 3.3% to 101.4 ± 2.9% by FRS, 113.8 ± 2.1% EPA, and 114.7 ± 1.5% JUB. The phenylthiourea (PTU) extracellular melanin inhibition result was 92.4 ± 2.4%, and it was 95.3 ± 30.2% intracellularly. The highest tyrosinase inhibition was found in FRS (45.7 ± 2.7%), followed by EPA (38.4 ± 3.1%), JUB (33.9 ± 4.5%), betulin (BTL) (11.2 ± 5.1%), and lastly jujuboside A (JUA) (7.4 ± 5.3%), while the reference value from PTU was 58.4 ± 1.0%.[7]

4.75. *Zizyphus lotus*. Marmouzi et al. found that *Zizyphus lotus* fruit extracts have superior antioxidant activity with a lower IC_{50} value compared to leaf extracts.[87] With regard to the DPPH and ABTS assays, the fruits extract showed stronger radical scavenging activities with IC_{50} values of 74.87 ± 16.74 and 46.31 ± 11.02 mg TE/g, respectively, compared to the leafs of 241.75 ± 17.37 and 301.34 ± 8.26 mg TE/g, respectively.[87] On the other hand, the FRAP results of fruit extract were 55.30 ± 2.30 mg AAE/g, while that for leaf extract was 160.10 ± 2.30 mg AAE/g.[87] Nevertheless, the *Zizyphus lotus* extracts possessed remarkable tyrosinase inhibition, as the IC_{50} value of fruit extract was 70.23 ± 5.94 μg/mL, while the leaf extract was 129.11 ± 9.40 μg/mL, compared to the quercetin 246.90 ± 1.90 μg/mL reference value.[87] These two findings revealed that the extracts with good antioxidant activity possessed significant antityrosinase activity.[87]

5. CONCLUSION AND OUR PERSPECTIVES

This review summarized information on the depigmentation effects of various natural plant species. Plants are rich in polyphenols including phenolic and flavonoid compounds that may have the potential to develop as a skin-whitening agent in the cosmeceutical and pharmaceutical industry.[92] From Table 1, we concluded that the use of natural plants as skin-whitening agents is highly effective as there is a significant correlation between the content of polyphenol compounds and antimelanogenesis, antityrosinase, and antioxidant activities.

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

However, it is worth noting that the use of extraction methods or types of solvents is very important in determining the biological activities of plants. Further research is required to explore the most suitable extraction methods and types of solvent to obtain extracts or bioactive compounds that exhibit the most promising biological activities. Thus, use of nonconventional extraction methods can be employed as they are faster and provide high extraction yields. Additionally, we can investigate the bioactive compounds in the plant extracts regarding their structure and function that may be responsible for different biological properties. By evaluating the structures, this can aid in understanding the structure−activity relationship between the bioactive compounds and depigmentation effects as well as the mechanism of inhibition effects. For instance, nuclear magnetic resonance (NMR) spectroscopy is very useful in understanding the structure and identity of bioactive compounds. Given the adverse effects of using skin-lightening products that are made of chemicals that are hazardous to humans and the environment, more research should be done to develop safe, environmentally friendly, and effective skin-whitening agents.

AUTHOR INFORMATION

Corresponding Author

Lai Ti Gew − *Department of Biological Sciences, School of Medical and Life Sciences, Sunway University, 47500 Petaling Jaya, Selangor, Malaysia;* orcid.org/0000-0001-6313-7889; Phone: +603-7491 8622; Email: janeg@sunway.edu.my

Authors

Xin Yee Tung − *Department of Biological Sciences, School of Medical and Life Sciences, Sunway University, 47500 Petaling Jaya, Selangor, Malaysia*

Jia Qi Yip − *Department of Biological Sciences, School of Medical and Life Sciences, Sunway University, 47500 Petaling Jaya, Selangor, Malaysia;* orcid.org/0000-0001-7545-8217

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.3c02994

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This research was funded by the Fundamental Research Grant Scheme (FRGS) (Grant no.: FRGS/1/2020/STG01/SYUC/02/1) awarded by Ministry of Higher Education Malaysia (MOHE).

REFERENCES

(1) Chao, W.-W.; Su, C.-C.; Peng, H.-Y.; Chou, S.-T. Melaleuca Quinquenervia Essential Oil Inhibits α-Melanocyte-Stimulating Hormone-Induced Melanin Production and Oxidative Stress in B16 Melanoma Cells. *Phytomedicine* **2017**, *34*, 191−201.

(2) Lee, J.; Ryu, H. S.; Kim, J.-M.; Jung, T.-H.; Park, S.-M.; Lee, Y.-M. Anti-Melanogenic Effect of Gomisin N from Schisandra Chinensis (Turcz.) Baillon (Schisandraceae) in Melanoma Cells. *Arch Pharm. Res.* **2017**, *40* (7), 807−817.

(3) Emami, S. A.; Sadeghi, M.; Yazdian-Robati, R.; Arab, A.; Tayarani-Najaran, Z. Anti-Melanogenic Activity of Different Extracts from Aerial Parts of Nepeta Glomerulosa on Murine Melanoma B16F10 Cells. *Iranian Journal of Pharmaceutical Sciences* **2017**, *13* (2), 61−74.

(4) Kim, Y.; Lee, S.; Ryu, J. H.; Yoon, K. D.; Shin, S. S. Effect of Aurea Helianthus Stem Extract on Anti-Melanogenesis. *Biosci Biotechnol Biochem* **2018**, *82* (11), 1871−1879.

(5) Li, H.; Park, J.; Su, X.; Kim, K.; Kang, J.; Kim, Y.; Kim, Y.; Yang, S. Identification of Anti-Melanogenesis Constituents from Morus Alba L. Leaves. *Molecules* **2018**, *23* (10), 2559.

(6) Juang, L.; Gao, X.; Mai, S.; Lee, C.; Lee, M.; Yao, C. Safety Assessment, Biological Effects, and Mechanisms of Myrica Rubra Fruit Extract for Anti-melanogenesis, Anti-oxidation, and Free Radical Scavenging Abilities on Melanoma Cells. *J. Cosmet Dermatol* **2019**, *18* (1), 322−332.

(7) Molagoda, I. M. N.; Lee, K.-T.; Athapaththu, A. M. G. K.; Choi, Y.-H.; Hwang, J.; Sim, S.-J.; Kang, S.; Kim, G.-Y. Flavonoid Glycosides from Ziziphus Jujuba Var. Inermis (Bunge) Rehder Seeds Inhibit α-Melanocyte-Stimulating Hormone-Mediated Melanogenesis. *Int. J. Mol. Sci.* **2021**, *22* (14), 7701.

(8) Park, J. U.; Yang, S. Y.; Guo, R. H.; Li, H. X.; Kim, Y. H.; Kim, Y. R. Anti-Melanogenic Effect of Dendropanax Morbiferus and Its Active Components via Protein Kinase A/Cyclic Adenosine Monophosphate-Responsive Binding Protein- and P38 Mitogen-Activated Protein Kinase-Mediated Microphthalmia−Associated Transcription Factor Downregulation. *Front Pharmacol* **2020**, DOI: 10.3389/fphar.2020.00507.

(9) Geoffrey, K.; Mwangi, A. N.; Maru, S. M. Sunscreen Products: Rationale for Use, Formulation Development and Regulatory Considerations. *Saudi Pharmaceutical Journal* **2019**, *27* (7), 1009−1018.

(10) Mutalik, S.; Shetty, P. K.; Venuvanka, V.; Jagani, H. V.; Gejjalagere, C. H.; Nayak, U. Y.; Musmade, P. B.; Reddy, M. S.; Kalthur, G.; Udupa, N.; Ligade, V. S.; Rao, C. M. Development and Evaluation of Sunscreen Creams Containing Morin-Encapsulated Nanoparticles for Enhanced UV Radiation Protection and Anti-oxidant Activity. *Int. J. Nanomedicine* **2015**, 6477.

(11) Eghbali-Feriz, S.; Taleghani, A.; Al-Najjar, H.; Emami, S.; Rahimi, H.; Asili, J.; Hasanzadeh, S.; Tayarani-Najaran, Z. Anti-Melanogenesis and Anti-Tyrosinase Properties of Pistacia Atlantica Subsp. Mutica Extracts on B16F10 Murine Melanoma Cells. *Res. Pharm. Sci.* **2018**, *13* (6), 533.

(12) Zhang, J.; Wang, C.; Wang, C.; Sun, B.; Qi, C. Understanding the Role of Extracts from Sea Buckthorn Seed Residues in Anti-Melanogenesis Properties on B16F10 Melanoma Cells. *Food Funct* **2018**, *9* (10), 5402−5416.

(13) Choi, M.-H.; Jo, H.-G.; Yang, J.; Ki, S.; Shin, H.-J. Antioxidative and Anti-Melanogenic Activities of Bamboo Stems (Phyllostachys Nigra Variety Henosis) via PKA/CREB-Mediated MITF Down-regulation in B16F10 Melanoma Cells. *Int. J. Mol. Sci.* **2018**, *19* (2), 409.

(14) Zhu, L.; Lu, Y.; Yu, W.-G.; Zhao, X.; Lu, Y.-H. Anti-Photoageing and Anti-Melanogenesis Activities of Chrysin. *Pharm. Biol.* **2016**, *54* (11), 2692−2700.

(15) Srisupap, S.; Chaicharoenpong, C. In Vitro Antioxidant and Antityrosinase Activities of Manilkara Kauki. *Acta Pharmaceutica* **2021**, *71* (1), 153−162.

(16) Page, M. J.; McKenzie, J. E.; Bossuyt, P. M.; Boutron, I.; Hoffmann, T. C.; Mulrow, C. D.; Shamseer, L.; Tetzlaff, J. M.; Akl, E. A.; Brennan, S. E.; Chou, R.; Glanville, J.; Grimshaw, J. M.; Hróbjartsson, A.; Lalu, M. M.; Li, T.; Loder, E. W.; Mayo-Wilson, E.; McDonald, S.; McGuinness, L. A.; Stewart, L. A.; Thomas, J.; Tricco, A. C.; Welch, V. A.; Whiting, P.; Moher, D. The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. *Syst. Rev.* **2021**, *10* (1), 89.

(17) Sasidharan, S; Chen, Y; Saravanan, D; Sundram, K.; Latha, L. Extraction, Isolation and Characterization of Bioactive Compounds from Plants' Extracts. *Afr J. Tradit Complement Altern Med.* **2010**, *8* (1), 1−10.

(18) Altemimi, A.; Lakhssassi, N.; Baharlouei, A.; Watson, D.; Lightfoot, D. Phytochemicals: Extraction, Isolation, and Identification of Bioactive Compounds from Plant Extracts. *Plants* **2017**, *6* (4), 42.

(19) Castro-Puyana, M.; Marina, M. L.; Plaza, M. Water as Green Extraction Solvent: Principles and Reasons for Its Use. *Curr. Opin Green Sustain Chem.* **2017**, *5*, 31−36.
(20) Abubakar, A.; Haque, M. Preparation of Medicinal Plants: Basic Extraction and Fractionation Procedures for Experimental Purposes. *J. Pharm. Bioallied Sci.* **2020**, *12* (1), 1.
(21) Luque de Castro, M. D.; Priego-Capote, F. Soxhlet Extraction: Past and Present Panacea. *J. Chromatogr A* **2010**, *1217* (16), 2383−2389.
(22) Richter, B. E.; Jones, B. A.; Ezzell, J. L.; Porter, N. L.; Avdalovic, N.; Pohl, C. Accelerated Solvent Extraction: A Technique for Sample Preparation. *Anal. Chem.* **1996**, *68* (6), 1033−1039.
(23) Sparr Eskilsson, C.; Björklund, E. Analytical-Scale Microwave-Assisted Extraction. *J. Chromatogr A* **2000**, *902* (1), 227−250.
(24) Gong, C.-F.; Wang, Y.-X.; Wang, M.-L.; Su, W.-C.; Wang, Q.; Chen, Q.-X.; Shi, Y. Evaluation of the Structure and Biological Activities of Condensed Tannins from Acanthus Ilicifolius Linn and Their Effect on Fresh-Cut Fuji Apples. *Appl. Biochem. Biotechnol.* **2019**, *189* (3), 855−870.
(25) Strzępek-Gomółka, M.; Gaweł-Bęben, K.; Angelis, A.; Antosiewicz, B.; Sakipova, Z.; Kozhanova, K.; Głowniak, K.; Kukula-Koch, W. Identification of Mushroom and Murine Tyrosinase Inhibitors from Achillea Biebersteinii Afan. Extract. *Molecules* **2021**, *26* (4), 964.
(26) Asghari, B.; Mafakheri, S.; Zengin, G.; Dinparast, L.; Bahadori, M. B. In-Depth Study of Phytochemical Composition, Antioxidant Activity, Enzyme Inhibitory and Antiproliferative Properties of Achillea Filipendulina: A Good Candidate for Designing Biologically-Active Food Products. *Journal of Food Measurement and Characterization* **2020**, *14* (4), 2196−2208.
(27) Pieczykolan, A.; Pietrzak, W.; Dos Santos Szewczyk, K.; Gawlik-Dziki, U.; Nowak, R. LC-ESI-MS/MS Polyphenolic Profile and In Vitro Study of Cosmetic Potential of Aerva Lanata (L.) Juss. Herb Extracts. *Molecules* **2022**, *27* (4), 1259.
(28) Nikkhahi, M.; Souri, E.; Sarkhail, P.; Baeeri, M.; Mohammadhosseini, N. Evaluation of Anti-Tyrosinase Activity of Allium Ursinum Extracts and Their Metal Complexes [Pdf]. *Acta Sci. Pol Technol. Aliment* **2018**, *17* (3), 219−226.
(29) Švarc-Gajić, J.; Cerdà, V.; Clavijo, S.; Suárez, R.; Zengin, G.; Cvetanović, A. Chemical and Bioactivity Screening of Subcritical Water Extracts of Chokeberry (Aronia Melanocarpa) Stems. *J. Pharm. Biomed Anal* **2019**, *164*, 353−359.
(30) Jeong, D.; Lee, J.; Jeong, S.-G.; Hong, Y. H.; Yoo, S.; Han, S. Y.; Kim, J. H.; Kim, S.; Kim, J. S.; Chung, Y. S.; Kim, J.-H.; Yi, Y.-S.; Cho, J. Y. Artemisia Asiatica Ethanol Extract Exhibits Anti-Photoaging Activity. *J. Ethnopharmacol* **2018**, *220*, 57−66.
(31) Woo, S. M.; Choi, W. R.; Lee, D.-R.; Kim, H.-S.; Yi, C.; Kim, K.-H.; Kim, H.-L.; Cheng, J.; Le, B.; Yang, S. H.; Suh, J.-W. Leukodin Isolated from Artemisia Capillaris Inhibits Alpha-Melanocyte Stimulating Hormone Induced Melanogenesis in B16F10 Melanoma Cells. *Eur. J. Integr Med.* **2019**, *25*, 85−91.
(32) Wang, G.-H.; Lin, Y.-M.; Kuo, J.-T.; Lin, C.-P.; Chang, C.-F.; Hsieh, M.-C.; Cheng, C.-Y.; Chung, Y.-C. Comparison of Biofunctional Activity of Asparagus Cochinchinensis (Lour.) Merr. Extract before and after Fermentation with Aspergillus Oryzae. *J. Biosci Bioeng* **2019**, *127* (1), 59−65.
(33) Zardi-Bergaoui, A.; Ben Nejma, A.; Harzallah-Skhiri, F.; Flamini, G.; Ascrizzi, R.; Ben Jannet, H. Chemical Composition and Biological Studies of the Essential Oil from Aerial Parts of Beta Vulgaris Subsp. Maritima (L.) < scp > Arcang</Scp>. Growing in Tunisia. *Chem. Biodivers* **2017**, *14* (10), No. e1700234.
(34) Liu, W.; Wang, M.; Xu, S.; Gao, C.; Liu, J. Inhibitory Effects of Shell of Camellia Oleifera Abel Extract on Mushroom Tyrosinase and Human Skin Melanin. *J. Cosmet Dermatol* **2019**, *18* (6), 1955−1960.
(35) Sinan, K. I.; Ferrarese, I.; Aktumsek, A.; Peron, G.; Glamocilja, J.; Sokovic, M.; Nenadić, M.; Dall'Acqua, S.; Zengin, G. NMR and LC-MSn Coupled with Pharmacological Network Analysis for the Assessment of Phytochemical Content and Biopharmaceutical Potential of Carapa Procera Extracts. *J. Pharm. Biomed Anal* **2021**, *203*, No. 114184.
(36) Viet, T. D.; Xuan, T. D.; Anh, L. H. α-Amyrin and β-Amyrin Isolated from Celastrus Hindsii Leaves and Their Antioxidant, Anti-Xanthine Oxidase, and Anti-Tyrosinase Potentials. *Molecules* **2021**, *26* (23), 7248.
(37) Yang, H.; Xu, P.; Song, W.; Zhai, X. Anti-Tyrosinase and Antioxidant Activity of Proanthocyanidins from Cinnamomum Camphora. *Int. J. Food Prop* **2021**, *24* (1), 1265−1278.
(38) Adhikari, D.; Panthi, V.; Pangeni, R.; Kim, H.; Park, J. Preparation, Characterization, and Biological Activities of Topical Anti-Aging Ingredients in a Citrus Junos Callus Extract. *Molecules* **2017**, *22* (12), 2198.
(39) Quan, N.; Van; Xuan, T. D.; Anh, L. H.; Tran, H.-D. Bio-Guided Isolation of Prospective Bioactive Constituents from Roots of Clausena Indica (Dalzell) Oliv. *Molecules* **2019**, *24* (24), 4442.
(40) Azwanida, Z. N. N.; Melanie-Jaynes, H.; Jonathan, O. E. Antioxidant, Anti-Collagenase, Anti-Elastase and Anti-Tyrosinase Activities of an Aqueous Cosmos Caudatus Kunth (Asteraceae) Leaf Extract. *Tropical Journal of Natural Product Research* **2021**, *4* (12), 1124−1130.
(41) Axiotis, E.; Angelis, A.; Antoniadi, L.; Petrakis, E. A.; Skaltsounis, L. A. Phytochemical Analysis and Dermo-Cosmetic Evaluation of Cymbidium Sp. (Orchidaceae) Cultivation By-Products. *Antioxidants* **2022**, *11* (1), 101.
(42) Silva, A. R.; Pinela, J.; Dias, M. I.; Calhelha, R. C.; Alves, M. J.; Mocan, A.; García, P. A.; Barros, L.; Ferreira, I. C. F. R. Exploring the Phytochemical Profile of Cytinus Hypocistis (L.) L. as a Source of Health-Promoting Biomolecules behind Its in Vitro Bioactive and Enzyme Inhibitory Properties. *Food Chem. Toxicol.* **2020**, *136*, No. 111071.
(43) Santi, M. D.; Peralta, M. A.; Mendoza, C. S.; Cabrera, J. L.; Ortega, M. G. Chemical and Bioactivity of Flavanones Obtained from Roots of Dalea Pazensis Rusby. *Bioorg. Med. Chem. Lett.* **2017**, *27* (8), 1789−1794.
(44) Chai, W.-M.; Huang, Q.; Lin, M.-Z.; Ou-Yang, C.; Huang, W.-Y.; Wang, Y.-X.; Xu, K.-L.; Feng, H.-L. Condensed Tannins from Longan Bark as Inhibitor of Tyrosinase: Structure, Activity, and Mechanism. *J. Agric. Food Chem.* **2018**, *66* (4), 908−917.
(45) Zengin, G.; Cvetanović, A.; Gašić, U.; Stupar, A.; Bulut, G.; Senkardes, I.; Dogan, A.; Seebaluck-Sandoram, R.; Rengasamy, K. R. R.; Sinan, K. I.; Mahomoodally, M. F. Chemical Composition and Bio-Functional Perspectives of Erica Arborea L. Extracts Obtained by Different Extraction Techniques: Innovative Insights. *Ind. Crops Prod* **2019**, *142*, No. 111843.
(46) Tanase; Mocan; Cosarcă; Gavan; Nicolescu; Gheldiu; Vodnar; Muntean. Biological and Chemical Insights of Beech (Fagus Sylvatica L.) Bark: A Source of Bioactive Compounds with Functional Properties. *Antioxidants* **2019**, *8* (9), 417.
(47) Saber, F. R.; Ashour, R. M.; El-Halawany, A. M.; Mahomoodally, M. F.; Ak, G.; Zengin, G.; Mahrous, E. A. Phytochemical Profile, Enzyme Inhibition Activity and Molecular Docking Analysis of Feijoa Sellowiana O. Berg. *J. Enzyme Inhib Med. Chem.* **2021**, *36* (1), 618−626.
(48) Parvez, S.; Amin, M. H.; Bae, H. Tyrosinase Inhibitors of Galla Rhois and Its Derivative Components. *Advances in Traditional Medicine* **2021**, *21* (2), 267−280.
(49) Chatatikun, M.; Supjaroen, P.; Promlat, P.; Chantarangkul, C.; Waranuntakul, S.; Nawarat, J.; Tangpong, J.; Chiabchalard, A. Antioxidant and Tyrosinase Inhibitory Properties of an Aqueous Extract of Garcinia Atroviridis Griff. Ex. T. Anderson Fruit Pericarps. *Pharmacognosy Journal* **2020**, *12* (1), 71−78.
(50) Wu, Q.-Y.; Wong, Z. C.-F.; Wang, C.; Fung, A. H.-Y.; Wong, E. O.-Y.; Chan, G. K.-L.; Dong, T. T.-X.; Chen, Y.; Tsim, K. W.-K. Isoorientin Derived from Gentiana Veitchiorum Hemsl. Flowers Inhibits Melanogenesis by down-Regulating MITF-Induced Tyrosinase Expression. *Phytomedicine* **2019**, *57*, 129−136.
(51) Menbari, A.; Bahramnejad, B.; Abuzaripoor, M.; Shahmansouri, E.; Zarei, M. A. Establishment of Callus and Cell Suspension Cultures

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

of Granny Smith Apple Fruit and Antityrosinase Activity of Their Extracts. *Sci. Hortic* **2021**, *286*, No. 110222.
(52) Kim, J. Y.; Lee, E. J.; Ahn, Y.; Park, S.; Kim, S. H.; Oh, S. H. A Chemical Compound from Fruit Extract of Juglans Mandshurica Inhibits Melanogenesis through P-ERK-Associated MITF Degradation. *Phytomedicine* **2019**, *57*, 57−64.
(53) Jeon, J. S.; Kang, H. M.; Park, J. H.; Kang, J. S.; Lee, Y. J.; Park, Y. H.; Je, B., Il; Park, S. Y.; Choi, Y. W. A Comparative Study on Photo-Protective and Anti-Melanogenic Properties of Different Kadsura Coccinea Extracts. *Plants* **2021**, *10* (8), 1633.
(54) Lee, J. Y.; Cho, Y.-R.; Park, J. H.; Ahn, E.-K.; Jeong, W.; Shin, H. S.; Kim, M.-S.; Yang, S. H.; Oh, J. S. Anti-Melanogenic and Anti-Oxidant Activities of Ethanol Extract of Kummerowia Striata: Kummerowia Striata Regulate Anti-Melanogenic Activity through down-Regulation of TRP-1, TRP-2 and MITF Expression. *Toxicol Rep* **2019**, *6*, 10−17.
(55) Lai, K.-Y.; Hu, H.-C.; Chiang, H.-M.; Liu, Y.-J.; Yang, J.-C.; Lin, Y.-A.; Chen, C.-J.; Chang, Y.-S.; Lee, C.-L. New Diterpenes Leojaponins G−L from Leonurus Japonicus. *Fitoterapia* **2018**, *130*, 125−133.
(56) Crespo, M. I.; Chabán, M. F.; Lanza, P. A.; Joray, M. B.; Palacios, S. M.; Vera, D. M. A.; Carpinella, M. C. Inhibitory Effects of Compounds Isolated from Lepechinia Meyenii on Tyrosinase. *Food Chem. Toxicol.* **2019**, *125*, 383−391.
(57) Bakhouche, I.; Aliat, T.; Boubellouta, T.; Gali, L.; Şen, A.; Bellik, Y. Phenolic Contents and in Vitro Antioxidant, Anti-Tyrosinase, and Anti-Inflammatory Effects of Leaves and Roots Extracts of the Halophyte Limonium Delicatulum. *South African Journal of Botany* **2021**, *139*, 42−49.
(58) Sinan, K. I.; Martinović, L. S.; Peršurić, Ž.; Pavelić, S. K.; Grbčić, P.; Matulja, D.; Etienne, O. K.; Mahomoodally, M. F.; Lobine, D.; Behl, T.; Zengin, G. Metabolite Characterization, Antioxidant, Anti-Proliferative and Enzyme Inhibitory Activities of Lophira Lanceolata Tiegh. Ex Keay Extracts. *Ind. Crops Prod* **2020**, *158*, No. 112982.
(59) Hsu, J.-Y.; Lin, H.-H.; Li, T.-S.; Tseng, C.-Y.; Wong, Y.; Chen, J.-H. Anti-Melanogenesis Effects of Lotus Seedpod In Vitro and In Vivo. *Nutrients* **2020**, *12* (11), 3535.
(60) Jo, Y. H.; Lee, S.; Ryu, S. H.; Yeon, S. W.; Turk, A.; Hwang, B. Y.; Lee, M. K. Xanthone and Flavonoid Derivatives from the Leaves of Maclura Tricuspidata with Antioxidant and Anti-Tyrosinase Activity. Natural Product. *Sciences* **2021**, *27* (4), 234−239.
(61) He, R.-J.; Li, J.; Huang, Y.-L.; Wang, Y.-F.; Yang, B.-Y.; Liu, Z.-B.; Ge, L.; Yang, K.-D.; Li, D.-P. Structural Characterization and Assessment of Anti-Inflammatory and Anti-Tyrosinase Activities of Polyphenols from Melastoma Normale. *Molecules* **2021**, *26* (13), 3913.
(62) Chaiyana, W.; Sirithunyalug, J.; Somwongin, S.; Punyoyai, C.; Laothaweerungsawat, N.; Marsup, P.; Neimkhum, W.; Yawootti, A. Enhancement of the Antioxidant, Anti-Tyrosinase, and Anti-Hyaluronidase Activity of Morus Alba L. Leaf Extract by Pulsed Electric Field Extraction. *Molecules* **2020**, *25* (9), 2212.
(63) Bose, B.; Tripathy, D.; Chatterjee, A.; Tandon, P.; Kumaria, S. Secondary Metabolite Profiling, Cytotoxicity, Anti-Inflammatory Potential and in Vitro Inhibitory Activities of Nardostachys Jatamansi on Key Enzymes Linked to Hyperglycemia, Hypertension and Cognitive Disorders. *Phytomedicine* **2019**, *55*, 58−69.
(64) Elkattan, A.; Gohar, A.; Amer, M.; Naeem, Z.; Ashour, A.; Shimizu, K. Melanin Synthesis Inhibitors from Olea Europeae. *Records of Natural Products* **2019**, *14* (2), 139−143.
(65) El Aanachi, S.; Gali, L.; Nacer, S. N.; Bensouici, C.; Dari, K.; Aassila, H. Phenolic Contents and in Vitro Investigation of the Antioxidant, Enzyme Inhibitory, Photoprotective, and Antimicrobial Effects of the Organic Extracts of Pelargonium Graveolens Growing in Morocco. *Biocatal Agric Biotechnol* **2020**, *29*, No. 101819.
(66) Masum, M. N.; Choodej, S.; Yamauchi, K.; Mitsunaga, T. Isolation of Phenylpropanoid Sucrose Esters from the Roots of Persicaria Orientalis and Their Potential as Inhibitors of Melanogenesis. *Medicinal Chemistry Research* **2019**, *28* (5), 623−632.
(67) Song, W.; Zhao, Y.-Y.; Ren, Y.-J.; Liu, L.-L.; Wei, S.-D.; Yang, H.-B. Proanthocyanidins Isolated from the Leaves of Photinia × Fraseri Block the Cell Cycle and Induce Apoptosis by Inhibiting Tyrosinase Activity in Melanoma Cells. *Food Funct* **2021**, *12* (9), 3978−3991.
(68) Mahomoodally, M. F.; Yerlikaya, S.; Llorent-Martínez, E. J.; Uğurlu, A.; Baloglu, M. C.; Altunoglu, Y. C.; Mollica, A.; Dardenne, K. K.; Aumeeruddy, M. Z.; Puchooa, D.; Zengin, G. Pharmacological and Polyphenolic Profiles of Phyllanthus Phillyreifolius Var. Commersonii Müll. Arg: An Unexplored Endemic Species from Mauritius. *Food Research International* **2019**, *115*, 425−438.
(69) Elloumi, W.; Maalej, A.; Ortiz, S.; Michel, S.; Chamkha, M.; Boutefnouchet, S.; Sayadi, S. Pistacia Lentiscus L. Distilled Leaves as a Potential Cosmeceutical Ingredient: Phytochemical Characterization, Transdermal Diffusion, and Anti-Elastase and Anti-Tyrosinase Activities. *Molecules* **2022**, *27* (3), 855.
(70) Rodrigues, M. J.; Matkowski, A.; Ślusarczyk, S.; Magné, C.; Poleze, T.; Pereira, C.; Custódio, L. Sea Knotgrass (Polygonum Maritimum L.) as a Potential Source of Innovative Industrial Products for Skincare Applications. *Ind. Crops Prod* **2019**, *128*, 391−398.
(71) Yang, D.; Wang, L.; Zhai, J.; Han, N.; Liu, Z.; Li, S.; Yin, J. Characterization of Antioxidant, α-Glucosidase and Tyrosinase Inhibitors from the Rhizomes of Potentilla Anserina L. and Their Structure−Activity Relationship. *Food Chem.* **2021**, *336*, No. 127714.
(72) Lee, H. P.; Kim, D. S.; Park, S. H.; Shin, C. Y.; Woo, J. J.; Kim, J. W.; An, R.-B.; Lee, C.; Cho, J. Y. Antioxidant Capacity of Potentilla Paradoxa Nutt. and Its Beneficial Effects Related to Anti-Aging in HaCaT and B16F10 Cells. *Plants* **2022**, *11* (7), 873.
(73) Park, S.; Choi, E.; Kim, S.; Kim, D.; Kim, J.; Chang, S.; Choi, J.; Park, K.; Roh, K.-B.; Lee, J.; Yoo, B.; Cho, J. Oxidative Stress-Protective and Anti-Melanogenic Effects of Loliolide and Ethanol Extract from Fresh Water Green Algae, Prasiola Japonica. *Int. J. Mol. Sci.* **2018**, *19* (9), 2825.
(74) Deguchi, T.; Tamai, A.; Asahara, K.; Miyamoto, K.; Miyamoto, A.; Nomura, M.; Kawata-Tominaga, T.; Yoshioka, Y.; Murata, K. Anti-Tyrosinase and Anti-Oxidative Activities by Asana: The Heartwood of Pterocarpus Marsupium. *Nat. Prod Commun.* **2019**, *14* (10), No. 1934578.
(75) Ma, H.; Xu, J.; DaSilva, N. A.; Wang, L.; Wei, Z.; Guo, L.; Johnson, S. L.; Lu, W.; Xu, J.; Gu, Q.; Seeram, N. P. Cosmetic Applications of Glucitol-Core Containing Gallotannins from a Proprietary Phenolic-Enriched Red Maple (Acer Rubrum) Leaves Extract: Inhibition of Melanogenesis via down-Regulation of Tyrosinase and Melanogenic Gene Expression in B16F10 Melanoma Cells. *Arch Dermatol Res.* **2017**, *309* (4), 265−274.
(76) Li, M.-X.; Xie, J.; Bai, X.; Du, Z.-Z. Anti-Aging Potential, Anti-Tyrosinase and Antibacterial Activities of Extracts and Compounds Isolated from Rosa Chinensis Cv. 'JinBian.'. *Ind. Crops Prod* **2021**, *159*, No. 113059.
(77) Grochowski, D. M.; Uysal, S.; Zengin, G.; Tomczyk, M. In Vitro Antioxidant and Enzyme Inhibitory Properties of Rubus Caesius L. *Int. J. Environ. Health Res.* **2019**, *29* (3), 237−245.
(78) Otang-Mbeng, W.; Sagbo, I. J. Anti-Melanogenesis, Antioxidant and Anti-Tyrosinase Activities of Scabiosa Columbaria L. *Processes* **2020**, *8* (2), 236.
(79) Sassi, A. B.; Elayeb, A.; Karaman, I.; Marzouk, B.; Mastouri, M. Phytochemical Profile and Antiproliferative, Anti-Tyrosinase, Anti-oxidant, and Antibacterial Potential of Schinus Terebinthifolius Growing in Tunisia. *J. Herbs Spices Med. Plants* **2020**, *26* (1), 61−76.
(80) Dall'Acqua, S.; Ak, G.; Sut, S.; Ferrarese, I.; Zengin, G.; Yıldıztugay, E.; Mahomoodally, M. F.; Sinan, K. I.; Lobine, D. Phenolics from Scorzonera Tomentosa L.: Exploring the Potential Use in Industrial Applications via an Integrated Approach. *Ind. Crops Prod* **2020**, *154*, No. 112751.
(81) Han, H. J.; Park, S. K.; Kang, J. Y.; Kim, J. M.; Yoo, S. K.; Heo, H. J. Anti-Melanogenic Effect of Ethanolic Extract of Sorghum Bicolor on IBMX−Induced Melanogenesis in B16/F10 Melanoma Cells. *Nutrients* **2020**, *12* (3), 832.

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201

(82) Younis, M. M.; Ayoub, I. M.; Mostafa, N. M.; El Hassab, M. A.; Eldehna, W. M.; Al-Rashood, S. T.; Eldahshan, O. A. GC/MS Profiling, Anti-Collagenase, Anti-Elastase, Anti-Tyrosinase and Anti-Hyaluronidase Activities of a Stenocarpus Sinuatus Leaves Extract. *Plants* **2022**, *11* (7), 918.
(83) Angelini, P.; Venanzoni, R.; Angeles Flores, G.; Tirillini, B.; Orlando, G.; Recinella, L.; Chiavaroli, A.; Brunetti, L.; Leone, S.; Di Simone, S. C.; Ciferri, M. C.; Zengin, G.; Ak, G.; Menghini, L.; Ferrante, C. Evaluation of Antioxidant, Antimicrobial and Tyrosinase Inhibitory Activities of Extracts from Tricholosporum Goniospermum, an Edible Wild Mushroom. *Antibiotics* **2020**, *9* (8), 513.
(84) Chutoprapat, R.; Malilas, W.; Rakkaew, R.; Udompong, S.; Boonpisuttinant, K. Collagen Biosynthesis Stimulation and Anti-Melanogenesis of Bambara Groundnut (Vigna Subterranea) Extracts. *Pharm. Biol.* **2020**, *58* (1), 1023−1031.
(85) Ferri, M.; Rondini, G.; Calabretta, M. M.; Michelini, E.; Vallini, V.; Fava, F.; Roda, A.; Minnucci, G.; Tassoni, A. White Grape Pomace Extracts, Obtained by a Sequential Enzymatic plus Ethanol-Based Extraction, Exert Antioxidant, Anti-Tyrosinase and Anti-Inflammatory Activities. *N Biotechnol* **2017**, *39*, 51−58.
(86) Sarikurkcu, C.; Kakouri, E.; Sarikurkcu, R. T.; Tarantilis, P. A. Study on the Chemical Composition, Enzyme Inhibition and Antioxidant Activity of Ziziphora Taurica Subsp. Cleonioides. *Applied Sciences* **2019**, *9* (24), 5515.
(87) Marmouzi, I.; Kharbach, M.; El Jemli, M.; Bouyahya, A.; Cherrah, Y.; Bouklouze, A.; Vander Heyden, Y.; Faouzi, M. E. A. Antidiabetic, Dermatoprotective, Antioxidant and Chemical Functionalities in Zizyphus Lotus Leaves and Fruits. *Ind. Crops Prod* **2019**, *132*, 134−139.
(88) Zolghadri, S.; Bahrami, A.; Hassan Khan, M. T.; Munoz-Munoz, J.; Garcia-Molina, F.; Garcia-Canovas, F.; Saboury, A. A. A Comprehensive Review on Tyrosinase Inhibitors. *J. Enzyme Inhib Med. Chem.* **2019**, *34* (1), 279−309.
(89) Lobo, V.; Patil, A.; Phatak, A.; Chandra, N. Free Radicals, Antioxidants and Functional Foods: Impact on Human Health. *Pharmacogn Rev.* **2010**, *4* (8), 118.
(90) Azab, A.; Nassar, A.; Azab, A. Anti-Inflammatory Activity of Natural Products. *Molecules* **2016**, *21* (10), 1321.
(91) An, S. M.; Lee, S. I.; Choi, S. W.; Moon, S.-W.; Boo, Y. C. p-Coumaric Acid, a Constituent of Sasa Quelpaertensis Nakai, Inhibits Cellular Melanogenesis Stimulated by -Melanocyte Stimulating Hormone. *British Journal of Dermatology* **2008**, *159* (2), 292−299.
(92) Ng, S. Y.; Eh Suk, V. R.; Gew, L. T. Plant polyphenols as green sunscreen ingredients: A systematic review. *Journal of Cosmetic Dermatology* **2022**, *21* (11), 5409−5444.

https://doi.org/10.1021/acsomega.3c02994
ACS Omega 2023, 8, 33115−33201