ISSN 1905-4637 (Print)
ISSN 3027-7922 (Online)
https://digital.car.chula.ac.th/tjps
Volume 48 **Issue** 1 (January - March 2024)

The Thai Journal of Pharmaceutical Sciences

(ไทยเภสัชสาร)

The Thai Journal of Pharmaceutical Sciences
Research Division, Faculty of Pharmaceutical Sciences,
Chulalongkorn University
254 Phayathai Road, Patumwan District,
Bangkok 10330

Journal Home
About This Journal
Aims and Scope
Editorial Board
Publication Ethics Statements
Author Instructions
Contact TJPS

Submit Article

Most Popular Papers

Receive Email Notices or RSS

Select an issue:
All Issues Browse

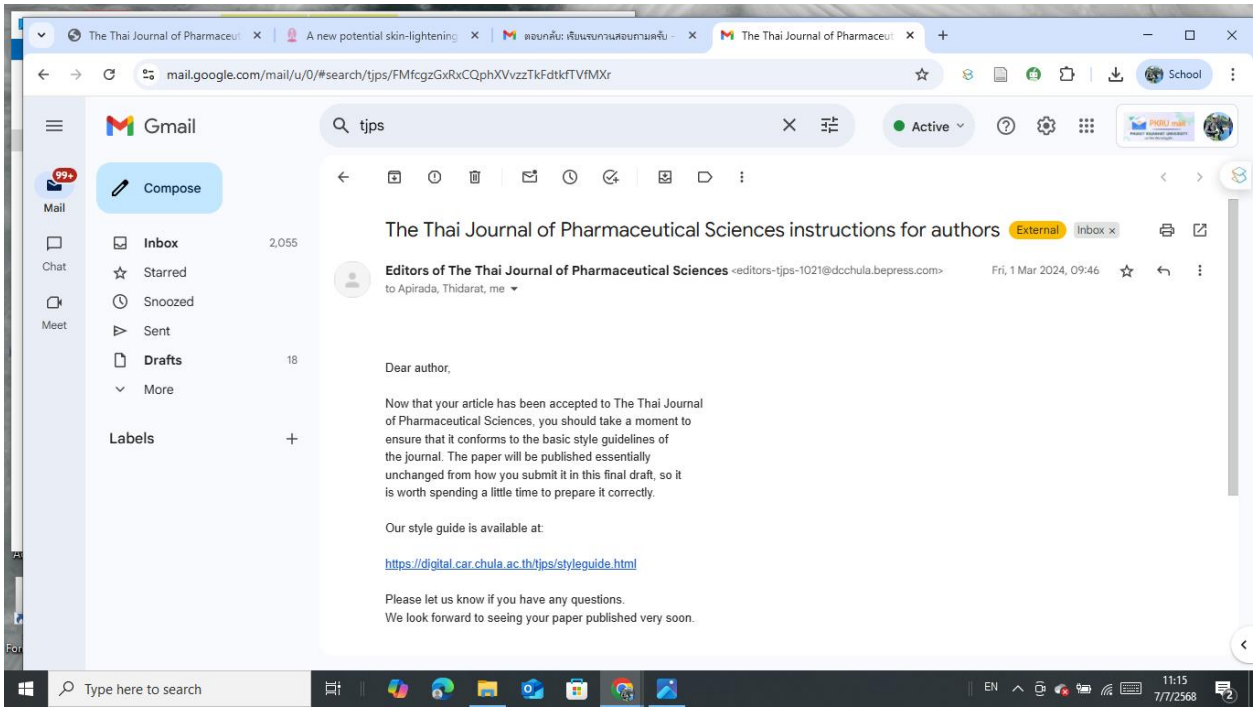
Search

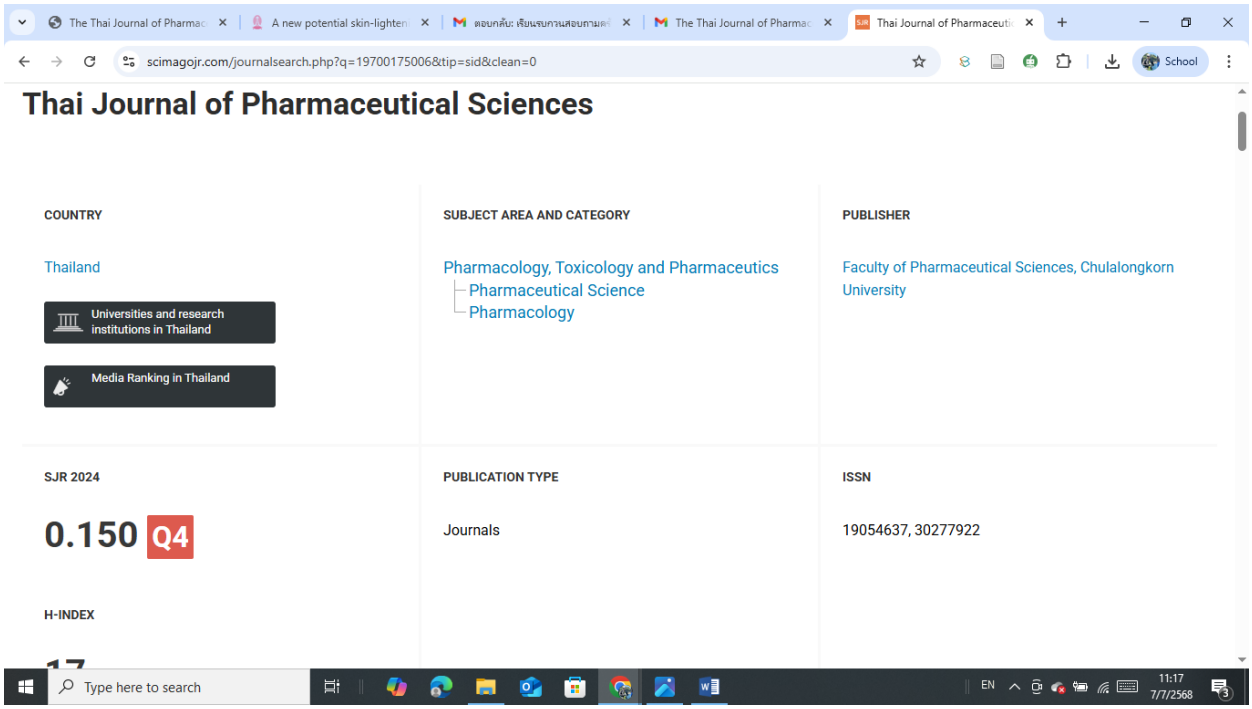
Enter search terms:
Search
in this journal

The Thai Journal of Pharmaceutical Sciences

Volume 48, Issue 1 (2024)

Articles


mail.google.com/mail/u/0/#search/tjps/FMfcgzGxRxCQphXVvzzTkFdtkfTVfMXr
Gmail
tjps
Compose
Inbox 2,055
Starred
Snoozed
Sent
Drafts 18
More
Labels
The Thai Journal of Pharmaceutical Sciences instructions for authors
Editors of The Thai Journal of Pharmaceutical Sciences <editors-tjps-1021@dcchula.bepress.com>
Fri, 1 Mar 2024, 09:46
to Apirada, Thidarat, me
Dear author,
Now that your article has been accepted to The Thai Journal of Pharmaceutical Sciences, you should take a moment to ensure that it conforms to the basic style guidelines of the journal. The paper will be published essentially unchanged from how you submit it in this final draft, so it is worth spending a little time to prepare it correctly.
Our style guide is available at:
https://digital.car.chula.ac.th/tjps/styleguide.html
Please let us know if you have any questions.
We look forward to seeing your paper published very soon.


scimagojr.com/journalsearch.php?q=19700175006&tip=sid&clean=0
Thai Journal of Pharmaceutical Sciences
COUNTRY
Thailand
Universities and research institutions in Thailand
Media Ranking in Thailand
SUBJECT AREA AND CATEGORY
Pharmacology, Toxicology and Pharmaceutics
Pharmaceutical Science
Pharmacology
PUBLISHER
Faculty of Pharmaceutical Sciences, Chulalongkorn University
SJR 2024
0.150 Q4
PUBLICATION TYPE
Journals
ISSN
19054637, 30277922
H-INDEX

The Thai Journal of Pharmaceutical Sciences

Volume 48 | Issue 1 Article 1

April 2024

A new potential skin-lightening extract from Artocarpus spp. fruit and skinlightening activity of Southern Thailand plant extracts.

Apirada Sucontphunt

Thidarat Phetmanee

Akkarapol Butsuri

Recommended Citation
Sucontphunt, Apirada; Phetmanee, Thidarat; and Butsuri, Akkarapol (2024) "A new potential skin-lightening extract from Artocarpus spp. fruit and skinlightening activity of Southern Thailand plant extracts.," *The Thai Journal of Pharmaceutical Sciences*: Vol. 48: Iss. 1, Article 1.
DOI: https://doi.org/10.56808/3027-7922.2857
Available at: https://digital.car.chula.ac.th/tjps/vol48/iss1/1

Original Article

Thai Journal of Pharmaceutical Sciences

A new potential skin-lightening extract from *Artocarpus* spp. fruit and skin-lightening activity of Southern Thailand plant extracts

Apirada Sucontphunt[1], Thidarat Phetmanee[2], Akkarapol Butsuri[3]

[1]Drug and Herbal Product Research and Development Center, College of Pharmacy, Rangsit University, Pathum Thani 12000, Thailand, [2]Department of Pharmacology, College of Pharmacy, Rangsit University, Pathum Thani 12000, Thailand, [3]Department of Science and Maths (Chemistry), Faculty of Science and Technology, Phuket Rajabhat University, Phuket 83000, Thailand

Corresponding Author:
Akkarapol Butsuri, Department of Science and Maths (Chemistry), Faculty of Science and Technology, Phuket Rajabhat University, Phuket 83000, Thailand.
E-mail: *akkarapol.b@pkru.ac.th*

Received: September 10, 2022
Accepted: February 29, 2024
Published: March 30, 2024

ABSTRACT

The global skin-lightening product market is expanding every year resulting in a high demand for skin-lightening herbal extracts that are effective and safe. Moreover, herbal plants are very popular in Thailand and can bring Thai farmers satisfactory income. This research hence aimed to discover new plant extracts with potential skin-lightening properties. Extractions of different parts of five plants originally cultivated in Southern Thailand including *Artocarpus integer* Spreng. (AI), *Artocarpus heterophyllus* Lam., *Garcinia atroviridis* Griff. Ex T. Anderson, *Glycyrrhiza glabra* Linn., and *Anacardium occidentale* L. were performed and determined for their anti-tyrosinase, anti-melanogenesis, anti-oxidant activity, and cell toxicity. It was found that a new extract from AI fruit peel had superior potential and could be used as an active ingredient in skin-lightening products when compared to other extracts due to its great anti-tyrosinase, anti-melanogenesis, anti-oxidant activities, and safety.

Key words: Anti-tyrosinase, *Artocarpus integer*, melanin, plant extract, skin lightening

INTRODUCTION

The global skin-lightening product market is expected to expand from 2022 to 2030. In 2021, the market value of skin-lightening products was USD 9.96 billion.[1] However, chemical compounds have been used in lightening products such as hydroquinone and corticosteroids which exhibit many adverse effects; consequently, herbal extracts exhibiting skin-lightening properties gain a lot of attention due to their safety.[2] Therefore, much research still searches for new skin-lightening herbal extracts.

Melanin is the main skin pigment synthesized from melanocytes and is responsible for skin color. Abnormality in melanogenesis and melanin accumulation results in many skin diseases. The rate-limiting step of melanogenesis is a tyrosinase enzyme catalyzation. Therefore, various studies attempt to investigate the anti-tyrosinase activity of many compounds.[3] This research, therefore, aimed to discover new herbal extracts exhibiting potential anti-tyrosinase and inhibiting melanin synthesis.

In this research, different parts of five plants originally cultivated in Southern Thailand including *Artocarpus integer* Spreng. (AI) or cempedak, *Artocarpus heterophyllus* Lam. (AH) or jackfruit, *Anacardium occidentale* L. (AO) or cashew nut, *Garcinia atroviridis* Griff. Ex T. Anderson (GA) or garcinia, and *Glycyrrhiza glabra* Linn. (GG) or licorice were selected. Phenolic compounds from AO were found to inhibit the mushroom tyrosinase activity.[4] The anti-tyrosinase activity of plants in *Artocapus* species, such as AI and AH, has been studied. Extracts from the root of AI and the sapwood of AH exhibited anti-tyrosinase activity.[5-7] However, these extracts were obtained from the wood and the roots of plants. This research aimed to discover new potential extracts from wasting parts of plants such as fruit peels to add value to plants or fruits that can easily be supplied to commercial production. Therefore, the activity of extracts from different parts of selected plants

from the south of Thailand and different solvents for extraction were studied. In addition, there has been no research on the skin-lightening activity of GA. Its crude extract exhibited anti-microbial, anti-oxidant, and anti-tumor activities[8] which are beneficial for cosmeceutical products. For the comparison of the activity of new plant extracts, GG extracts were tested in parallel with others. In many studies, GG and glabridin, a chemical compound found in the root extract of licorice, have been investigated for its therapeutic activities including anti-tyrosinase activity, inhibition of melanin synthesis, and anti-inflammatory activity.[9-11] It is widely used in cosmeceuticals.[12] Therefore, skin-lightening activity including anti-tyrosinase, anti-melanogenesis, anti-oxidant activities, and cytotoxicity of selected plant extracts was investigated.

MATERIALS AND METHODS

Material and Chemicals

Collected plants as the raw materials were cultivated in Phuket Province, Thailand. Dr. Piya Chalermglin, authentication the plants at the Department of Science and Mathematics, Faculty of Science and Technology, Phuket Rajabhat University, AI Spreng, (PKRU-AK-001) and AH Lam., (PKRU-AK-002), family *Moraceae*, AO L., (PKRU-AK-003), family *Anacardiaceae*, GA Griff. Ex T. Anderson., (PKRU-AK-004), family *Clusiaceae*, GG Linn., (PKRU-AK-005), family *Leguminoseae*, DPPH (2,2-Diphenyl-1-picrylhydrazyl), mushroom tyrosinase, a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), dimethyl sulfoxide (DMSO), standard ascorbic acid, and kojic acid were purchased from Sigma Aldrich, MO, USA. Dulbecco's Modified Eagle Medium (DMEM), fetal bovine serum, penicillin, streptomycin, and glutamine were purchased from Gibco, MD, USA.

Extractions

Fresh or dried plants were finely ground. Then, 1 kg of fine plant powder was extracted through reflux extraction with 1000 mL of ethanol and heated at 50°C for 8 h. Filtered extracts then were evaporated by a rotary evaporator to obtain ethanol crude extracts (ECE). Further extractions were accomplished by liquid–liquid extraction. 50 g of ECE was dissolved in a combination of 1,000 mL of water and 1,000 mL of hexane. It was shaken in a separation funnel. The hexane part was extracted 3 times. The collected hexane part was then evaporated until dry to obtain hexane extract (HE). The water part was further extracted using ethyl acetate and *n*-butanol, to obtain ethyl acetate extract (EE), *n*-butanol extract (BE), and water part extract (WE), respectively.

DPPH Anti-oxidant Assay

To investigate the anti-oxidant activity of the extracts, DPPH free radical scavenging assay was performed by the modified method applied by previous studies.[13] Briefly, different concentrations of standard ascorbic acid and samples were prepared by diluting ethanol. 100 µL of each sample was mixed with DPPH 100 µL of 0.1 mM of DPPH in ethanol in 96 well plates. After the samples were left at room temperature in the dark for 30 min, absorbance at 517 nm was measured and the percentages of DPPH free radical inhibition compared to the control were calculated. To obtain IC_{50} from the anti-oxidant activity of each extract, the linear regression equation was calculated by plotting % inhibition against the concentration of the extract.

In vitro Anti-tyrosinase Assay

Tyrosinase inhibitory activity was investigated by the dopachrome method modified from a previous study.[14] Briefly, various concentrations of extracts and the standard kojic acid were prepared. 20 µL of each sample was mixed with 20 µL of mushroom tyrosinase solution (333 unit/mL) in 96 well plates. After the samples were stored at 45°C for 10 min, 20 µL of 5 mM of tyrosine was added, and phosphate buffer (pH 6.8) was used to adjust the total volume to 200 µL. Absorbance at 492 nm was measured after 60 min of final mixing. The percentages of anti-tyrosinase activity compared to the control were calculated. To obtain the IC_{50} value, anti-tyrosinase activity of each extract was determined using the linear regression equation by which % inhibition was plotted against the concentration of extract.

Cell Culture and Treatments

Melanoma cell line B16F10 American Type Culture Collection (ATCC® CRL-6745) was obtained from the (ATCC, Manassas, VA, USA). Cells were cultured in DMEM with 10% fetal bovine serum, 100 U/mL of penicillin, 100 U/mL of streptomycin, and 2 mM of glutamine and maintained in 5% CO_2 environment at 37°C.[15] Cells were subcultured at 80–90% confluence.

After 24 h of cell plating, the old medium was removed. The control was replaced with a new medium whereas the treatment was replaced with a new medium containing various concentrations of samples and a new medium containing standard kojic acid.

Cellular Melanin Content Assay

To compare melanin inhibition activity among the samples, melanin in cells was photographed and analyzed. Melanin inhibition assay was performed with melanoma cell line B16F10 at a concentration of 6×10^4 cells/6 well plate. After treatment for 72 h, cells were washed twice in phosphate buffer saline pH 7.4 (PBS). To remove the cells from the plates, trypsin (0.5 mL) was used, and the plates were rinsed twice in 0.5 mL of PBS. All cell solutions were collected in 1.5 mL centrifuge tubes and centrifuged at 12,000 rpm. The supernatant was removed and photographs of the cell pellet were recorded and compared for melanin content in cells. After that, 1 ml of 1N sodium hydroxide was added, and the cells were boiled for 15 min and sonicated for 15 min, then the absorbance at 450 nm was read. The percentage of melanin content compared to the control was calculated. The EC_{50} of the anti-melanogenesis activity of each extract was determined using the linear regression equation by which % inhibition was plotted against the concentration of extract.

Cell Viability Measurement

The cell viability of the extracts and standard were determined using MTT assay.[16] B16F10 in 96 well plates at a concentration of 2×10^3 cells/well was left overnight. After that, various

concentrations of the extracts were added to the medium, and cells were incubated for 72 h. Then, the medium was removed and 100 µL of MTT solution (5.0 mg/mL in PBS) was added to each well. After 4 h of incubation at 37°C, MTT solution was removed and 100 µL of DMSO was added to solubilize formazan crystal. Absorbance at 570 nm was measured and % cell viability compared to the control was calculated.

Statistical Analysis

Data were collected from triplicate independent measurements and cell viability was expressed as mean ± standard deviation. Repeated measurements were conducted, and one-way analysis of variance with a *post hoc* test at a significance level of 0.05S was performed by the SPSS program to statistically analyze data.

RESULTS AND DISCUSSION

Extractions

Herbal extracts from five selected plants originally cultivated in Southern Thailand were investigated for their cosmeceutical activities including *in vitro* tyrosinase inhibitory activity, inhibition of melanogenesis and cytotoxicity in melanoma cell line, and anti-oxidant activity. In the extraction process, parts of different plants were extracted using ethanol to obtain ethanol extracts (ECE) and then further extracted using different solvents such as hexane, ethyl acetate, *n*-butanol, and water to partially purify crude extract by compound solubility property.

The extraction yield of each plant is shown in Table 1. It was found that for ethanol extracts, GA had the highest yield and the dried peel of AI had the lowest yield. After further extractions using various solvents, the highest yield was obtained from the water part (WE).

Anti-oxidant Activity

For anti-oxidant assay, the IC_{50} values of plant extracts are shown in Table 2. An EE dried fruit peel of AI exhibited the strongest anti-oxidant activity with IC_{50} of 0.0262 ± 0.001 mg/mL, followed by an EE of fresh fruit of AO (0.0529 ± 0.002 mg/mL) and an EE of fresh fruit peel of AI (0.0738 ± 0.000 mg/mL), respectively. These extracts had strong anti-oxidant activities as well as the standard ascorbic acid (IC_{50} = 0.0086 ± 0.000 mg/mL).

In vitro Anti-Tyrosinase Activity

Results from *in vitro* anti-tyrosinase activity test [Table 3] showed that an EE of the dried GG root had the most

Table 1: Extraction yield of different parts of selected plants extracted by various solvents

Plant	Part	Weight (g)	% Yield	% Yield from ECE			
			ECE	HE	EE	BE	WE
AI	Fresh fruit peel	2000	3.54	1.60	0.91	13.62	83.94
	Dried fruit peel	200	15.14	0.66	4.66	9.20	83.94
	Fresh fruit	1000	15.81	0.30	0.36	5.14	94.22
AH	Fresh fruit peel	1000	2.32	12.36	4.16	9.70	73.80
	Dried fruit peel	213.8	15.61	25.40	8.36	14.30	48.60
GA	Dried fruit	1000	27.42	0.30	3.98	12.04	83.68
GG	Dried root	1000	24.00	1.72	18.68	25.18	54.42
AO	Fresh fruit	1000	19.00	0.10	1.84	21.08	76.96
	Dried fruit	144.5	59.37	1.60	8.44	17.70	72.20

HE: Hexane extract, BE: Butanol extract, WE: Water part extract, EE: Ethyl acetate extract

Table 2: Anti-oxidant activities of various plant extracts

Plant	Part	IC_{50} of DPPH (µg/mL)				
		ECE	HE	EE	BE	WE
AI	Fresh fruit peel	0.258±0.028	0.132±0.004	0.073±0.000	0.229±0.003	9.093±0.466
	Dried fruit peel	0.271±0.022	0.605±0.038	0.026±0.001	0.075±0.005	1.275±0.045
	Fresh fruit	18.674±0.483	17.051±1.042	0.525±0.003	3.593±0.186	0.432±0.033
AH	Fresh fruit peel	0.555±0.005	1.844±0.165	0.283±0.001	0.140±0.004	0.902±0.050
	Dried fruit peel	0.872±0.031	2.537±0.059	1.112±0.091	1.345±0.013	3.669±0.233
GA	Dried fruit	8.555±0.243	1.330±0.051	1.112±0.091	0.758±0.040	2.004±0.075
GG	Dried root	0.148±0.004	0.166±0.005	1.403±0.005	0.985±0.035	3.694±0.181
AO	Fresh fruit	0.241±0.007	-	0.052±0.002	0.658±0.013	0.559±0.049
	Dried fruit	1.740±0.050	1.151±0.164	0.665±0.011	0.856±0.039	3.530±0.211
Ascorbic acid		0.008±0.000				

HE: Hexane extract, BE: Butanol extract, WE: Water part extract, EE: Ethyl acetate extract

Table 3: Anti-tyrosinase activities of various plant extracts

Plant	Part	IC_{50} of anti-tyrosinase (μg/ml)				
		ECE	HE	EE	BE	WE
AI	Fresh fruit peel	381.152±7.066	104.466±0.047	1.203±0.083	327.270±0.177	867.771±0.371
	Dried fruit peel	27.457±0.036	27.754±1.813	6.811±0.617	605.086±1.978	No inhibition
	Fresh fruit	No inhibition	No inhibition	No inhibition	No inhibition	No inhibition
AH	Fresh fruit peel	348.778±0.725	941.615±0.028	53.998±0.806	949.930±0.024	978.359±0.040
	Dried fruit peel	88.087±0.488	122.001±1.614	51.055±1.180	No inhibition	No inhibition
GA	Dried fruit	996.761±0.594	962.357±0.935	874.394±0.746	209.109±0.023	No inhibition
GG	Dried root	97.518±0.190	2.883±0.078	1.157±0.093	103.755±0.131	150.064±0.437
AO	Fresh fruit	103.045±0.832	-	93.7011±0.384	368.598±0.789	342.712±0.991
	Dried fruit	No inhibition	No inhibition	51.055±1.180	No inhibition	No inhibition
Kojic acid				27.293±0.986		

BE: Butanol extract, WE: Water part extract, EE: Ethyl acetate extract

superior activity with IC_{50} at 1.157 ± 0.093 μg/mL; the IC_{50} of EE from the fresh peel of AI and an HE of the dried GG root were 1.203 ± 0.083 μg/mL and 2.883 ± 0.078 μg/mL, respectively. Meanwhile, the standard kojic acid exhibited IC_{50} at 27.293 ± 0.986 μg/mL. Therefore, these extracts had superior anti-tyrosinase activity than the standard kojic acid. Each plant extract exhibiting the highest anti-tyrosinase activity was selected for further experiments to investigate their effect on the reduction of cellular melanin content.

Cellular Melanin Content

Various concentrations of selected plant extracts including EE of AI fresh fruit peel (AI-EE-P), EE of AH fresh fruit peel (AH-EE-P), EE of GG root (GG-EE-R), EE of AO fruit (AO-EE-F), BE of GA dried fruit (GA-BE-F), and kojic acid were tested for their inhibition of melanogenesis activity in melanoma cell line as shown in Figures 1 and 2; Table 4, respectively. GG-EE-R exhibited the most potent melanogenesis inhibition activity with EC_{50} at a concentration of 17.60 μg/mL. AI-EE-P and AH-EE-P also showed anti-melanogenesis activity with EC_{50} at concentrations of 35.93 μg/mL and 62.43 μg/mL, respectively. Meanwhile, GA-BE-F and AO-EE-F could not reduce cellular melanin content. This result was related to our *in vitro* anti-tyrosinase activity result.

Cell Viability

Various concentrations of selected plant extracts including EE of AI fresh fruit peel (AI-EE-P), EE of AH fresh fruit peel (AH-EE-P), EE of GG root (GG-EE-R), EE of AO fruit (AO-EE-F), BE of GA dried fruit (GA-BE-F), and kojic acid were tested for their cytotoxicity in melanoma cell lined by incubating cell with treatment for 72 h. The duration of treatment was the same as in the melanin content experiment therefore the result can be compared with two experiments. Percent cell viability is shown in Figure 3. It was found that the percent viability of kojic acid, AI-EE-P, and AO-EE-F was

Table 4: Slope, intercept, R^2, and EC_{50} for melanogenesis inhibition of samples calculated by linear regression equation

Sample	Slope	Intercept	R^2	EC_{50} (μg/mL)
AI-EE-P	−1.4976	103.78	0.9801	35.932
GG-EE-R	−5.421	145.43	0.9801	17.604
AH-EE-P	−1.2734	129.50	0.8918	62.431
Kojic acid	−0.1848	101.83	0.9858	280.465

AI: EE: Ethyl acetate extract

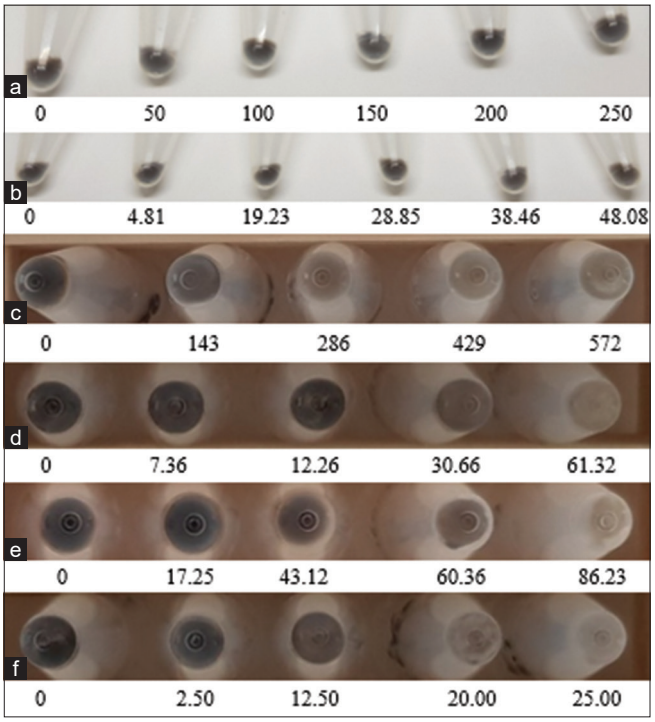


Figure 1: Melanin content inhibition of various concentrations (μg/mL) of *Garcinia atroviridis*-butanol extract-F (a), *Anacardium occidentale*-ethyl acetate extract (EE)-F (b), kojic acid (c), *Artocarpus integer*-EE-P (d), *Artocarpus heterophyllus*-EE-P (e), *Glycyrrhiza glabra*-EE-R (f)

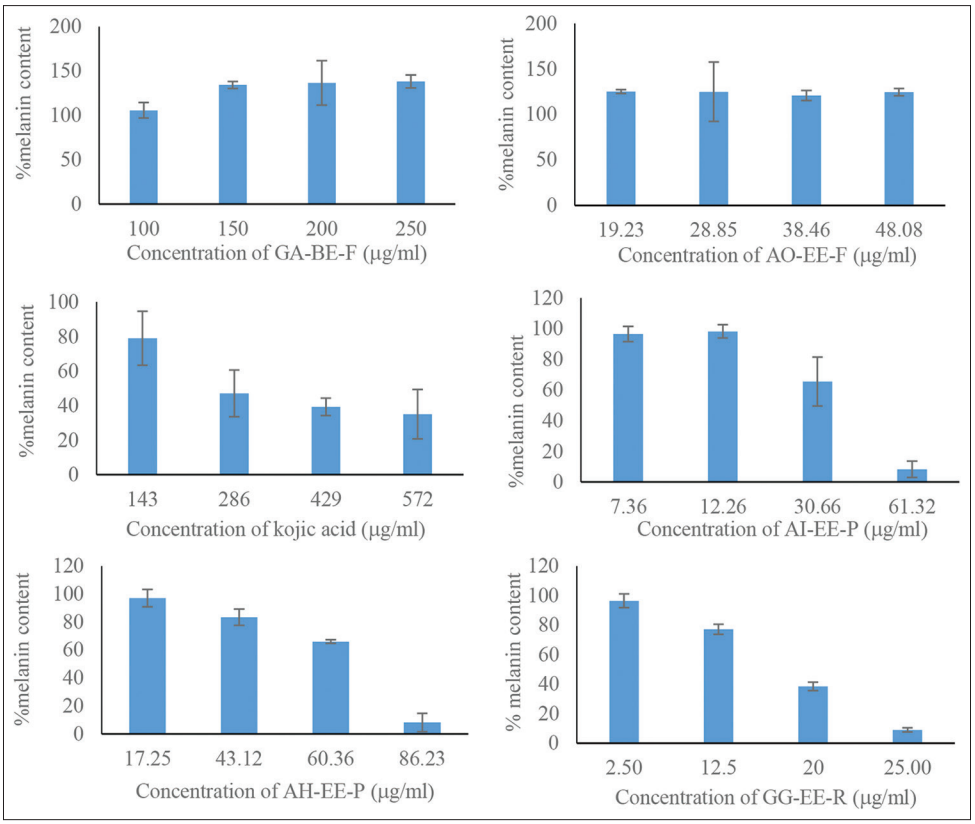


Figure 2: Percent of melanin content of cells treated with various concentrations (µg/mL) of extracts compared to control

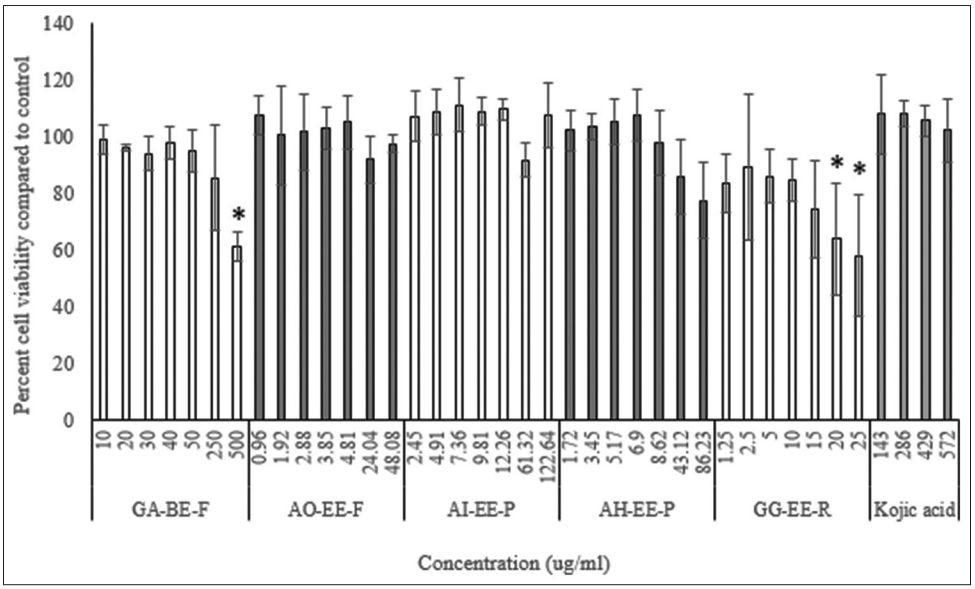


Figure 3: Cell viability of melanoma cell line B16F10 treated with various concentrations of selected extracts for 24 h. The percentage of cell viability is represented as means of three independent triplicate samples ± SE (*$P < 0.05$ when compared to control cells)

higher than 80% in all tested concentrations. However, AH-EE-P and GG-EE-R exhibited cell cytotoxicity at the effective dose. Cell cytotoxicity of GG-EE-R might result from its flavonoids. Glycyrrhetinic acid inhibited cell proliferation of B16 melanoma cells.[17] Isoliquiritigenin induced cell apoptosis of B16F10 melanoma cells.[18] Isoangustone A and glycyrrhizin suppressed the growth of human melanoma cells.[19] After the comparison of the results from all tests, AI-EE-P was a new potential skin-lightening active ingredient as its potential was superior to other extracts due to its anti-tyrosinase activity, anti-oxidant activity, and safety. Further studies on isolation and pharmacological activity investigation of active biomarkers of AI-EE-P should be further studied.

CONCLUSION

Extracts of different parts of five plants cultivated in Southern Thailand including AI Spreng., AH Lam., GA Griff. Ex T. Anderson, GG Linn., and AO L. were evaluated for their anti-tyrosinase, anti-melanogenesis, anti-oxidant activity, and cell toxicity. It was found that an ethanol-EE of AI peel could be used as an active ingredient in skin-lightening products as its potential was superior to other extracts due to its great anti-tyrosinase, anti-melanogenesis, and anti-oxidant activities, and safety.

ACKNOWLEDGMENTS

The researchers are very grateful to Phuket Abalone Co., Ltd., for its support in the direction trend of research in South-West Thailand. The researchers would like also to express their gratitude to the Research Development Institute, Phuket Rajabhat University, and the Research Institute, Rangsit University for their support of research facilities.

REFERENCES

1. Skin Lightening Products Market Size and Share Report; 2030. Available from: https://www.grandviewresearch.com/industry-analysis/skin-lightening-products-market [Last accessed on 2022 Sep 01].
2. Zhu W, Gao J. The use of botanical extracts as topical skin-lightening agents for the improvement of skin pigmentation disorders. J Investig Dermatol Symp Proc 2008;13:20-4.
3. Mukherjee PK, Biswas R, Sharma A, Banerjee S, Biswas S, Katiyar CK. Validation of medicinal herbs for anti-tyrosinase potential. J Herb Med 2018;14:1-16.
4. Kubo I, Kinst-Hori I, Yokokawa Y. Tyrosinase inhibitors from *Anacardium occidentale* fruits. J Nat Prod 1994;57:545-51.
5. Arung ET, Shimizu K, Kondo R. Inhibitory effect of artocarpanone from *Artocarpus heterophyllus* on melanin biosynthesis. Biol Pharm Bull 2006;29:1966-9.
6. Arung ET, Shimizu K, Tanaka H, Kondo R. 3-Prenyl luteolin, a new prenylated flavone with melanin biosynthesis inhibitory activity from wood of *Artocarpus heterophyllus*. Fitoterapia 2010;81:640-3.
7. Dej-Adisai S, Meechai I, Puripattanavong J, Kummee S. Antityrosinase and antimicrobial activities from Thai medicinal plants. Arch Pharm Res 2014;37:473-83.
8. Mackeen MM, Ali AM, Lajis NH, Kawazu K, Hassan Z, Amran M, *et al.* Antimicrobial, antioxidant, antitumour-promoting and cytotoxic activities of different plant part extracts of *Garcinia atroviridis* griff. ex *T. anders*. J Ethnopharmacol 2000;72:395-402.
9. Kang MH, Jang GY, Ji YJ, Lee JH, Choi SJ, Hyun TK, *et al.* Antioxidant and anti-melanogenic activities of heat-treated licorice (Wongam, *Glycyrrhiza glabra* × *G. uralensis*) extract. Curr Issues Mol Biol 2021;43:1171-87.
10. Pan C, Liu X, Zheng Y, Zhang Z, Li Y, Che B, *et al.* The mechanisms of melanogenesis inhibition by glabridin: Molecular docking, PKA/MITF and MAPK/MITF pathways. Food Sci Hum Wellness 2023;12:212-22.
11. Yokota T, Nishio H, Kubota Y, Mizoguchi M. The inhibitory effect of glabridin from licorice extracts on melanogenesis and inflammation. Pigment Cell Res 1998;11:355-61.
12. Cerulli A, Masullo M, Montoro P, Piacente S. Licorice (*Glycyrrhiza glabra*, *G. uralensis,* and *G. inflata*) and their constituents as active cosmeceutical ingredients. Cosmetics 2022;9:7.
13. Lourith N, Kanlayavattanakul M, Chanpirom S. Free radical scavenging efficacy of tamarind seed coat and its cosmetics application. J Health Res 2009;4:159-62.
14. Likhitwitayawuid K, Sritularak B, De-Eknamkul W. Tyrosinase inhibitors from *Artocarpus gomezianus*. Planta Med 2000;66:275-7.
15. Li L, Liu Y, Xue Y, Zhu J, Wang X, Dong Y. Preparation of a ferulic acid-phospholipid complex to improve solubility, dissolution, and B16F10 cellular melanogenesis inhibition activity. Chem Cent J 2017;11:26.
16. Chaikhumwang P, Nilubol D, Tantituvanont A, Chanvorachote P. A new cell-to-cell interaction model for epithelial microfold cell formation and the enhancing effect of epidermal growth factor. Eur J Pharm Sci 2017;106:49-61.
17. Abe H, Ohya N, Yamamoto KF, Shibuya T, Arichi S, Odashima S. Effects of glycyrrhizin and glycyrrhetinic acid on growth and melanogenesis in cultured B16 melanoma cells. Eur J Cancer Clin Oncol 1987;23:1549-55.
18. Wang Y, Ma J, Yan X, Chen X, Si L, Liu Y, *et al.* Isoliquiritigenin inhibits proliferation and induces apoptosis via alleviating hypoxia and reducing glycolysis in mouse melanoma B16F10 cells. Recent Pat Anticancer Drug Discov 2016;11:215-27.
19. Song NR, Lee E, Byun S, Kim JE, Mottamal M, Park JH, *et al.* Isoangustone A, a novel licorice compound, inhibits cell proliferation by targeting PI3K, MKK4, and MKK7 in human melanoma. Cancer Prev Res (Phila) 2013;6:1293-303.