

**Review Article**

# A review on tyrosinase inhibition potential of plant extracts for skin whitening

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**Abstract:** Fair skin is considered a trait of beauty in many cultures all over the world. Hence, there is an increased demand for skin whitening products. Since synthetic skin whitening products which are available in the market are associated with adverse effects, attention has shifted towards plant extracts with tyrosinase inhibitory potencies, as natural products are safe and effective. This study was conducted as a systematic review of plants with skin-whitening properties using a tyrosinase inhibitory assay. Research articles that were published between the years 2010-2021 were studied for this review article. The review was based on two inclusion criteria and two exclusion criteria. When it comes to inclusion criteria, tyrosinase inhibitory assay was used for extract assessment, and only the English articles were revised. The research papers that lack half maximal inhibitory concentration analysis were rejected, and only plant extracts were considered, while compounds were rejected. From a total of 70 articles that were studied, only 23 were considered relevant.  $IC_{50}$  values of tyrosinase inhibitory assay in different plant extracts were considered, and the details were tabulated. The highest tyrosinase inhibitory potency was recorded from the methanol extract of *Quercus infectoria* galls with an  $IC_{50}$  value of 3.34  $\mu\text{g/ml}$ , while the second highest tyrosinase inhibitory potency was recorded from the methanol extract of *Terminalia chebula* fruit with an  $IC_{50}$  value of 3.87  $\mu\text{g/ml}$ . The families Balanophoraceae and Caprifoliaceae showed high tyrosinase inhibitory potencies, while the families Sapotaceae, Clusiaceae, Fabaceae, Solanaceae, and Malvaceae showed moderate tyrosinase inhibitory potencies. Therefore, it can be concluded that the plants from the above-mentioned families possess active tyrosinase inhibition properties. It was also observed that even when comparing the same plant part of the same species when the polarity of the solvent used for extract preparation is low that the  $IC_{50}$  value tends to be high.

**Keywords:**  $IC_{50}$ , Plants, Tyrosinase inhibition.

## 1. Introduction

Skin whitening or skin lightening is the process of using synthetic or natural substances which can even lighten the skin tone. (Burger et al., 2016). The use of various substances to whiten the skin dates back to 3000 years ago when archaeologists found records of skin protection ointments in the pyramids of ancient Egypt. (Baditha et al., 2009). Even after all these years in many countries, white skin is considered a prized asset. Over the past years, an increasing trend in skin whitening has been observed in South Asian countries such as Sri Lanka, India, Pakistan, and Bangladesh. (Baditha et al., 2009).

Over the past years, the production and marketing of skin whitening products has become a multi-billion-dollar industry. (Aramide et al., 2019). Skin whitening is done for many reasons, including white supremacy, slavery, Eurocentric beauty standards, colonization, external racism by white people, internal racism by black people, and stereotyping of femininity and masculinity. (Aramide et al., 2019). Sources suggest that the belief in darker skin is associated with lower status and lesser beauty, resulting in feelings of poor identity, inferiority, and low self-esteem, which leads people towards skin whitening. (Lewis et al., 2011).

The primary determinant of skin color is called Melanin, which protects the skin by absorbing UV radiation.

(Liyanaarachchi et al., 2018). Melanin is produced through a process called melanogenesis, and Melanin is synthesized in the basal layer of the epidermis in the melanocytes. (Napagoda et al., 2018). Melanogenesis is initiated by an enzyme called tyrosinase. (Perera et al., 2017). Studies have proven that substances that possess the ability to inhibit the catalytic activity of tyrosinase can interrupt the synthesis and release of Melanin. Therefore, tyrosinase inhibition is a commonly used strategy in skin whitening. (Burger et al., 2016).

Synthetic skin whitening products available in the market contain various harmful compounds which can have adverse effects such as acne breakouts, uneven skin, and dullness. Long-term use of these products can lead to tumors, kidney diseases, and many undesirable effects. (Wijesekara and De Silva, 2019). Increased demand for whitening skin products has been observed across Asia, making identifying new compounds with skin-whitening properties necessary. (Perera et al., 2018). Skin whitening properties have been observed in both natural and artificial sources. Many natural sources such as plants, fungi, bacteria, and algae have proven to consist skin-whitening properties. Both medicinal and non-medicinal plants have proven to consist skin-whitening properties with low toxicity and high efficiency. (Hashemi and Zarei, 2014).



## 2. Methodology

This review article revises the published studies between the years 2010 to 2021. These were retrieved from the database Google Scholar using the keywords "Plants", "tyrosinase inhibitory assay" and "IC<sub>50</sub>".

The inclusion criteria used when assessing the articles was that the inhibitory activity of the extract had been determined by mushroom tyrosinase inhibitory assay, which is the currently accepted procedure for screening the skin-whitening properties of a certain extract or compound. Also, only the English research papers were revised. The research papers that lack half maximal inhibitory concentration or the analysis of the IC<sub>50</sub> values were rejected. Only the plant extracts were considered for this review study.

A total of 70 articles were studied, of which 23 were considered relevant for the data analysis based on the inclusion and exclusion criteria mentioned above. The IC<sub>50</sub> values of extracts were analyzed based on their inhibitory activity, starting with the highest inhibitory potency. The results were tabulated with the details, including the plant species, family name, the extract, and IC<sub>50</sub> value they possess.

The tables were tabulated based on the high potency (IC<sub>50</sub> < 20 µg/ml), moderate potency (20 µg/ml < IC<sub>50</sub> < 200 µg/ml), low potency (200 µg/ml < IC<sub>50</sub> < 1000 µg/ml) tyrosinase inhibitory activity.

## 3. Results and discussions

The plant extracts that showed IC<sub>50</sub> values less than 20 µg/ml in tyrosinase inhibitory assay were considered as plant extracts with high tyrosinase inhibitory potencies. The methanol extract of *Quercus infectoria* (Fagaceae) galls on leaves showed the highest tyrosinase inhibitory potency with an IC<sub>50</sub> value of 3.34 µg/ml. (Ansari et al., 2011). This plant is best suited to produce a skin whitening product such as a cream, a lotion, or a soap. Also, other plant species from the family Fagaceae might contain high tyrosinase inhibitory potencies, thus, effective skin whitening properties. The methanol extract of *Terminalia chebula* (Combretaceae) showed an IC<sub>50</sub> value of 3.87 µg/ml. (Ansari et al., 2011). Since the plant *Terminalia chebula* showed the second highest tyrosinase inhibitory potency, this plant might also be highly effective when it comes to skin whitening product development. Furthermore, other plant species from the family Combretaceae might contain high tyrosinase inhibitory potencies. The ethyl acetate of the *Balanophora laxiflora* (Balanophoraceae) plant showed an IC<sub>50</sub> value of 7.90 µg/ml. In contrast, the butanol extract of the plant showed an IC<sub>50</sub> value of 15.12 µg/ml (Hang et al., 2016). The flowers, leaves, and branches of the species *Lonicera japonica* (Caprifoliaceae) showed high tyrosinase inhibitory potencies. Because many plant parts from the species *Lonicera japonica* show high tyrosinase inhibitory potencies, this plant can be valuable for

skin whitening product development. Further studies are needed to evaluate the full potential of this plant. The aqueous extract of leaves of *Eugenia dysenterica* (Myrtaceae) showed a high tyrosinase inhibitory potency with an IC<sub>50</sub> value of 11.88 µg/ml. (Sauza et al., 2012). The aqueous extract of *Quercus infectoria* showed an IC<sub>50</sub> value of 14.7 µg/ml. (Ansari et al., 2011).

Even though the methanol extract of *Quercus infectoria* galls showed the highest tyrosinase inhibitory potency when considering the obtained results, it was observed that the aqueous extract of the *Quercus infectoria* galls gave a lesser tyrosinase inhibitory activity in comparison. Therefore, methanol extracts are more potent than aqueous extracts and, thus, more suitable for further research on the skin-whitening properties of plants and natural skin-whitening product development.

When considering the overall results, it was observed that the methanol extract of plants is more suitable for tyrosinase inhibitory assay since methanol extracts of plant parts show high tyrosinase inhibitory potencies. This can be due to the difference in polarities in organic solvents which are used for extract preparation. When considering the plant species mentioned above, many of these plants belong to the plant families Balanophoraceae and Caprifoliaceae. Therefore, these two plant families might contain high tyrosinase inhibitory potencies. Furthermore, other plant species which belong to the families mentioned above might possess high tyrosinase inhibitory potencies. When considering the evaluated plant parts, leaves and flowers had shown high tyrosinase inhibitory potencies. Therefore, leaves and flowers from plants that belong to the families Balanophoraceae and Caprifoliaceae might possess high tyrosinase inhibitory potencies, thus effective skin whitening properties. Moreover, once known for certain, if they contain skin-whitening properties, leaves and flowers from plants that belong to the above-mentioned families can be used for novel skin-whitening product development.

The plant extracts that showed IC<sub>50</sub> values within the range of (20 µg/ml < IC<sub>50</sub> < 200 µg/ml) in tyrosinase inhibitory assay were considered as plant extracts with moderate tyrosinase inhibitory potencies. When considering the moderate tyrosinase inhibitory potencies, *Pouteria torta* and *Pouteria caimito*, which belong to the family Sapotaceae, showed moderate tyrosinase inhibitory potencies. The aqueous extract of leaves of *Pouteria torta* showed an IC<sub>50</sub> value of 30.01 µg/ml, while the aqueous extract of leaves of *Pouteria caimito* showed an IC<sub>50</sub> value of 50.01 µg/ml. (Souza et al., 2012). The species *Garcinia atroviridis*, *Calophyllum symingtonianum*, and *Calophyllum depressinervosum*, which belong to the family Clusiaceae, showed moderate tyrosinase inhibitory potencies. The plant family Fabaceae showed moderate tyrosinase inhibitory potencies, whereas the species *Cassia auriculata*, *Stryphodendron adstringens*, *Saraca asoca* showed moderate tyrosinase inhibitory potencies. The methanolic hydro extract

**Table 1:** High tyrosinase inhibitory potencies of plant species ( $IC_{50} < 20 \mu\text{g/ml}$ )

Plant species	Family name	Extracts	Plant part	$IC_{50}$ ( $\mu\text{g/ml}$ )	Reference
<i>Quercus infectoria</i>	Fagaceae	Methanol	Galls on leaves	3.34	(Ansari et al., 2011)
<i>Terminalia chebula</i>	Combretaceae	Methanol	Fruit	3.87	(Ansari et al., 2011)
<i>Balanophora laxiflora</i>	Balanophoraceae	Ethyl acetate	Plant	7.90	(Hang et al., 2016)
<i>Crocus sativus</i>	Iridaceae	Methanol	Flower	10.78	(Sariri et al., 2011)
<i>Lonicera japonica</i>	Caprifoliaceae	Ethanol	Flower	11.16	(Dung et al., 2011)
<i>Eugenia dysenterica</i>	Myrtaceae	Aqueous	Leaves	11.88	(Sauza et al., 2012)
<i>Quercus infectoria</i>	Fagaceae	Aqueous	Galls	14.7	(Ansari et al., 2011)
<i>Balanophora laxiflora</i>	Balanophoraceae	Butanol	Plant	15.12	(Hang et al., 2016)
<i>Lonicera japonica</i>	Caprifoliaceae	Ethanol	Leaves	15.81	(Dung et al., 2011)
<i>Lonicera japonica</i>	Caprifoliaceae	Ethanol	Branches	17.18	(Dung et al., 2011)

**Table 2:** Moderate tyrosinase inhibitory potencies of plant species ( $20 \mu\text{g/ml} < IC_{50} < 200 \mu\text{g/ml}$ )

Plant species	Family name	Extracts	Plant part	$IC_{50}$ ( $\mu\text{g/ml}$ )	Reference
<i>Pouteria torta</i>	Sapotaceae	Aqueous	Leaves	30.01	(Sauza et al., 2012)
<i>Balanophora laxiflora</i>	Balanophoraceae	Hexane	Plant	31.81	(Hang et al., 2016)
<i>Stachys lavandulifolia</i>	Lamiaceae	Ethanol	Aerial parts	33.4	(Tundis et al., 2015)
<i>Garcinia atroviridis</i>	Clusiaceae	Aqueous	Fruit pericarp	40.72	(Chatatikun et al., 2020)
<i>Cassia auriculata</i>	Fabaceae	Hydro methanolic	Flower	42.49	(Napagoda et al., 2018)
<i>Stryphodendron adstringens</i>	Fabaceae	Ethanol	Bark stem	48.45	(Sauza et al., 2012)
<i>Pouteria caimito</i>	Sapotaceae	Aqueous	Leaves	50.01	(Sauza et al., 2012)
<i>Stachys lavandulifolia</i>	Lamiaceae	Methanol	Aerial parts	51.8	(Tundis et al., 2015)
<i>Eugenia dysenterica</i>	Myrtaceae	Ethanol	Leaves	51.54	(Sauza et al., 2012)
<i>Saraca asoca</i>	Fabaceae	Methanol	Leaves	53.5	(Perera et al., 2017)
<i>Saraca asoca</i>	Fabaceae	Methanol	Seed	54.2	(Perera et al., 2017)
<i>Bergenia pacumbis</i>	Saxifragaceae	Methanol	Plant	58.25	(Pandey et al., 2020)
<i>Stachys lavandulifolia</i>	Lamiaceae	Dichloromethane	Aerial parts	64.3	(Tundis et al., 2015)
<i>Lycopersicon esculentum</i> (Var. Eva F1)	Solanaceae	Methanol	Leaves	65	(Omotoyinbo et al., 2020)
<i>Calophyllum symingtonianum</i>	Clusiaceae	Dichloromethane	Heartwood	65.08	(Aminudin et al., 2015)
<i>Saraca asoca</i>	Fabaceae	Methanol	Bark	75.5	(Perera et al., 2017)
<i>Ficus erecta</i>	Moraceae	Ethyl acetate	Branch	75.7	(Park et al., 2012)
<i>Physalis alkekengi</i>	Solanaceae	Ethanol	Aerial parts	90	(Namjoyan et al., 2015)
<i>Calophyllum symingtonianum</i>	Clusiaceae	Methanol	Heartwood	96.31	(Aminudin et al., 2015)
<i>Calophyllum depressinervosum</i>	Clusiaceae	Dichloromethane	Stem bark	98.90	(Aminudin et al., 2015)
<i>Calophyllum symingtonianum</i>	Clusiaceae	Dichloromethane	Leaves	99.88	(Aminudin et al., 2015)
<i>Pouteria torta</i>	Sapotaceae	Ethanol	Fruit peel	104.34	(Sauza et al., 2012)
<i>Citrus sinensis</i> Osbeck cv Newhall	Rutaceae	Ethyl acetate	Peel	108.24	(Guo et al., 2020)
<i>Balanophora laxiflora</i>	Balanophoraceae	Aqueous	Plant	128.42	(Hang et al., 2016)
<i>Hibiscus tiliaceus</i>	Malvaceae	Dichloromethane	Leaves	130	(Lim et al., 2011)
<i>Hancornia speciosa</i>	Apocynaceae	Hexane	Leaves	146.60	(Sauza et al., 2012)
<i>Rhizophora mucronata</i>	Rhizophoraceae	Dichloromethane	Leaves	150	(Lim et al., 2011)
<i>Eugenia dysenterica</i>	Myrtaceae	Hexane	Leaves	151.37	(Sauza et al., 2012)
<i>Bergenia pacumbis</i>	Saxifragaceae	Aqueous	Plant	168.81	(Pandey et al., 2020)
<i>Thespesia populnea</i>	Malvaceae	Methanol	Bark	190	(Perera et al., 2018)
<i>Lycopersicon esculentum</i> (Var. Hausa)	Solanaceae	Methanol	Leaves	198	(Omotoyinbo et al., 2020)

of flowers of *Cassia auriculata* showed an  $IC_{50}$  value of 42.49  $\mu\text{g/ml}$ . (Napagoda et al., 2018) The methanol

**Table 3:** Moderate tyrosinase inhibitory potencies of plant species (200 µg/ml < IC<sub>50</sub> < 1000 µg/ml)

Plant species	Family name	Extracts	Plant part	IC <sub>50</sub> (µg/ml)	Reference
<i>Blumea balsamifera</i>	Asteraceae	Ethyl acetate	Leaves	206	(Saewan et al., 2011)
<i>Pouteria ramiflora</i>	Sapotaceae	Ethanol	Leaves	249.83	(Souza et al., 2012)
<i>Citrus sinensis</i> Osbeck cv Newhall	Rutaceae	Petroleum ether	Peel	250.31	(Guo et al., 2020)
<i>Phyllanthus emblica</i>	Phyllanthaceae	Methanol	Fruit	251	(Perera et al., 2018)
<i>Pouteria torta</i>	Sapotaceae	Ethanol	leaves	258.53	(Souza et al., 2012)
<i>Stachys lavandulifolia</i>	Lamiaceae	Hexane	Aerial parts	272.7	(Tundis et al., 2015)
<i>Rhizophora apiculata</i>	Rhizophoraceae	Methanol	Leaves	280	(Lim et al., 2021)
<i>Bergenia pacumbis</i>	Saxifragaceae	Ethyl acetate	Plant	280.36	(Pandey et al., 2020)
<i>Codariocalyx motorius</i>	Fabaceae	Methanol	Leaves	282.29	(Wijesekara and De Silva, 2019)
<i>Polygonum sachalinense</i>	Polygonaceae	Methanol	Root	289	(Choi et al., 2020)
<i>Citrus sinensis</i> Osbeck cv Newhall	Rutaceae	Ethanol	Peel	290.07	(Guo et al., 2020)
<i>Polygonum sachalinense</i>	Polygonaceae	Methanol	Fruit	308.8	(Choi et al., 2020)
<i>Blumea balsamifera</i>	Asteraceae	Hexane	leaves	319	(Saewan et al., 2011)
<i>Blumea balsamifera</i>	Asteraceae	Aqueous	Leaves	345	(Saewan et al., 2011)
<i>Citrus sinensis</i> Osbeck cv Newhall	Rutaceae	Aqueous	Peel	360.95	(Guo et al., 2020)
<i>Genipa americana</i>	Rubiaceae	Hexane	Fruit	361.23	(Souza et al., 2012)
<i>Syzygium grande</i>	Myrtaceae	Acetone	Leaves	380	(Lim et al., 2021)
<i>Alcea rosea</i>	Malvaceae	Ethanol	Aerial parts	380	(Namjoyan et al., 2015)
<i>Syzygium grande</i>	Myrtaceae	Dichloromethane	Leaves	440	(Lim et al., 2021)
<i>Persicaria sieboldi</i>	Polygonaceae	Methanol	Fruit	445.4	(Choi et al., 2020)
<i>Hibiscus tiliaceus</i>	Malvaceae	Methanol	leaves	460	(Lim et al., 2021)
<i>Syzygium grande</i>	Myrtaceae	Methanol	Leaves	480	(Lim et al., 2021)
<i>Polygonum cuspidata</i>	Polygonaceae	methanol	Seed	483.9	(Choi et al., 2020)
<i>Fragaria ananassa</i>	Rosaceae	Ethanol	Fruit	492.68	(Lukitaningsih et al., 2020)
<i>Tagetes erecta</i>	Asteraceae	Ethyl acetate	Flower	509.43	(Phrutivorapongkul et al., 2013)
<i>Hibiscus tiliaceus</i>	Malvaceae	Acetone	Leaves	540	(Lim et al., 2021)
<i>Sonneratia alba</i>	Lythraceae	Acetone	Leaves	550	(Lim et al., 2021)
<i>Polygonum alpinum</i>	Polygonaceae	Methanol	Aerial parts	564.8	(Choi et al., 2020)
<i>Sonneratia alba</i>	Lythraceae	Dichloromethane	Leaves	600	(Lim et al., 2021)
<i>Rhizophora apiculata</i>	Rhizophoraceae	Dichloromethane	Leaves	600	(Lim et al., 2021)
<i>Prunus spinosa</i> L	Rosaceae	Methanol	Fruit	636.51	(Stankovic et al., 2019)
<i>Rhizophora apiculata</i>	Rhizophoraceae	Acetone	Leaves	640	(Lim et al., 2021)
<i>Sonneratia alba</i>	Lythraceae	Methanol	Leaves	650	(Lim et al., 2021)
<i>Rhizophora mucronata</i>	Rhizophoraceae	Acetone	Leaves	660	(Lim et al., 2021)
<i>Rhizophora mucronata</i>	Rhizophoraceae	Methanol	Leaves	790	(Lim et al., 2021)
<i>Prunus spinosa</i> L	Rosaceae	Ethanol	Fruit	865.68	(Stankovic et al., 2019)
<i>Prunus spinosa</i> L	Rosaceae	Aqueous	Fruit	982.40	(Stankovic et al., 2019)

extract of leaves of *Saraca asoca* showed an IC<sub>50</sub> value of 53.5 µg/ml. (Perera et al., 2017).

When it comes to the family Solanaceae, the species *Lycopersicon esculentum* and *Physalis alkekengi* showed moderate tyrosinase inhibitory potencies. Under the species *Lycopersicon esculentum*, the varieties Eva F1 and Hausa were considered. When comparing the two varieties, Eva F1 variety showed a high tyrosinase inhibitory potency with the IC<sub>50</sub> value of 65 µg/ml for methanol extract of the leaves. (Omatoyinbo et al., 2020). In the family Malvaceae, the species *Thespesia populnea*

and *Hibiscus tiliaceus* showed moderate tyrosinase inhibitory potencies, where methanol extract of *Thespesia populnea* bark showed the IC<sub>50</sub> value of 190 µg/ml (Perera et al., 2018) while the dichloromethane extract of leaves of *Hibiscus tiliaceus* showed the IC<sub>50</sub> value of 130 µg/ml. (Lim et al., 2021). Since the leaves and fruit peel of *Pouteria torta*, as well as leaves, seeds, and bark of *Saraca asoca*, showed moderate tyrosinase inhibitory potencies, these two plant species contain considerable skin whitening properties; thus, these two species can be used for product development in skin whitening products. When considering the families these plants be-

long to, it was observed that many plants with moderate tyrosinase inhibitory potency belong to the families of Sapotaceae, Clusiaceae, Fabaceae, Solanaceae, and Malvaceae. Therefore, the above-mentioned families contain considerable skin-whitening properties.

Furthermore, other plant species belonging to the above-mentioned plant families might also contain many skin-whitening properties. When considering the plant parts, leaves contain a considerable amount of tyrosinase inhibitory potency in many plant species. Therefore, the leaves show higher tyrosinase inhibitory potency and skin-whitening properties compared to other plant parts. The plant species' aerial parts, bark stem, bark, and fruit peel also showed many skin-whitening properties. Given that, leaves from plants that belong to families Sapotaceae, Clusiaceae, Fabaceae, Solanaceae, and Malvaceae might contain moderate or even high tyrosinase inhibitory properties, thus skin whitening properties. Leaves from the plants belonging to the above-mentioned families can be used to produce skin-whitening products.

The plant extracts that showed  $IC_{50}$  values within the range of ( $200 \mu\text{g/ml} < IC_{50} < 1000 \mu\text{g/ml}$ ) in tyrosinase inhibitory assay were considered as plant extracts with low tyrosinase inhibitory potencies. *Blumea balsamifera* and *Tagetes erecta*, which belong to the family Asteraceae showed low tyrosinase inhibitory potencies. When considering the family Sapotaceae, the species *Pouteria ramiflora* and *Pouteria torta* were evaluated for their tyrosinase inhibitory potencies. When comparing the two varieties, the species *Pouteria ramiflora* showed a high tyrosinase inhibitory potency compared with the ethanol extract of leaves showing the  $IC_{50}$  value of  $249.83 \mu\text{g/ml}$ . In contrast, the ethanol extract of the *Pouteria torta* leaves showed an  $IC_{50}$  value of  $258.53 \mu\text{g/ml}$ . (Souza et al., 2012). The petroleum ether extract of *Citrus sinensis* Osbeck cv Newhall (Rutaceae) peel showed an  $IC_{50}$  value of  $250.31 \mu\text{g/ml}$ .

The ethanol extract of the peel and the aqueous extract of the peel showed significantly lower  $IC_{50}$  values than the petroleum ether extract. (Guo et al., 2020). This can be due to the polarities of the solvent, where petroleum ether has significantly less polarity (non-polar) when compared to the other two solvents. Ethanol has a polarity less than water but higher than petroleum ether. Therefore, the ethanol extract of the *Citrus sinensis* peel showed an  $IC_{50}$  value higher than the aqueous extract but lesser than the petroleum ether extract. This theory about less polarity of the organic solvent correlating with a higher  $IC_{50}$  value can be proven further, where the acetone extract of *Sonneratia alba* (Lythraceae) leaves showed the  $IC_{50}$  value of  $550 \mu\text{g/ml}$ .

In comparison, the methanol extract of *Sonneratia alba* leaves showed an  $IC_{50}$  value of  $650 \mu\text{g/ml}$ . (Lim et al., 2021). Acetone has a lesser polarity than methanol; thus, it gave a high  $IC_{50}$  value even for the same

plant part of the same species. In the family Rhizophoraceae, *Rhizophora apiculata*, and *Rhizophora mucronata* species were evaluated for their tyrosinase inhibitory potencies. When comparing the two species, *Rhizophora apiculata* showed considerably high tyrosinase inhibitory potencies in comparison to *Rhizophora mucronata* where the methanol extract of *Rhizophora apiculata* leaves showed the  $IC_{50}$  value of  $280 \mu\text{g/ml}$ . In contrast, the methanol extract of *Rhizophora mucronata* showed an  $IC_{50}$  value of  $790 \mu\text{g/ml}$  (Lim et al., 2021).

The majority of plants that showed low tyrosinase inhibitory potencies belong to the family Polygonaceae, where four species, namely, *Polygonum sachalinense*, *Persicaria sieboldi*, *Polygonum alpinum* and *Polygonum cuspidata* were evaluated for tyrosinase inhibitory potencies. When comparing the tyrosinase inhibitory potencies of those above-mentioned four plants the species *Polygonum sachalinense* showed significantly high tyrosinase inhibitory potencies in comparison to other species from the family Polygonaceae. In the family Malvaceae, the species *Alcea rosea* and *Hibiscus tiliaceus* were evaluated for tyrosinase inhibitory potencies. When considering the family Rosaceae, the species *Fragaria ananassa* and *Prunus spinosa* L were evaluated for tyrosinase inhibitory potencies, where the species showed low tyrosinase inhibitory potencies. The methanol extract of the fruit of the *Prunus spinosa* L showed an  $IC_{50}$  value of  $636.51 \mu\text{g/ml}$ .

When considering plant families these plant species belong to many of these plants belong to the family Polygonaceae. Therefore, other plant species that belong to the family Polygonaceae might have low yet considerable tyrosinase inhibitory activities, thus skin whitening properties. More research is needed on this matter, and once known, certain plants from the family Polygonaceae can be used for product development on skin whitening products. Furthermore, the families Asteraceae, Sapotaceae, Rhizophoraceae, Malvaceae, and Rosaceae also showed a considerable number of plants with tyrosinase inhibitory potency.

So, the other plants which belong to the above-mentioned families might contain tyrosinase inhibitory potencies. When considering the plant parts, leaves contain a considerable amount of tyrosinase inhibitory potency in many plant species. Due to that observation, leaves tend to have considerable tyrosinase inhibitory potencies in plants.

Furthermore, leaves from plants that belong to families Polygonaceae, Asteraceae, Sapotaceae, Rhizophoraceae, Malvaceae, and Rosaceae might possess tyrosinase inhibitory activities, which might lead to the development of novel skin whitening products. Even though not as much as leaves, both fruits and aerial parts of the plants considered showed considerable tyrosinase inhibitory potency. Therefore, the fruits and aerial parts from plants that belong to the above-mentioned families might possess tyrosinase inhibitory activities. This area requires

more studies which might lead to the development of natural skin whitening products with fewer adverse effects and better safety.

#### 4. Conclusion

When considering the analyzed data, it was observed that the majority of the plants reviewed contained moderate or low tyrosinase inhibitory potencies. The highest tyrosinase inhibitory potency was recorded from the methanol extract of *Quercus infectoria* galls on leaves with the IC<sub>50</sub> value of 3.34 µg/ml. In comparison, the second-highest tyrosinase inhibitory potency was recorded from the methanol extract of *Terminalia chebula* fruit with an IC<sub>50</sub> value of 3.87 µg/ml. The species *Quercus infectoria* is the best plant species that can be used to develop skin whitening products. The species *Quercus infectoria* belongs to the family Fagaceae. Hence, the family Fagaceae needs more attention and research, which will help develop novel skin-whitening products.

Furthermore, the families Balanophoraceae and Caprifoliaceae showed high tyrosinase inhibitory potencies. The families Sapotaceae, Clusiaceae, Fabaceae, Solanaceae, and Malvaceae showed moderate tyrosinase inhibitory potencies. Therefore, further research is required on other plants belonging to the families mentioned above as they might also contain considerable tyrosinase inhibitory potencies. In all plants, the leaves showed higher, if not considerable, tyrosinase inhibitory potencies, thus skin whitening properties. It was also observed that even when comparing the same plant part of the same species when the polarity of the solvent used for extract preparation is low, the IC<sub>50</sub> value tends to be high. Since many plant parts of the species *Lonicera Japonica*, *Pouteria torta*, and *Saraca asoca*, including flowers, leaves, and branches of *Lonicera Japonica*, leaves and fruit peel of *Pouteria torta* and leaves, seed, the bark of *Saraca asoca* showed tyrosinase inhibitory potencies these species need to be more attentive.

#### References

- Aminudin, N.I., Ahmad, F. and Taher, M., 2015. In vitro antioxidant, cholinesterase and tyrosinase inhibitory activities of *Calophyllum symingtonianum* and *Calophyllum depressinervosum* (Guttiferae). *Journal of Coastal Life Medicine*, 3(2):126-131.
- Ansari, M., Etelaie, F. and Sharififar, F., 2011. Tyrosinase kinetic in the presence of three inhibitory medicinal plants. *International Journal of Green Pharmacy (IJGP)*, 5(2):103-106.
- Aramide, k.O., Olatunji, O. and Ayandele, O. (2019). Health information literacy on the risks of using skin bleaching products. *International Journal of e-healthcare Information Systems*, 6(1):159-163.
- Baditha, S., Shin, J. and Kim, E. (2009). Potential Skin Whitening Agents of Natural Origin from South Asian Region. *Journal of Society of Cosmetic Scientist of Korea*, 35(1):1-9.
- Burger, P., Landreau, A., Azoulay, S., Michel, T. and Fernandez, X. (2016). Skin Whitening Cosmetics: Feedback and Challenges in the Development of Natural Skin Lighteners. *Cosmetics*, 3(36):1-24.
- Chatatikun, M., Supjaroen, P., Promlat, P., Chantarangkul, C., Waranuntakul, S., Nawarat, J., Tangpong, J. and Chiabchalard, A. (2020). Antioxidant and Tyrosinase Inhibitory Properties of an Aqueous Extracts of *Gracinia atroviridis* Griff.ex.T.Anderson Fruit Pericarps. *Pharmacognosy Journal*, 12(1):71-78.
- Choi, Y., Lee, J., Lee, J., Jung, Y., Jeong, W., Hong, S., Cho, Y. and Choi, C. (2020). Skin-Related Properties and Constituents from the Aerial Parts Extracts of *Persicaria senticosa*. *Oxidative Medicine and Cellular Longevity*, 2020:1-9.
- Dung, N., Bajpai, V., Rahman, A., Yoon, J. and Kang, S. (2011). Phenolic Contents, Antioxidants and Tyrosinase Inhibitory Activities of *Lonicera japonica* Thumb. *Journal of Food Biochemistry*, 35:148-160.
- Guo, C., Shan, Y., Yang, Z., Zhang, L., Ling, W., Liang, Y., Ouyang, Z., Zhong, B. and Zhang, J. (2020). Chemical composition, antioxidant, antibacterial and tyrosinase inhibition activity of extracts from Newhall naval orange (*Citrus sinensis* Osbeck cv.Newhall) peel. *Journal of the Science of Food and Agriculture*, 100:2664-2674.
- Hang, T., Quyen, T., Huy, N. and Hoa, L. (2016). Second Metabolic Composition, Antioxidative, Tyrosinase inhibitory, Antibacterial and Anticancer Activity of *Balanophora laxiflora* Extract. *VNU Journal of Science: Natural Science and Technology*, 32(2):6-14.
- Hashemi, F., and Zarei, M.A. (2014). Tyrosinase inhibitory activity within hexane extract of ten screened plants from Kurdistan province of Iran. *International Journal of Advanced Biological and Biomedical Research*, 2(11), 2795-2799.
- Lewis, K.M., Robkin, N., Gaska, K. and Njoki, L.C. (2011). Investigating motivations for women's skin bleaching in Tanzania. *Psychology of Women Quarterly*, 35(1):29-37.
- Lim, W., Chan, E., Phan, C. and Wong, C. (2021). Tyrosinase Inhibiting extracts from Coastal Plants as Potential Additives in Skin Whitening Formulations. *Current Applied Science and Technology*, 21(3):481-494.
- Liyanaarachchi, G.D., Samarasekera, J.K.R.R., Mahanama, K.R.R., and Hemalal, K.D.P. (2018). Tyrosinase, elastase, hyaluronidase inhibitory and antioxidant activity of Sri Lanka medicinal plants for novel cosmeceuticals. *Industrial Crops and Products*, 111, 597-605.

- Lukitaningsih, E., Nur, S., Qonithah, F., Zulbayu, A., Kuswahyuning, R. and Rumiati. (2020). In vitro Anti-Wrinkle and Tyrosinase Inhibitory Activities of Grapefruit Peel and Strawberry Extracts. *Traditional Medicine Journal*, 25(3):180-187.
- Namjoyan, F., Jahangiri, A., Azemi, M., Arkian, E. and Mousavi, H. (2015). Inhibitory Effects of *Physalis alkekengi* L., *Alcea rosea* L., *Bunium persicum* B.Fedstch. and *Marrunium vulgare* L. on Mushroom Tyrosinase. *Jundishapur Journal of Natural Pharmaceutical Products*, 10(1):1-6.
- Napagoda, M., Kumari, M., Qader, M., Soyza, S. and Jayasinghe, L. (2018). Evolution of tyrosinase inhibitory potential in flowers of *Casila auriculata* L. for the development of natural skin whitening formulation. *European Journal of Integrative Medicine*, 21:39-42.
- Omotoyinbo, O., Awojulu, E. and Sanni, D. (2020). Phytochemical screening, antioxidant and tyrosinase inhibitory studies of methanol leaf extracts of two tomato varieties. *Highlights in Bioscience*, 3:1-7.
- Pandey, B., Pradhan, S., Adhikari, K. and Nepal, S. (2020). *Bergenia pacumbis* from Nepal, an astonishing enzyme inhibitor. *BMC Complementary Medicine and Therapies*, 20(198):1-12.
- Park, S., Oh, T., Kim, S., Kim, J., Lee, S. and Lee, N. (2012). Constituents with tyrosinase inhibitory activities from branched of *Ficus erecta* var. *sieboldii* king. *Journal of Enzyme Inhibition and Medicinal Chemistry*, 27(3):390-394.
- Perera, H., Pradeep, A., Devinda, K., Rathnayake, R. and Gunawardhana, D. (2017). Tyrosinase inhibitory effects of *Saraca asoca* bark, leaf, and seed. *Journal of Complementary Medicine and Alternative Healthcare*, 4(3):1-3.
- Perera, H., Pradeep, A., Devinda, K., Rathnayake, R., Gunawardhana, D. and Jayasinghe, J. (2018). Antityrosinase activities of *Thespesia populnea* bark and *Phyllanthus emblica* fruit. *Journal of advances in Medical and Pharmaceutical*, 16(3):1-8.
- Phrutivorapongkul, A., Kiattisin, K., Jantrawut, P., Chansakaow, S., Vejabhikul, S. and Leelapornpisid, P. (2013). Appraisal of biological activities and identification of phenolic compound of African marigold (*Tagetes erecta*) flower extract. *Pakistan Journal of Pharmaceutical Sciences*, 26(6):1071-1076.
- Saewan, N., Koysomboon, S. and Chantrapromma, K. (2011). Anti-tyrosinase and anti-cancer activities of flavonoids from *Blumea balsamifera* DC. *Journal of Medicinal Plants Research*, 5(6):1018-1025.
- Sariri, R., Sabbaghzadeh, R. and Poumohmad, F. (2011). In-vitro antioxidant and anti-tyrosinase activity of methanol extracts from *Crocus sativus* flowers. *Pharmacologyonline*, 3:1-11.
- Souza, P., Elias, S., Simeoni, L., Paula, J., Sueli, M., Guerra, E., Fonesca, Y., Silva, E., Silvera, D. and Magalhaes, P. (2012). Plants from Brazilian Cerrado with potent tyrosinase inhibitory activity. *PLOS ONE*, 7(11):1-7.
- Stankovic, M., Savic, V., Zivkovic, J., Tadic, V. and Arsic, I. (2019). Tyrosinase inhibitory and antioxidant activity of wild *Prunus spinosa* L. fruit extracts as natural source of bioactive compounds. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*, 47(3):651-657.
- Tundis, R., Bonsei, M., Pulgiese, A., Nadjafi, F., Menichini, F. and Loizzo, M. (2015). Tyrosinase, acetyl- and butyryl- cholinesterase inhibitory activity of *Stachys lavandulifolia* Vahl (Lamiaceae) and its major constituents. *Records of Natural Products*, 9(1):81-93.
- Wijesekara, K. and De Silva, W. (2019). Preliminary screening of telegraph (*Odariocalyx motorius*) plant extract for skin whitening property and anti-cytotoxicity activity. *GARI International Journal of Multidisciplinary Research*, 4(7):33-42.