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# Research Article
# Evaluation of Anti-Tyrosinase Activity of *Pyrus communis* Leaves Extract and Cosmetic Formulation

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## Abstract

**Background and Objective:** Melanin is the dark pigment created by melanocytes and skin whitening agents can influence different stages of melanin synthesis during melanogenesis. Many are acknowledged as tyrosinase competitive inhibitors. This study had three main objectives: First, to assess the anti-tyrosinase activity of an ethanolic extract derived from *Pyrus communis* leaves; second, to create a whitening cream using this extract and finally, to evaluate user satisfaction. **Materials and Methods:** A whitening cream containing 2% w/w *Pyrus communis* leaf extract was developed and tested on 25 volunteers for one month, with a comparison to a base cream. The findings indicated that the volunteers expressed a high level of satisfaction with the properties of the *Pyrus communis* leaves cream, including its moisturization, absorption, spreadability and texture while the satisfaction level for its odor properties was moderate. The overall preference for the *Pyrus communis* leaves cream was rated as high. **Results:** After one month of using the *Pyrus communis* leaves cream, an improvement in the volunteer's skin color was observed through a skin color bar assessment. The study used Mexameter® to measure skin melanin levels before applying creams and one month after usage. The findings indicated that the *Pyrus communis* leaves cream decreased melanin pigment by 35.47%. Importantly, none of the volunteers experienced any irritation during the testing period. **Conclusion:** *Pyrus communis* leaves extract has the potential to be utilized in the cosmetic industry for the formulation of natural whitening creams.

Key words: *Pyrus communis*, anti-tyrosinase, whitening cream, plant extract, melanin inhibitor

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

The skin, the body's largest organ, functions as a vital shield, separating the inner environment from the outside world. The outermost layer, known as the epidermis, acts as a waterproof protective barrier and constantly renews itself through a process called epidermal turnover. Within the epidermis, there are specialized cells called melanocytes that generate melanin, the pigment responsible for determining skin color[1]. Commercially available skin whitening solutions for cosmetic usage are available to achieve a lighter skin tone. They also help with the treatment of pigmentation issues like post-inflammatory hyperpigmentation and melasma. Hyperpigmentation occurs when there is an elevated production and buildup of melanin or an augmentation in the melanocyte count. Melanin is the dark pigment created by melanocytes and skin whitening agents can influence different stages of melanin synthesis during melanogenesis. Many are acknowledged as tyrosinase competitive inhibitors[2]. All skin types are susceptible to the common skin problem known as hyperpigmentation. This condition is marked by an elevated production and dispersion of melanin, the pigment responsible for the coloration of human skin. Many human cultures have hyperpigmentation, which includes skin conditions like melasma; many human cultures have hyperpigmentation, which includes skin conditions like age spots, sun lentigo, melisma and post-inflammatory hyperpigmentation[3]. Numerous depigmenting medications have been used to treat hyperpigmentation problems, including hydroquinone, arbutin, kojic acid and corticosteroids[4]. Numerous adverse effects, including contact dermatitis, sensitization and a mutagenic effect with prolonged exposure, are frequently reported for a number of these agents, despite their efficacy[5]. The study of natural products has led to the identification of numerous phytochemicals, such as licorice, polyphenols, flavonoids, arbutin, kojic acid, hesperidin and yeast derivatives, in the search for novel depigmenting with fewer side effects. Studies have demonstrated that plants are more effective melanogenesis inhibitors than arbutin, kojic acid and linoleic acid in the absence of melanocytotoxicity. Due to their role in preventing the formation of free radicals and reducing the production of oxidative enzymes like collagenase, elastase and tyrosinase, which typically cause the breakdown of the skin's extracellular matrix. These enzymes include inductive nitric oxide synthase, which is linked to inflammation and inflammatory disease. The enzyme that catalysis the most crucial step in melanin production is gaining popularity as a skin care ingredient[6]. As a result, there is an increasing desire to discover natural origins that can impede these enzymes and incorporate them as potential components in cosmetics. Ingredients in topical creams and lotions constitute an intriguing topic[7].

*Pyrus communis* is a member of the Rosaceae family with 3000 species and 110 genera. The plant commonly known as the European pear or common pear serves as a parent to numerous pear varieties cultivated for their fruit. It is also known as nashpati in Pakistan. It can tolerate temperatures as low as -290°C and requires at least 25 weeks without frost. *Pyrus communis* is native to Europe South of the Netherlands and to Southwestern Asia. It contains an abundance of fatty acids, folate, vitamin C, copper, potassium, tocochromanols, carotenoids, phytosterols and squalene. It was used in diabetes management. Its extract has the same beneficial effects on blood glucose as the normal. Additionally, it lowers elevated biochemical parameters such as triacylglycerol, LDL, VLDL and total cholesterol (TC) and maintains body weight[8]. *Pyrus communis* phytochemical analysis revealed the presence of 14.5 µg GAE $mg^{-1}$ phenolic acids, 10.3 µg CE $mg^{-1}$ flavonoids, 6.58 g/100 g alkaloids and 0.55 g/100 g saponins[9].

The purpose of this study was to evaluate the anti-tyrosinase activity of hydroalcoholic/fraction crude extract of *Pyrus communis* leaves and cosmetics formulation. The present research will help us to explore the various processes responsible for the efficacy of hydroalcoholic crude extract of *Pyrus communis* for anti-tyrosinase activity. This study will help us to screen phytochemicals and understand the effectiveness of new natural cosmetics products for the skin against tyrosinase so that people can have these natural cosmetics products at very low cost and it will also help to avoid other problems caused by synthetic cosmetics with strong formulation proves.

## MATERIALS AND METHODS

**Study area:** The study was conducted at Muhammad Institute of Medical and Allied Sciences, Multan, Pakistan. The total duration of the study was two months from July, 2023 to September, 2023.

**Chemicals:** Different chemicals such as alcohol, emulbase (Polyacrylamide and Laureth-7), cream flow (hydrogenated polydecene), propylene glycol, glycerol, preservative (concentrated paraben) and water were used in this study. The chemicals employed were of analytical quality and possessed the utmost purity.

**Instruments:** The electrical shaker, rotatory evaporator, electrical weighing balance, electrical grinder, Mexameter® MX18, Luschan's chromatic scale, incubator and hot air oven were used in this experimental method.

**Plant material collection:** Fresh *Pyrus communis* leaves, which have a long-standing reputation in traditional medicine, were gathered in the Hazara Region of Khyber Pakhtunkhwa. To ensure their authenticity, they were verified with the assistance of an expert botanist at Bahaudin Zakriya University's Department of Botany in Multan and a herbarium specimen was recorded. These freshly gathered leaves were then naturally dried in the shade. Before being transformed into a coarse powder using a specialized herbal grinder, any foreign substances or unwanted plant material were meticulously removed from the dried vegetation. The resulting crushed leaf powder was carefully stored in airtight containers until the extraction process.

**Preparation of crude extract:** To produce an alcoholic extract, 50 g of plant powder was socked in 200 mL of ethanol and the resulting mixture was stirred with an electronic shaker for 2 hrs for consecutive three days at a temperature between 20 and 25°C. After that mixture was filtered through Whatman filter paper and the filtrate was added to the rotatory evaporator to remove solvent. The obtained dry extract was kept at a temperature of 4°C until further use[2].

**Tyrosinase inhibition assay:** To assess the anti-tyrosinase activity of *Pyrus communis* leaf extract using an improved method, the experiment involved using L-Dopa as the substrate and kojic acid as the standard. In a 50 mm phosphate buffer at pH 6.8, one KU (1000 unit $mL^{-1}$) of mushroom tyrosinase was pre-incubated with different doses of *Pyrus communis* extract or kojic acid for 5 min. Then, L-Dopa (25 and 0.20 mM) was added to the reaction mixture, which was then incubated for 10 min at 37°C. The formation of DOPA chrome, detected by measuring absorbance at 475 nm, indicated the enzymatic process. The percentage inhibition of tyrosinase activity was calculated using the following formula[2]:

$$\text{Inhibition (\%)} = \frac{\text{A (475) control-A (475) sample}}{\text{A (475) control}} \times 100$$

**Formulation of whitening cream containing *Pyrus communis* leaves extract:** Table 1 showed the ingredients of the cream base and cream with *Pyrus communis* leaves extract. First of all cream flow and emulbase were mixed while being stirred to make a cream base. After that glycerol and propylene glycol were added and thoroughly mixed. After adding the preservative and color, water was added slowly while being continuously stirred. The process for making cream, including *Pyrus communis* leaves extract, was the same as for making the cream base, with the addition of an additional 2% w/w plant extract in the formula. Creams that were formulated were stored at ambient room temperature during the testing phase[2].

**Stability test:** To calculate the mechanical stress, the stability of the cream was tested by centrifugation at 4000 rpm and 20°C for 30 min. Additionally, stability testing was carried out at 4, 45°C and room temperature, as well as six heating/cooling cycles (45°C for 48 hrs followed by 4°C for 48 hrs for each cycle). The physiochemical appearance of the cream was assessed during stability testing, including any color or odor changes, pH, dye test, spreadability, homogeneity, appearance and removal[10].

**Subjects:** A total of twenty-five female volunteers (ages ranging from 20 to 25 years) were selected for the experimental study. The research was carried out following the endorsement of the Ethical Committee at the Muhammad Institute of Medical and Allied Sciences in Multan, Pakistan.

**Skin irritation test:** A closed patch test was performed to evaluate skin irritation. The test materials (cream base, *Pyrus communis* cream, *Pyrus communis* leaf extract and DI water) were evenly distributed on each aluminum disc and placed on the legs of volunteers. After 24 hrs of occlusion, the patches were removed to observe any inflammatory signs[2].

Table 1: Composition of the *Pyrus communis* extract-containing cream and the cream base

| Ingredients | Cream base (g) | *Pyrus communis* extract cream (g) |
|---|---|---|
| Emulbase (polyacrylamide and laureth-7) | 5.0 | 5.0 |
| Cream flow (hydrogenated polydecene) | 5.0 | 5.0 |
| *Pyrus communis* extract | - | 2.0 |
| Propylene glycol | 2.5 | 2.5 |
| Glycerol | 2.5 | 2.5 |
| Preservative (con.paraben) | 0.5 | 0.5 |
| Water | 84.5 | 82.5 |

**User satisfaction test:** In a randomized controlled study, 25 participants assessed their contentment with a cream containing *Pyrus communis* leaf extract against a standard cream. They were instructed to apply the standard cream to one leg and the extract-containing cream to the other leg twice daily for a month. Satisfaction levels were measured using categorized intervals: Low (scores between 1.81 and 2.60), medium (scores between 2.61 and 3.40), high (scores between 3.41 and 4.20) and very high (scores between 4.21 and 5.00)[2].

**Improvement of skin color level:** Volunteers' skin color was assessed using a modified version of Luschan's chromatic scale before and one month after applying the cream[2].

**Efficacy test:** Before assessing melanin pigment levels in the skin, the Mexameter® MX18 device was employed, which relies on the absorption and reflection of three distinct wavelengths (red: $\lambda = 660$ nm, infrared: $\lambda = 870$ nm and green: $\lambda = 568$ nm). The emitted light intensity was established, enabling the determination of the quantity of light absorbed by the skin, indicative of melanin pigment content. This measurement was conducted both before and after a one month application of topical cream.

**Statistical analysis:** The statistical analysis was done by using the Statistical Package for the Social Sciences (SPSS),version 10 for Windows. Viscosity data was analyzed by the use of a One-way Analysis of Variance (ANOVA) with Tukey's HSD test. Statistical significance was determined at $p \leq 0.05$.

## RESULTS

**Anti-tyrosinase activity assay:** The *Pyrus communis* leaves extract was examined for anti-tyrosinase activity compared with kojic acid. The $IC_{50}$ of kojic acid was 10.74 μg $mL^{-1}$ (Fig. 1) whereas, $IC_{50}$ of *Pyrus communis* leaves extract was 250.51 μg $mL^{-1}$ (Fig. 2) which was less effective than kojic acid (23.32 times).

**Stability testing:** The pH of the cream was found to be in the range of 6 to 6.7 which is good for skin pH. All prepared formulations produce uniformity of cream. Homogeneity was confirmed by appearance and by touch. When the formulation was kept for a long time, it found no change in the color of the cream. Emolliency, slipperiness and amount of residue left after the application of a fixed amount of cream were found. After application of the cream, the type of smear formed on the skin was non-greasy. The cream applied on the skin was easily removed by washing with tap water. Therefore, this cream could be stored long-term without any change in the physiochemical properties (Table 2).

**Irritation test:** Before launching new skincare products and ingredients, it is crucial to conduct tests for potential adverse skin reactions, such as irritation and allergies. In this context, a dermatological assessment was carried out to evaluate the irritation potential on human skin, ensuring consumer safety. The outcome indicated that none of the tested materials, including the cream base, *Pyrus communis* cream, crude extract and DI water, caused skin irritation under the specified testing conditions. Additionally, no volunteers reported any irritation during the testing period. Consequently, it can be inferred that the cream is likely to cause skin irritation when used as directed.

**User satisfaction test:** Twenty-five volunteers participated in a survey to assess their satisfaction with a cream they had used. The volunteer's satisfaction levels were measured using a 5-point Likert scale. Regarding the cream's physical appearance, the volunteers expressed a high level of satisfaction with its texture, while they rated the odor of the cream as moderately satisfying. However, their overall preference for the cream was rated as highly satisfying. When it came to the experience of using the cream, the volunteers were extremely satisfied with its spreadability. Furthermore, they found the cream's absorbability and moisturizing properties to be highly satisfying. In summary, the volunteers reported a high level of satisfaction with the cream. Additionally, there were no observed changes in the appearance of the extract-based cream of throughout a one month test. To enhance the product, it is suggested to consider adding fragrance for a more pleasant odor.

**Improvement of skin color level:** The research examined the improvement in skin tone by employing a skin color chart adapted from von Luschan's chromatic scale, both before and following the application of cream over the duration of one month. The scores were determined based on the degree of improvement in skin color. The findings demonstrated that *Pyrus communis* cream had a greater impact on improving skin color (with a difference of $1.85 \pm 0.93$) compared to the cream base (with a difference of $0.79 \pm 0.64$). In conclusion, the *Pyrus communis* extract cream exhibited a more pronounced whitening effect than the cream base and the majority of participants (86%) expressed satisfaction with the skin whitening properties of *Pyrus communis* cream compared to the cream base.

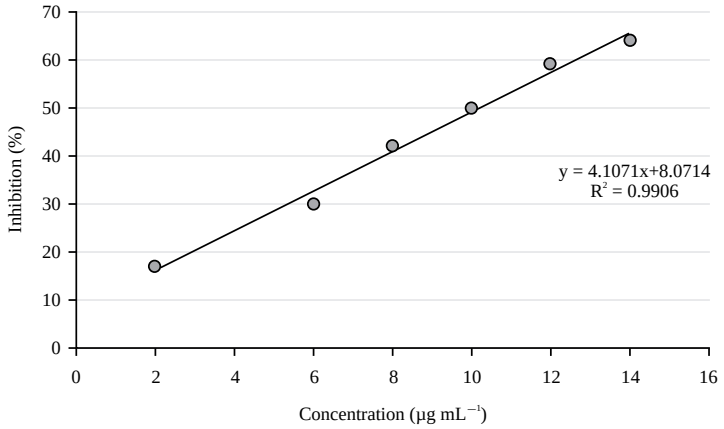


Fig. 1: Tyrosinase inhibitory activity of kojic acid at different concentrations

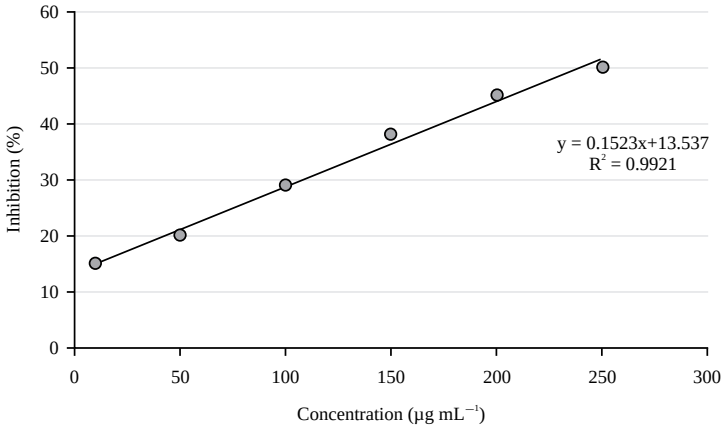


Fig. 2: Tyrosinase inhibitory activity of *Pyrus communis* leaves extract at different concentrations

Table 2: Stability test of the cream

| Days | Temperature | Formulation | pH | Xl | X2 | X3 | X4 | X5 | X6 |
|---|---|---|---|---|---|---|---|---|---|
| 0 | RT | Base cream | 6.2 | ** | NCC | ** | E | NG | ES |
| | | Extract cream | 6.3 | ** | NCC | ** | E | NG | ES |
| | 45°C+4°C | Base cream | 6.2 | ** | NCC | ** | E | NG | ES |
| | | Extract cream | 6.2 | ** | NCC | ** | E | NG | ES |
| 5 | RT | Base cream | 6.1 | ** | NCC | ** | E | NG | ES |
| | | Extract cream | 6.2 | ** | NCC | ** | E | NG | ES |
| | 45°C+4°C | Base cream | 6.2 | * | NCC | ** | E | NG | ES |
| | | Extract cream | 6.3 | ** | NCC | ** | E | NG | ES |
| 10 | RT | Base cream | 6.0 | ** | NCC | ** | E | NG | ES |
| | | Extract cream | 6.3 | ** | NCC | ** | E | NG | ES |
| | 45°C+4°C | Base cream | 6.2 | ** | NCC | ** | E | NG | ES |
| | | Extract cream | 6.3 | ** | NCC | ** | E | NG | ES |
| 15 | RT | Base cream | 6.7 | * | NCC | ** | E | NG | ES |
| | | Extract cream | 6.2 | ** | NCC | ** | E | NG | ES |
| | 45°C+4°C | Base cream | 6.1 | ** | NCC | ** | E | NG | ES |
| | | Extract cream | 6.3 | ** | NCC | ** | E | NG | ES |
| 20 | RT | Base cream | 6.2 | * | NCC | ** | E | NG | ES |
| | | Extract cream | 6.2 | ** | NCC | ** | E | NG | ES |
| | 45°C+4°C | Base cream | 6.0 | ** | NCC | ** | E | NG | ES |
| | | Extract cream | 6.2 | ** | NCC | ** | E | NG | ES |

X1: Homogeneity, X2: Appearance, X3: Spreadability, X4: After feel, X5: Type of smear, X6: Removal, *Satisfactory, **Good, E: Emollient, NG: Non-greasy, ES: Easy and NCC: No change in color

**Efficacy test using Mexameter®:** The research examined how applying both creams affected skin melanin production. Skin melanin levels were assessed using Mexameter® before and after one month of using two creams. The findings, given in arbitrary units, clearly showed that the creams had an impact on melanin levels. Specifically, after a month of using a standard cream, melanin content decreased from 185.7±1.4 to 162.4±1.6, indicating a reduction of 12.55%. In contrast, when *Pyrus communis* cream was used, melanin content decreased from 194±0.5 to 125.2±0.7, showing a more significant reduction of 35.47%. These findings lead to the conclusion that *Pyrus communis* cream had stronger skin whitening effects compared to the base cream.

## DISCUSSION

There is a growing interest in using natural products for cosmetics, particularly skin-whitening products, due to their ability to inhibit melanin synthesis. Various skin conditions, such as lentigo (flat brown spots), neurofibromatosis (congenital nodular lesions) and ephelis (freckles), are associated with localized hyperpigmentation. Hyperpigmentation can also cause inflammation e.g., acne and atopic dermatitis. Melasma is another source of hyperpigmentation which is localized at facial-hyper pigmentation appearing during pregnancy or hormone use[11]. Commercially available skin-whitening solutions for cosmetic usage are available to achieve a lighter skin tone. They also help with the treatment of pigmentation issues like post-inflammatory hyperpigmentation and melasma. Hyperpigmentation occurs when there is an elevated production and buildup of melanin or an augmentation in the melanocyte count[8].

Melanin is the dark pigment created by melanocytes and skin-whitening agents can influence different stages of melanin synthesis during melanogenesis. Many are acknowledged as tyrosinase competitive inhibitors[2]. Tyrosinase is an enzyme that activates the oxidation of tyrosine to DOPA and the production of dopaquinone. Whitening chemicals such as azelaic acid, hydroquinone, arbutin and kojic acid, are commonly used in cosmetics as acute ingredients[12]. Tyrosinase inhibitors are chemicals that can decrease enzymatic processes like browning in food and the formation of melanin in human skin. Consequently, these substances hold significant commercial promise in both the food processing and cosmetics sectors. The positive control in this study was the methanolic leaf extract of *Hibiscus tiliaceus*, chosen because it exhibited the most potent tyrosinase inhibition activity out of 39 medicinal plants analyzed by Masuda *et al.*[13]. Conversely, tyrosinase has a crucial function in regulating the synthesis of melanin[14]. Therefore, targeting tyrosinase has become crucial in the treatment of pigment-related disorders and the creation of novel skin-lightening products[15].

In addition, numerous plant extracts, such as *Glycyrrhiza glabra* or *Morus alba* L., inhibit melanin synthesis and are employed as whitening agents. Previous studies have shown that *Pyrus communis* contains antioxidants and anti-tyrosinase activity[16]. In melanin synthesis, tyrosinase is the rate-limiting enzyme (EC 1.14.1.18.1). This enzyme contains copper and plays a role in carrying out two hydroxylation reactions on tyrosine and oxidizing 3,4-dihydroxyphenylalanine (L-DOPA) into O-dopaquinone, which is its diphenolase activity. The oxidative polymerization of this dopaquinone derivative results in the production of melanin. Due to the central role of tyrosinase in the melanin pathway, tyrosinase inhibitors are gaining importance in the pharmaceutical and cosmetic industries as potent skin whitening agents for the treatment of skin disorders[17]. All skin types are susceptible to the common skin problem known as hyperpigmentation. It involves a rise in the generation and dispersal of melanin, the substance responsible for the coloration of human skin. Many human cultures have hyperpigmentation, which includes skin conditions like melisma, many human cultures have hyperpigmentation, which includes skin conditions like age spots, sun lentigo, melisma and post-inflammatory hyperpigmentation and post-inflammatory hyperpigmentation[3]. Numerous depigmenting medications have been used to treat hyperpigmentation problems, including hydroquinone, arbutin, kojic acid and corticosteroids[4]. The study of natural products has led to the identification of numerous phytochemicals, such as licorice, polyphenols, flavonoids, arbutin, kojic acid, hesperidin and yeast derivatives, in the search for novel depigmenting with fewer side effects.

Studies have demonstrated that plants are more effective melanogenesis inhibitors than arbutin, kojic acid and linoleic acid in the absence of melanocytoxicity. Due to their role in preventing the formation of free radicals and reducing the production of oxidative enzymes like collagenase, elastase and tyrosinase, which typically cause the breakdown of the skin's extracellular matrix. These enzymes include inductive nitric oxide synthase, which is linked to inflammation and inflammatory disease. The enzyme that catalysis the most crucial step in melanin production is gaining popularity as a skincare ingredient[6]. *Pyrus communis* (Rosaceae family) is commonly called European Pear (English), Nashpati (Urdu), Babu gosha and Naka. This fruit is commonly enjoyed in its fresh, canned, juiced or dried forms, offering valuable dietary fiber and vitamin C. Different components of the

*Pyrus communis* plant, including its leaves, bark, flowers and roots, exhibit anti-inflammatory properties against various diseases. The leaves contain a wealth of phytochemicals such as tannin, ursolic acid, astragalin, isoquercitrin, sorbitol and arbutin[18].

Arbutin is a naturally occurring compound with phenolic properties. It is employed in urinary therapy, acts as a skin whitening agent and has been observed to play a role in protecting against bacterial infections[19]. *Pyrus communis* is abundant in vitamin C, also known as ascorbic acid and serves as an antioxidant, combating reactive oxygen species. Its fruits provide ample pectins, which assist in regulating the body's ideal acid levels. It has been reported that *Pyrus communis* is a medicinal plant and it has several active constituents which are used for several diseases like diabetes[20]. The α-arbutin, also known as 4-hydroxy phenyl α-D-glucopyranoside, is a substance found in *Pyrus communis* that exhibits high tyrosine inhibition. It is considered the anomer of naturally occurring arbutin. The α-arbutin is a powerful melanin production inhibitor in human skin and it has been reported to be more effective at suppressing human tyrosine compared to arbutin, all without causing any side effects[21]. In the future, this study will help to prepare an efficient whitening cream at the commercial level with no side effects and lowest cost.

## CONCLUSION

The current research found that the crude extract from *Pyrus communis* leaves exhibited anti-tyrosinase effects and the ability to lighten the skin. This study highlights the potential benefits of utilizing pear leaves. However, more investigations are required to identify the specific active compounds in *Pyrus communis* leaves, which could potentially serve as novel ingredients for skin whitening agents in cosmetics.

## SIGNIFICANCE STATEMENT

The study of natural products had led to the identification of numerous phytochemicals, such as licorice, polyphenols, flavonoids, arbutin, Kojic acid and hesperidin and yeast derivatives, in the search for novel depigmenting with fewer side effects. The current research found that the crude extract from *Pyrus communis* leaves exhibited anti-tyrosinase effects and the ability to lighten the skin. This study highlights the potential benefits of utilizing pear leaves. However, more investigations are required to identify the specific active compounds in *Pyrus communis* leaves, which could potentially serve as novel ingredients for skin whitening agents in cosmetics.

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