A COMPARATIVE STUDY OF THE EFFICACY OF 4% WHITE RADISH ROOT EXTRACT CREAM VERSUS 2% ALPHA ARBUTIN CREAM IN FACIAL WHITENING

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MASTER OF SCIENCE
IN
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THIS THESIS IS A PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN DERMATOLOGY

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Wint Nandar Thein

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Author	Wint Nandar Thein
Degree	Master of Science (Dermatology)
Advisor	Professor Thamthiwat Nararatwanchai, Ph. D.
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ABSTRACT

Nowadays, fair skin is becoming popular among both men and women. The difference in skin color is due to the melanogenic activities in the melanocytes, the proportion of mature melanocytes and the distribution to the surrounding keratinocytes. The ability to control skin hyperpigmentation disorders is the most important research goals in cosmetic formulations. Currently, Alpha Arbutin is one of the most popular whitening ingredients in the world, it is used to treat many hyper pigmentation disorders. α-Arbutin has a high market value due to its wide applicability in the cosmetic and pharmaceutical industries.

In recent years, cosmetics containing herbal medicines and botanical ingredients are said to be safer than those containing synthetic ingredients and are attracting consumer interest. High quality studies with larger sample sizes are needed to confirm the safety and clinical efficacy of herbal medicines with high therapeutic indices. Previous studies have shown that radish root extract inhibits the tyrosinase enzyme, a key enzyme in melanogenesis, and it also has antioxidant properties. White radish is inexpensive and easy to grow in Thailand. The purpose of this study is to investigate the efficacy of radish root extract for facial whitening. Objective: To compare the facial whitening efficacy of a cream containing 4% radish root extract versus 2% alpha arbutin, which is widely recognized as a standard treatment for skin whitening.

In this study, a total of 24 volunteers between the ages of 20 and 50, men and women with Fitzpatrick II-V skin, diagnosed by a dermatologist who wanted to voluntarily whiten their face, were collected to participate in this study for 12 weeks.

White radish root extract 4% and 2% alpha-arbutin creams were instructed to apply twice daily to the entire face, parallel group study design for 12 weeks. Improvement was measured by Mexameter® MX18 and VISIA® analysis and the results were statistically analyzed. As a result, 4% white radish extract reduced the melanoma index after 12 weeks. No complications or side effects were noted during and after the study.

Keywords: 4% White Radish Extract Cream, Raphanus Sativus L, Tyrosinase Inhibitor, Skin Whitening

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CHAPTER 1

INTRODUCTION

1.1 Background

In today's world, people, particularly women, often use makeup as a means of expressing their modern sense of identity and independence. Cosmetics have become an essential part of modern women's lives, serving not only as a tool for self-expression but also to show respect and impress others. According to a recent study, the Thai cosmetics industry is expected to reach to a value of 10 billion USD in 2030, reflecting the increasing popularity of cosmetics among Thai consumers (Department of International Trade Promotion Ministry of Commerce, 2023).

Market research indicates that Asians, particularly women, prefer fair skin, which has contributed to the rising demand for skin-lightening products in the region. Whitening care has become an integral aspect of daily life for many women who are concerned about their beauty and appearance. The science behind skin lightening is complex, with factors such as genetics, sun exposure, blood circulation, skin trauma, diet, stress, and lifestyle all influencing skin tone. Moreover, skin tone serves as a critical protective barrier for the skin, which is highly resistant to the loss of this protection (Li et al., 2008).

Tyrosinase, a copper-containing glycoprotein found in the membranes of melanosomes, is a key enzyme in the melanogenesis pathway and plays a significant role in skin hyperpigmentation. As a result, tyrosinase inhibitors have become highly sought after in the cosmetic industry as depigmenting agents. One widely used tyrosinase inhibitor is Alpha arbutin, which is commonly incorporated into skin care products. The tyrosinase enzyme catalyzes two key reactions in melanin synthesis: the conversion of tyrosine to dopa through hydroxylation, and the oxidation of dopa to dopaquinone. Environmental and hormonal factors can further promote melanin synthesis (Solano et al., 2006).

Melanocytes produce melanin, the pigment responsible for skin color. Excess melanin accumulation not only alters the color of the skin but can also trigger skin issues such as age spots, solar keratosis, and melasma. To address these concerns, people use either synthetic substances or traditional plant-based remedies as skin whitening agents. Many of these agents are tyrosinase inhibitors, which target the key enzyme in melanogenesis. Melanosome transfer inhibitors, such as soy and niacinamide, also exhibit skin whitening effects by inhibiting the transfer of melanosomes from melanocytes to adjacent keratinocytes. Additionally, substances like retinoic acid can induce skin desquamation, helping to reduce excessive melanin content in the skin (Gillbro & Olsson, 2011).

Radishes (Raphanus sativus L.), traditionally known for their culinary uses, have long been recognized in East Asia for their medicinal properties. The root can be consumed raw, cooked, or pickled, and is used in traditional medicine to treat rheumatic pains, burns, and bruises. In Thailand, women have used fresh radish slices on their faces to treat melasma. Research has shown that radish extract possesses both anti-tyrosinase and antioxidant activities (Jakmatakul et al., 2009).

As public awareness of the complexities surrounding synthetic chemicals grows, the cosmetic industry is increasingly shifting towards natural, plant-based products as alternatives to traditional skin bleaching agents. The use of herbal remedies for skin whitening has become a global trend.

Recent studies have demonstrated that white radish extract cream significantly lightens skin with fewer side effects in vivo.

1.2 Research Question

Does 4% white radish extract cream have a better effect in facial skin whitening than 2% Alpha Arbutin cream?

1.3 Objectives

1.3.1 General Objective

To study the efficacy and satisfaction of 4% white radish extract cream for facial skin whitening while comparing with standard cream (2% alpha arbutin) in 20-50 years old people.

1.3.2 Specific Objective

1.3.2.1 Primary Outcome

To compare the effect of facial skin whitening between 4% white radish extract and 2% alpha arbutin in 20-50 years old, men and women.

1.3.2.2 Secondary Outcome

To discover the complications of 4% White Radish extract cream for whitening of facial skin.

1.4 Research Hypothesis

4% White Radish Extract Cream has better result than 2% Alpha Arbutin Cream for facial skin brightening.

1.5 Benefits

1.5.1 As a altrenative treatment for facial skin whitening

1.5.2 To record data for future research studies

1.6 Conceptual Framework

Tyrosinase inhibitors such as hydroquinone, melanocyte cytotoxic agents, and retinoids are currently used as skin lightening agents, most of which are synthetic chemicals. As a result, many unwanted complications have occurred. Therefore, dermatologists and scientists have sought to find a harmless and effective skin

lightening agent. Natural compounds have been proven to be safe and effective depigments. The white radish extract has been proven to have many skin benefits including whitening effect, antioxidant effect, UV protection effect and anti-inflammatory effect. This natural compound may be an alternative treatment for hyperpigmentation. Therefore, comparative study was performed for the future whitening agent that is more effective and safer.

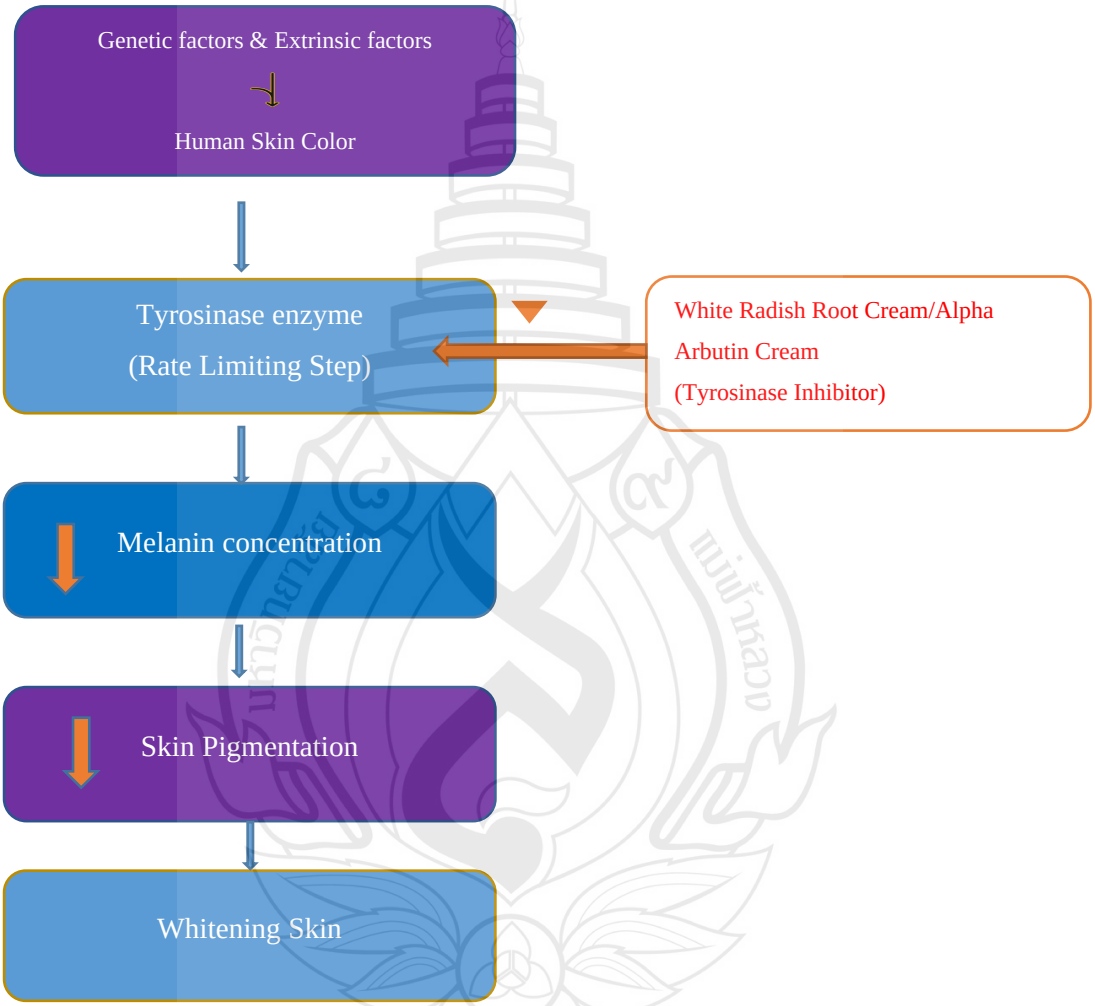


Figure 1.1 Conceptual framework

1.7 Scope of Research

24 volunteers of both male and female within the age range from 20 to 50 years old with Fitzpatrick skin type II-V were consulted with dermatologist researcher. Volunteers are selected through inclusion and exclusion criteria. By using randomization method,4% white radish extract cream and 2% Alpha Arbutin were applied on whole face according to assigned group. Apply respective cream twice daily for 12 weeks. In addition, subjects received sunscreen and a mild facial cleanser. At the beginning of the study, at weeks 4, 8 and 12, the subjects were examined on Mexameter® MX18 to determine mean and melanin values and compare images from the VISIA® analysis. Three dermatologists reviewed and analyzed the satisfaction scores and side effects recorded during the study period.

1.8 Limitation of the Study

The small sample size and short duration may limit the depth of the results,with a longer study potentially providing more definitive outcomes. Moreover, there was no strict control over factors such as sun exposure, sleep routines, health habits, age, and stress. These uncontrolled variables might lead to more prominent effects on the study's results.

1.9 Definitions

The Tyrosinase Enzyme is the Rate-Limiting Step Enzyme in Melanogenesis.

2% Alpha Arbutin Cream is a standard cream with anti-tyrosinase activity for whitening. Arbutin (hydroquinone-O-beta-D-glucopyranoside) is isolated from the fresh fruit of California horse chestnut and horse chestnut, which inhibits melanin synthesis by inhibiting tyrosinase activity.

4% White radish root extract Cream is a face cream containing 4% white radish root extract added in standard cream base approved by FDA.

Sunscreens are SPF 60, PA+++ creams that are applied to the skin to protect against the sun's harmful UV rays.

Satisfied means meeting expectations or needs

Efficacy is the extent to which an intervention produces the expected results under ideal conditions in a controlled environment.

Effect is the measurable impact or influence that one factor (cause, treatment, or condition) has on another variable within a research study, often used to test hypotheses about relationships or causality.

Complication refers to an unforeseen issue or complexity that interferes with the execution, analysis, or interpretation of a research study, potentially impacting its outcomes or validity.

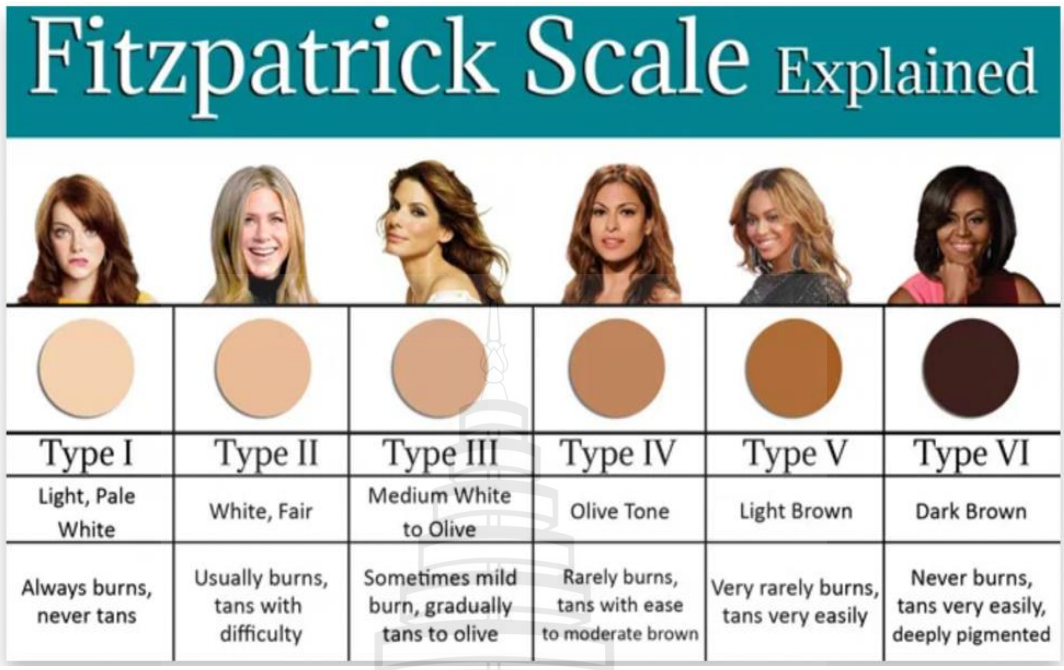
Satisfaction is the subjective evaluation of how well an research meets the expectations or needs of an individual or group, often measured through self-report or survey instruments.

Mean Melanin Index (M-Index) is a visual skin parameter related to melanin content in tissues.

Mexameter® MX18 is a very quick, simple and economical tool to measure the main components that determine the skin color: melanin and hemoglobin by reflectance. The analyses are performed in an area of 19.6 mm2, i.e. a disc of 5mm in diameter. The probe is applied to the skin surface with a spring device adjusted to constant pressure using black and white calibration plates.

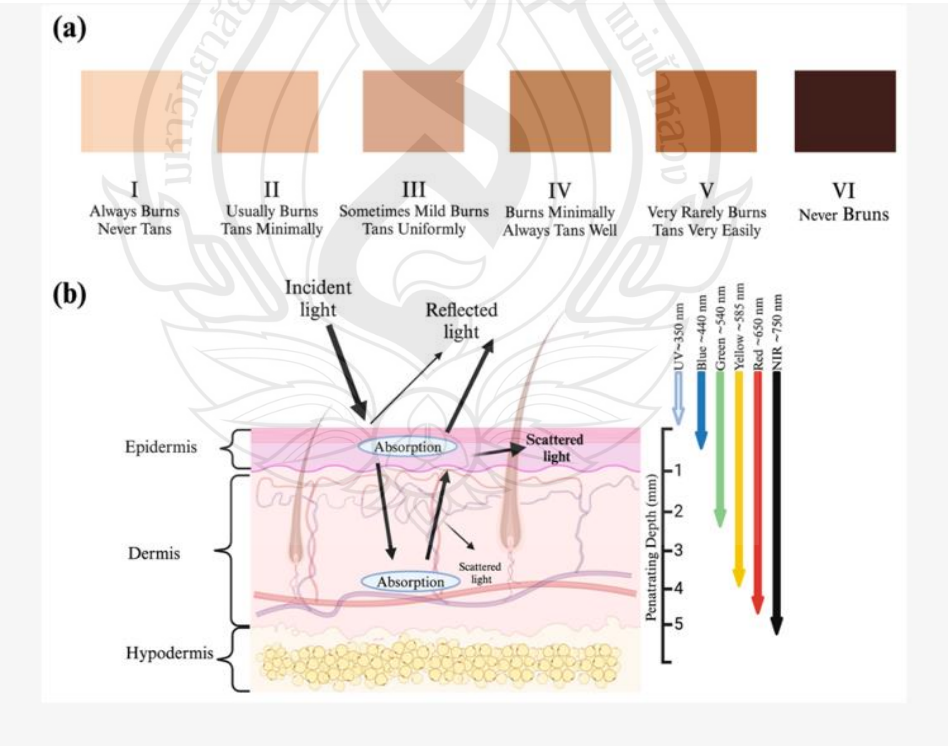
The VISIA® Complexion Analysis System is a skin scanning tool that provides multispectral imaging and analysis of eight areas including pigmentation, appearance, pore size, porphyrins, UV spots and photodamage of affected skin. This system can record important visual information like wrinkles and texture in the same situation.

Fitzpatrick Skin Phototype is a numerical classification commonly used to describe a person's skin type in terms of its response to ultraviolet radiation (UVR). There are six types of skin color, which are determined by the density of melanin in the skin.



Source Yu et al. (2024)

Figure 1.2 Fitzpatrick skin type scale (I–VI)



Source Yu et al. (2024)

Figure 1.3 Generalized penetration depths of various wavelengths of light through tissue structures of interest

A patch test is a way to determine if a substance that comes into contact with the skin is causing skin irritation (contact dermatitis). Each observed reaction is scored according to the International Contact Dermatitis Research Group System as follows: = suspicious reaction: only slight redness, += weak, positive reaction: skin reddened and slightly thickened, ++ = strong positive reaction: skin reddened, swelling with a few small blisters, +++ = Very Positive Reaction: Intense redness and swelling due to large coalesced bubbles or diffuse reaction, IR = irritant reaction, red skin improves upon removal of patch, NT = not tested.

CHAPTER 2

REVIEW LITERATURE

2.1 Human Skin Color

The skin is the largest organ of the integumentary system and forms the outermost layer of the human body. Human skin tones can range from colorless (light white) to various shades of "colored" skin, such as tan, dark brown, and black.

Skin color is a result of several skin chromophores, including red (oxyhemoglobin), blue (deoxygenated hemoglobin), yellow-orange (carotene, an external pigment), and brown (melanin). However, melanin is the primary determinant of skin color. The pigmentation of the epidermis is determined by the presence or absence of melanosomes in melanocytes and melanin in keratinocytes, while dermal macrophages and melanocyte melanin contribute to overall skin pigmentation (Ortonne, 2012).

2.2 Melanocyte

Melanocytes are the primary cells responsible for pigment production in the skin, originating from embryonic neural crest cells. Melanin is synthesized within melanosomes, which are membrane-bound organelles located in the cytoplasm of melanocytes. These cells are predominantly found in the basal layer of the epidermis and in the matrix of hair follicles. The molecular structure of melanin enables it to effectively absorb ultraviolet (UV) and visible light, thereby serving as a protective barrier against ultraviolet radiation (UVR) from sunlight (DeMello et al., 2016).

Ultrastructural investigations have revealed the presence of melanosome-containing cells in the fetal epidermis as early as 8-10 weeks of gestation. Clinically, this can manifest as conditions such as Mongolian spots, which are bluish-black marks commonly seen in the sacral region of infants of Oriental and African descent.

Epidermal analysis indicates that melanocytes constitute approximately 10% of the cells in the basal layer (Bolognia & Pawelek, 1988).

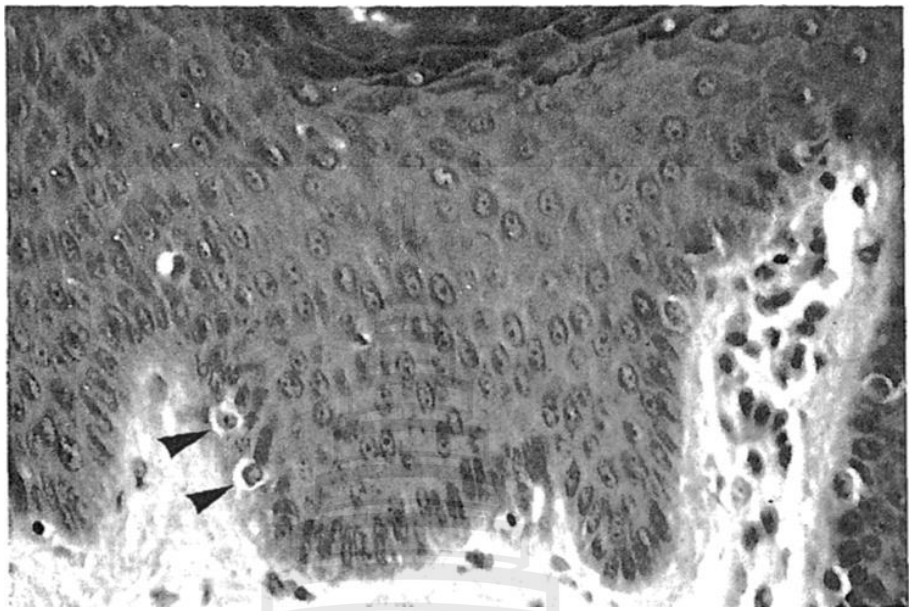


Figure 2.1 Melanocytes are in the basal layer of the epidermis. They are characterized by a distinct cytoplasm (arrows). (Hematoxylin and eosin-stained section, X400)

2.3 Melanogenesis

Melanogenesis is the process of production of melanin pigment. They are mainly produced by cells called melanocytes which contain melanosomes. Melanosomes require a specific set of enzymes and structural proteins to form mature melanin (Figure 2.2). Melanin production is initiated and regulated by a number of signaling systems and transcription factors including the tyrosine kinase receptor KIT, its ligand SCF, as well as MITF. Among them, TYR and TYRP2 are the critical enzymes that influence the quantity and quality of melanin during melanogenesis.

Tyrosinase is a copper-containing enzyme and functions as key enzyme in melanogenesis. Hydroxylation of L-tyrosine to L-DOPA is the rate-limiting step in melanin synthesis When L-phenylalanine is catalyzed by the PAH enzyme (phenylalanine hydroxylase) and converts L-tyrosine to L-3,4-dihydroxyphenylalanine

(DOPA). DOPA is then oxidized to DOPA-quinone. Homeostasis of melanogenesis is maintained by controlling L-Tyrosine and L-dopa production levels.

There are two types of melanin: eumelanin (brownish black color) and pheomelanin (reddish yellow color). The difference in the synthesis of pheomelanin from eumelanin lies in the L-dopaquinone phase. In the presence of cysteine, L-dopaquinone is converted to cysteinyl dopa, which is later converted to a benzothiazine derivative and subsequent polymerization produces pheomelanin. Eumelanin to pheomelanin ratio may contribute the human skin pigmentation (D'Mello et al., 2016).

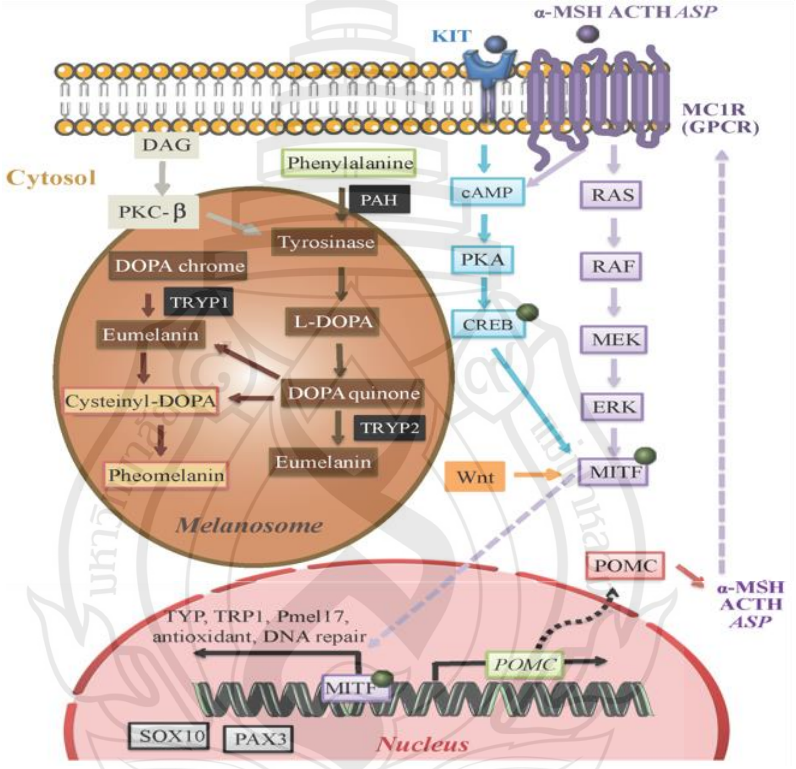


Figure 2.2 Melanogenesis pathway and its signaling system

2.4 Transportation of Melanosome

Melanosome transport in the skin involves the movement of melanin-containing organelles from melanocytes to keratinocytes, contributing to skin pigmentation. Melanosomes are formed in melanocytes and transported along microtubules and actin filaments with the help of motor proteins, such as kinesins and dyneins. The transport process is essential for transferring melanosomes to keratinocytes, where they distribute

melanin and protect the skin from UV radiation. This process is crucial for determining skin and hair pigmentation (Kondo & Hearing, 2011).

2.5 Tanning Response

Tanning is generally understood as the increased epidermal melanization observed in the skin after exposure to UV light. Tanning also acts host response process to protect against further UV induced damage (Gilchrest, 2011). Environmental factor like Ultraviolet light is the most important factor on melanocyte survival proliferation and differentiation functions. There are two types of tanning: immediate tanning and delayed tanning (Park & Yaar, 2012).

Immediate tanning occurs within 5-10 minutes under sunlight (mainly UVA or visible light) and fades within 24hours depending on UV dose and individual's complexion (for example, more visible in darker skin and undetectable in fair skin). It is caused by a change in melanin already present in the skin.

Delayed tanning, induced mainly by UVB exposure, first becomes visible 3-4 days after UV exposure and subtle in 10-28 days. Both UVA and UVB radiation can create an excited condition in the melanocyte which in turn releases more melanin in the skin (Park & Yaar, 2012).

2.6 UV Irradiation

Ultraviolet (UV) irradiation impacts not only melanogenesis but also the proliferation and survival of melanocytes by acting on keratinocytes, which, in turn, stimulate the synthesis and secretion of paracrine factors. UV exposure enhances the activity of epidermal melanin units by increasing both the size and number of melanosomes, although it does not affect the overall number of melanocytes. Previous studies have shown a direct correlation between the number of tyrosinase enzymes and the amount of melanin produced, which is also linked to skin pigmentation. Comparative studies indicate that DOPA levels are higher in tanned skin compared to untanned skin. Additionally, UV exposure induces significant alterations in cytokine

levels, growth factors, and hormones. UV radiation promotes the oxidation of tyrosine to DOPA and the subsequent reduction of sulfhydryl compounds in the epidermis, leading to a decrease in the natural inhibitors of the tyrosinase enzyme. Furthermore, elevated skin temperature resulting from UV exposure can also enhance melanin production (Kameyama et al., 1996).

2.7 Skin Whitening Agents

2.7.1 Tyrosinase Inhibitors

Tyrosinase plays a crucial role in the synthesis of melanin through the process of melanogenesis. Consequently, tyrosinase inhibitors have emerged as significant and effective targets for melanogenesis inhibitors, as they directly inhibit the enzyme's catalytic activity. Most over-the-counter cosmetics or skin whitening agents are tyrosinase inhibitors (Kanlayavattanakul & Lourith, 2018).

1. Hydroquinone

Hydroquinone functions by inhibiting approximately 90% of tyrosinase activity and inducing cytotoxic effects on melanocytes. It is naturally present in various foods such as vegetables, fruits, grains, coffee, tea, beer, and wine. Historically, hydroquinone has been a primary treatment for post-inflammatory hyperpigmentation and chloasma. It reduces skin pigmentation by binding to histidine at the active site of the tyrosinase enzyme.

Additionally, hydroquinone promotes the generation of reactive oxygen species, leading to oxidative damage to membrane lipids and proteins, specifically those associated with tyrosinase. It also reduces pigmentation by depleting glutathione levels and inhibiting DNA and RNA synthesis, which contributes to melanosome degradation and melanocyte damage. Despite its efficacy, hydroquinone carries the risk of causing permanent damage to melanocytes, potentially resulting in irreversible loss of natural skin pigmentation. Consequently, the use of hydroquinone has been declining. Furthermore, prolonged use of hydroquinone has been linked to the induction of extrinsic neoplasia and the development of drug resistance (Barsh & Attardi, 2007; Kramer et al., 2000).

2. Aloesin

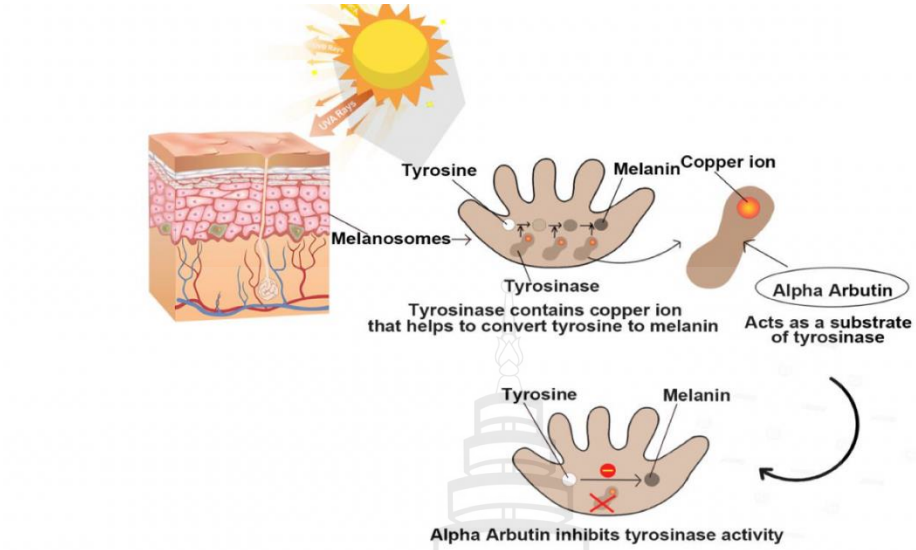
Aloesin is a natural extract from aloe vera. It acts as a tyrosinase inhibitor by inhibiting not only the hydroxylation of tyrosine to DOPA, but also the oxidation of DOPA to DOPA-quinone. Aloesin is more potent than kojic acid and arbutin in inhibiting tyrosinase. When aloesin is used with arbutin, the combination can synergistically inhibit UV-induced melanin synthesis (Jones et al., 2002).

3. Arbutin

Arbutin is a hydroquinone beta-D-glucopyranoside found naturally in plants such as pear leaves, bearberries, and wheat, where it contains hydroquinone molecules bound to glucose. Arbutin functions by inhibiting the synthesis and expression of tyrosinase, thereby reversibly inhibiting the enzyme's activity. Compared to hydroquinone, arbutin is less cytotoxic to human melanocytes. There are two forms of arbutin: alpha-arbutin (4-hydroxyphenyl-a-D-glucopyranoside) and beta-arbutin (4-hydroxyphenyl-a-D-glucopyranoside). Beta-arbutin is typically extracted from the leaves and fruit peels of various plants.

However, α-arbutin does not exist naturally and is biosynthesized by microbial enzymes and microorganisms. Interestingly, α-arbutin inhibits tyrosinase activity much more effectively than natural arbutin. The inhibitory effects of α-arbutin on melanin biosynthesis were examined in cultured melanoma cells and human skin models, demonstrating that α-arbutin effectively reduced melanin production without causing cytotoxicity. A concentration of 2% α-arbutin has been shown to be safe and is commonly used in popular skin whitening cosmetics.

Arbutin inhibits melanin synthesis in α-MSH-induced B16 cells and reduces tyrosinase activity in cell-free systems. Furthermore, the hyperpigmentation induced by α-MSH was reversed when arbutin was applied to guinea pig and human skin tissues. These findings suggest that arbutin could serve as an effective agent for skin lightening. The use of 2% α-arbutin is recognized as safe and continues to be incorporated into trending whitening products (Lim et al., 2009).



Source Chandorkar et al. (2021)

Figure 2.3 Mechanism of action of alpha-arbutin in skin lightening

4. Acelaic Acid

Azelaic acid is a naturally occurring dicarboxylic acid that reduces skin pigmentation by inhibiting mitochondrial oxidoreductase activation, DNA synthesis, and acting as a competitive, reversible tyrosinase inhibitor. Its lightening effect primarily targets highly active melanocytes, with minimal impact on normally pigmented skin. Azelaic acid is well tolerated for long-term use, though common side effects like erythema, scaling, itching, and burning typically resolve within one month (Parvez et al., 2006).

5. Kojic Acid

Kojic acid occupies different families of Aspergillus, Penicillium and Acetobacter. It works as a bleaching agent by chelating copper d inhibiting the tyrosinase enzyme. Kojic acid and its derivatives are used as antioxidants, antiproliferative, anti-inflammatory agents, and dental care products. Kojic acid is used to treat skin hyperpigmentation such as wrinkles, scars, melasma and freckles. However, there is a risk of contact dermatitis and erythema, and even cramps from kojic injections (Woolery-Lloyd & Kammer, 2011).

6. Licorice extract

Licorice can be obtained from the root of Glycyrrhiza glabra linneva. Licorice extract inhibits tyrosinase activity without damaging DNA. It has anti-inflammatory properties, protects the skin from UVB radiation and removes free radicles. In addition, it also has antibacterial, antiulcer and antioxidant properties (Lee et al., 2021).

7. Paper mulberry or mulberry extract

Paper mulberry belongs to the mulberry family and was obtained from the Broussonetiapapyrifera tree. These extracts interfere with the tyrosinase activity that converts dopa to dopachrome. It also has antibacterial and anti-tumor effects and slows down aging. Although it has anti-tyrosinase activity, its use in skin lightening is still poorly studied. Its efficacy in skin depigmentation still falls short of that of kojic acid. (Lee et al., 2002)

8. Emblicanin

Emblicanin is derived from an edible fruit called Phyllanthus cemblica fruit. It's two main components, Emblicanin A and Emblicanin B, have anti-tyrosinase effects and antioxidant properties. Emblicanin is a safer and more effective skin lightening agent than kojic acid and hydroquinone (Bhattacharya et al., 2001).

9. Flavonoid

Flavonoids are found in various parts of plants such as the bark, flowers, and leaves. The six main groups of flavonoids are flavones, flavanones, isoflavones, flavanols, flavonols and anthocyanidins. Flavonoids are direct tyrosinase inhibitors and have antioxidant effects, so they are good at lightening the skin. They are also used in numerous naturopathic treatments due to their many beneficial effects such as anti-cancer, anti-inflammatory, and UV protection (Solano et al., 2006).

2.7.2 Melanosome-transfer Inhibitors

1. Niacinamide

Niacinamide (nicotinamide) is the active form of vitamin B3 and found in the roots of vegetables and yeast. Niacinamide has several effects on the skin: anti-inflammatory action in acne, acts as an antioxidant, prevents photo immunosuppression and photo carcinogenesis, and increases intercellular lipid synthesis (Hakozaki et al., 2002) Niacinamide exerts its whitening effect by inhibiting the migration of

melanosomes to keratinocytes. Previous studies have shown that niacinamide reduces skin pigmentation by up to 68% by inhibiting melanosome migration (Greatens et al., 2005).

2. Soy

Soy is associated with health and nutrition, and there is growing evidence that soy-based products play a role in skin care. Soy extract inhibits protease-activated receptor-2 (PAR-2) activation. Soy compounds can inhibit the transfer of melanosomes from melanocytes to keratinocytes. While soy is known for its potential in inhibiting melanin production by targeting enzymes like tyrosinase, it may also affect the process of melanosome transport, thus contributing to skin lightening effects by preventing the distribution of melanin to surrounding skin cells. It has a depigmenting effect on the skin (Leyden & Wallo, 2011).

2.7.3 Antioxidants

Normal skin contains several antioxidants that can be depleted with UV exposure and cause oxidative damage. Applying topical antioxidants capable of preventing oxidative damage to the skin. There is an increasing trend to incorporate antioxidants into sunscreens and skin care products to replenish the skin's natural reserves. Vitamin A, Vitamin C, Vitamin E, Selenium and green tea are major antioxidants used in skin care products (Chen et al., 2012).

2.7.4 Epidermal Turnover Acceleration or Desquamation

Epidermal turnover is the process by which keratinocytes are generated in the basal layer of the epidermis and eventually lost from the surface of the skin as corneocytes (Maeda, 2017). Chemical exfoliants such as AHA, BHA, retinoic acid, and linoleic acid can be used to remove melanin in the epidermis. Not only do these acids hasten desquamation, but they also affect the tyrosinase enzyme. Linoleic acid reduces tyrosinase levels. Retinoic acid inhibits tyrosinase transcription and AHA directly inhibits tyrosinase without affecting mRNA or protein expression (Parvez et al., 2006).

2.8 Herbal Remedies for Skin Depigmentation

Recently, various tropical plants, such as paper mulberry, emblicanin extract, and radish root extract, have been tested for their potential anti-tyrosinase activity, particularly for use in skin whitening. Whitening cosmetics made with plant-derived natural ingredients are very popular because they are suitable for long-term use and have few side effects (Bhattacharya et al., 2001)

2.9 White Radish Root Extract

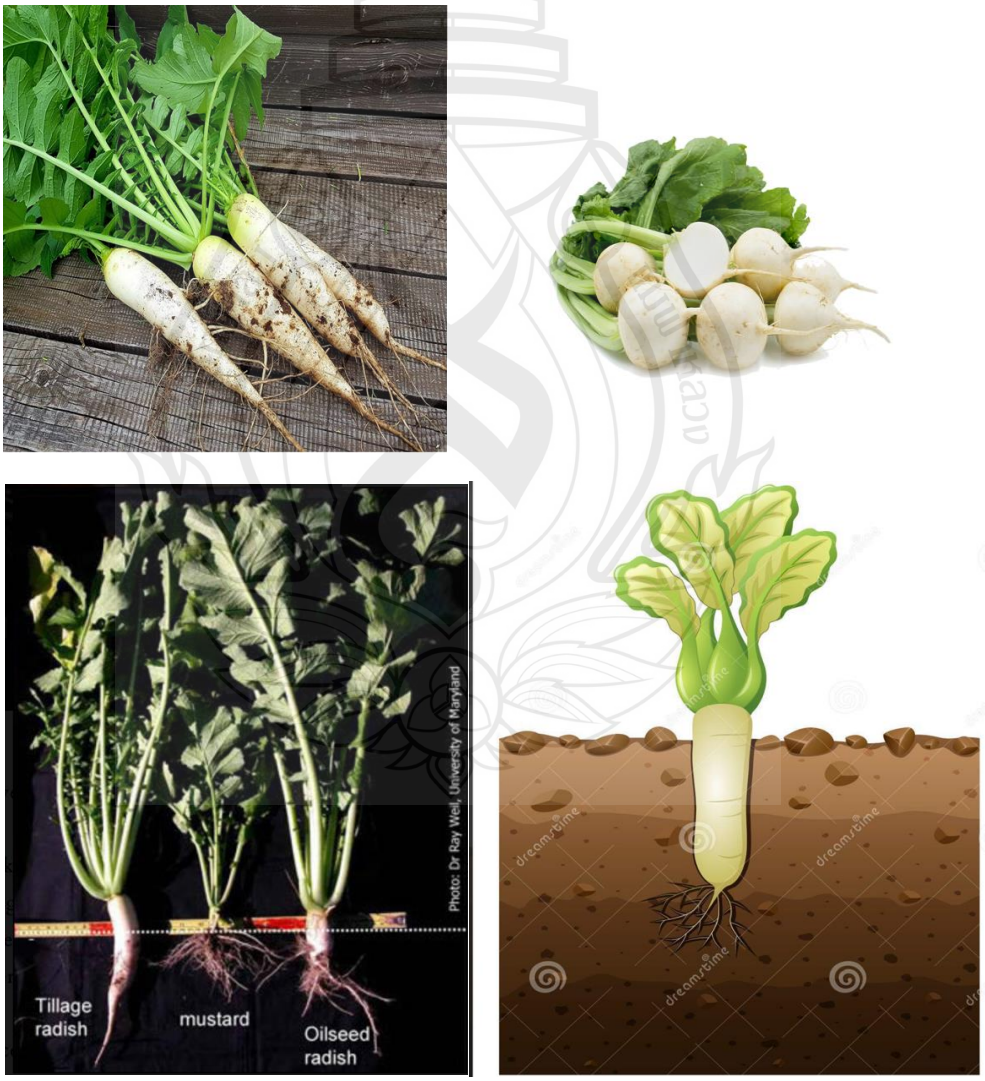


Figure 2.4 White radish root (Raphanus sativus L.)

2.9.1 General Information

White Radish (Raphanus sativus L.) belongs to the cruciferous vegetable family, which includes broccoli, cauliflower, cabbage, and kale. Raphanus sativus L. is originally comes from Europe and Asia. It grows in temperate climates at an altitude of 190-1240 m, 30-90 cm tall, with thick roots and varying in size, shape, and color. Radish (Raphanus sativus L.) is continuously consumed as a root vegetable. White and green radishes, also called mu, have been used in traditional Korean cuisine for over 1500 years. Seeds, leaves and roots of the radish have been used for therapeutic purposes (Park et al., 2022).

The long root variety, which is best suited for cooking, can grow up to 15 cm in length, while the smaller, rounded variety is typically consumed raw in salads. The flesh has a sweet taste initially, but it becomes bitter if the vegetable is left in the ground for an extended period. The leaves are arranged in rosettes, measuring 10-15 cm in small varieties and up to 45 cm in larger varieties. They have a lyrical shape, being pinnately divided with larger terminal lobes and smaller lateral lobes. The plant produces white flowers arranged in racemes (Gutiérrez & Perez, 2004).

2.9.2 Chemical Constituents of White Radish Root

White radish root is rich in chemical compounds such as

1. Four major organic acids; oxalic, malonic, malic, erythorbic acids
2. Phenolic compounds; Flavonoid, ascorbic acid, Cyadinin, Kaempferol, Lutolin, Myricetin, Quercetin and Pelargonidin
3. Coumarins; Aesculetin and Scopoletin (Gutiérrez & Perez, 2004)

Also rich in a variety of nutrients

Table 2.1 Phytochemical composition of radish (Raphanus sativus L)

Phytochemical/Nutrient	Radish* (root)	Radish* (leaves)
Proteins	570	3810
Fat	70	370
Carbohydrates	3030	4040
Fiber	320	610
Potasium	380	495
Calcium	148	752

Table 2.1 (continued)

Phytochemical/Nutrient	Radish* (root)	Radish* (leaves)
Vitamin C	38.8**	38.6
β-carotene	NA	3.96***

Source Hanlon and Barnes (2011)

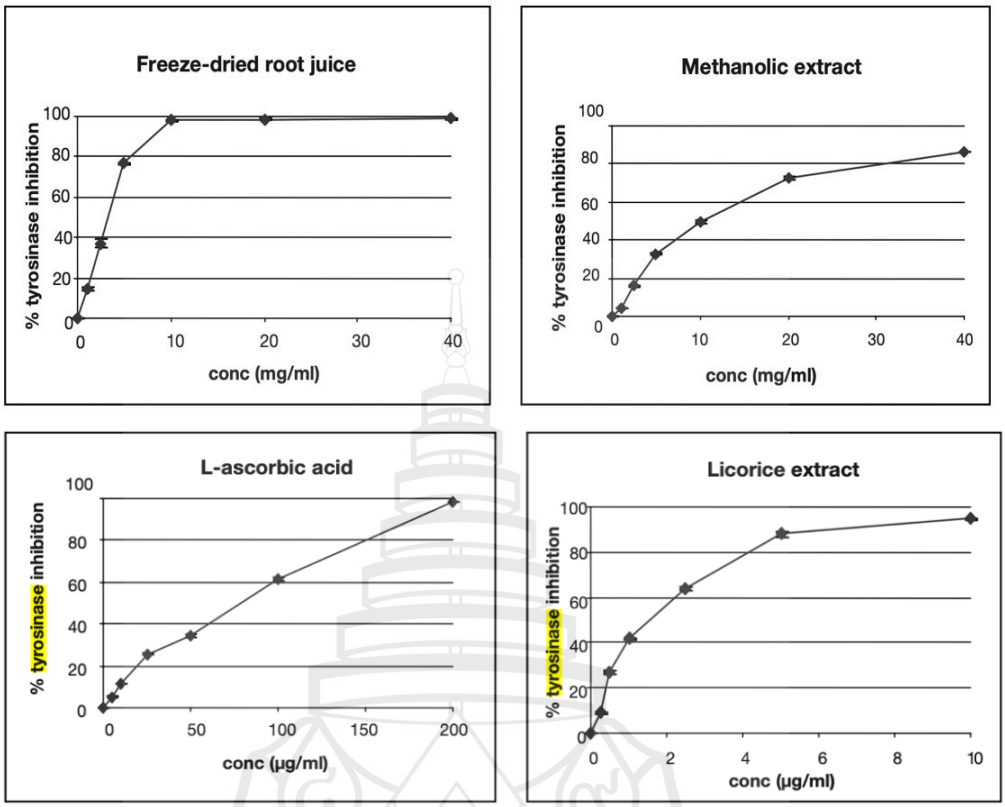
2.9.3 Biological Activities of White Radish Root

2.9.3.1 Pharmacological properties of white radish root compounds

1. Antioxidant activity (Hanlon & Barnes, 2011)
2. Anti-inflammatory activity (Gutiérrez & Perez, 2004)
3. Anti-wrinkle activity
4. Anti-tyrosinase activity (Jakmatakul et al., 2009)

2.9.3.2 Skin Lightening Effects

R. sativus root extract can use as a natural skin lightening/skin aging agent due to its ability to inhibit tyrosinase and scavenge multiple types of reactive oxygen species. One previous study proved that anti-tyrosinase activity of R.sativus extract using reference anti-tyrosinase agents like L-ascorbic acid and Licorice extract (Jakmatakul et al., 2009).



Source Jakmatakul et al. (2009).

Figure 2.5 Relationship between % tyrosinase inhibition and concentration of freeze-dried root juice, methanolic extract, and reference inhibitors (L-ascorbic acid and licorice extract) (mean ± SD, n = 3)

Another study proved and compared anti-tyrosinase activity of white radish root extract. The results of anti-tyrosinase activity of 16 plant extracts in 4 different organic solvents as percentage (%) of fungal tyrosinase inhibition. Among them, Raphanus sativus (in 50% propylene glycol) exhibit relatively high tyrosinase inhibition levels (88.50%).

Table 2.2 Sixteen tropical vegetables selected for screening of anti-tyrosinase inhibition

Common name	Scientific name	Family	Parts used
Lemongrass	*Cymbopogon citrates* (DC.) Stapf.	Poaceae	stem
Indian long pepper, Javanese long pepper	*Piper longum* Blume	Piperaceae	fruit
Chinese radish	*Raphanus sativus* Linn.	Brassicaceae	root
Aloe	*Aloe vera* Linn.	Aloaceae	leaf
Vegetable Humming Bird, Sesban	*Sesbania grandiflora* (L.) Pers.	Fabaceae	flower
Sweet basil	*Ocimum basilicum* Linn.	Apiaceae	leaf
Bitter cucumber, bitter gourd	*Momordica charantia* Linn.	Cucurbitaceae	fruit
Okra	*Hibiscus esculentus* Linn. *Abelmoschus esculentus* L. Moench.	Malvaceae	fruit
Krachai (Thai name)	*Boesenbergia pandurata* (Roxb.) Schltr.	Zingiberaceae	rhizome
Winged bean	*Psophocarpus tetragonolobus* (L.) DC.	Fabaceae	fruit
Tomato	*Lycopersicon esculentum* Mill.	Solanaceae	
Cilantro, coriander, Chinese parsley	*Coriandrum sativum* Linn.	Apiaceae	leaf
Cucumber	*Cucumis sativus* Linn.	Cucurbitaceae	fruit
Holy basil	*Ocimum sanctum* Linn.	Labiatae	leaf

Table 2.2 (continued)

Common name	Scientific name	Family	Parts used
Kitchen mint, March mint	*Mentha cordifolia* Opiz.	Labiatae	leaf
Carrot	*Daucus sativus* Hoffm.	Apiaceae	root

Source Kamkaen et al. (2007)

Table 2.3 Effect of sixteen vegetable extracts with four different organic solvents on mushroom tyrosinase inhibition

Scientific name	Inhibition of mushroom tyrosinase (%)			
	Hexane	Ethyl acetate	Methanol	50% Propylene glycol
Cymbopogon citratus	46.57	14.24	7.57	10.51
Piper longum	12.24	160.26	-89.73	-44.91
Raphanus sativus	38.43	68.73	53.51	88.50
Aloe vera	15.07	159.76	10.00	0.44
Sesbania grandiflora	-3.65	10.64	28.03	13.06
Ocimum basilicum	4.19	149.88	-371.34	-0.998
Momordica charantia	2.67	169.74	78.98	68.17
Hibiscus esculentus	25.52	-56.26	18.47	20.65
Boesenbergia pandurata	21.44	-437.50	6.80	7.82
Psophocarpus tetragonolobus	4.92	-489.29	-157.77	-13.95
Lycopersicon esculentum	4.27	-193.75	2.91	-1.70
Coriandrum sativum	13.56	-412.50	-24.76	9.32
Cucumis sativus	3.47	33.13	-21.60	-18.78
Ocimum sanctum	14.98	156.81	-98.30	-3.01
Mentha cordifolia	10.20	208.43	-218.20	36.27
Daucus sativus	16.18	39.84	2.18	-7.86
Kojic acid (reference)	87.65	96.12	65.24	82.02

Source Kamkaen et al. (2007)

Table 2.4 Previous studies of Raphanus sativus (Radish)

Author, Year	Type	Method	Outcome
Martha et al. (2004)	Review article	-	Radish roots contain phenolic compound and antioxidant properties
Pirodamornchai et al. (2005)	Laboratory	The anti-tyrosinase activity of nine vegetables was tested using the mushroom tyrosinase inhibition method, with results compared to the standard kojic acid.	Raphanus sativus L. exhibits significant tyrosinase inhibition, surpassing 60%, when compared to the standard kojic acid.
Kamkaen at el. (2007)	Laboratory	The anti-tyrosinase activity of 16 vegetables was tested using four different solvents—hexane, ethyl acetate, methanol, and 50% propylene glycol—through the mushroom tyrosinase inhibition method, with results compared to the standard kojic acid.	Raphanus sativus L. in 50% propylene glycol shows significant tyrosinase inhibition (88%), surpassing the performance of standard kojic acid in the same solvent.

Table 2.4 (continued)

Author, Year	Type	Method	Outcome
Jakmatakul et al. (2009)	Laboratory	The antityrosinase, antioxidant, and cytotoxic activities of Thai radish root were tested using freeze-drying and methanolic extraction methods.	Levels of total phenols, total flavonoids, and L-ascorbic acid were analyzed in freeze-dried and methanolic radish root extracts, along with potency of tyrosinase inhibition with IC 50 = 3.09 and 9.62, as well as scavenging effects on DPPH radicals, superoxide. Analyzed. Anion radicals and singlets have found oxygen to reflect antioxidant activity. Leakage of LDH from fibroblasts indicated low cytotoxicity of both extracts.

2.9.3.3 Side Effects

White Radish extracts are known to be safe with minimal side effects. But contact dermatitis to radish extract has been mentioned in some studies. The radish, Raphanus sativus L., is a member of the mustard family (Cruciferae), and the root material and seeds produce mustard oil (isothiocyanates). It has been reported to cause allergic contact dermatitis and associated sensitizing chemicals have been identified. The risk of exposure to several plants providing such mustard oil is tabulated.

Therefore, patch test should be performed prior to the research study (Mitchell & Jordan, 1974).

2.9.3.4 Genotoxicity of White Radish

There is limited research specifically addressing the genotoxicity of white radish (Raphanus sativus). However, radish in general, including white radish, is typically considered safe for consumption. The majority of studies on white radish focus on its nutritional benefits, antioxidant properties, and potential in promoting skin health, rather than its genotoxicity.

A study on fresh radish showed that after extracting the edible portion with hexane, chloroform, and methanol, none of the fractions were mutagenic to S. typhimurium strains TA98 and TA100, with or without the S-9 mix. The hexane and chloroform extracts contained both direct and indirect mutagens but exhibited antimutagenic effects, reducing mutagenicity. However, they did not inhibit the mutagenicity of benzo[a]pyrene. The findings suggest that radish lacks mutagenic compounds but contains nonpolar compounds with antimutagenic properties (Rojanapol & Tepsuwan, 1993).

2.9.3.5 Carcinogenicity of white radish root extract

To evaluate teratogenicity, pregnant rats were administered radish extract at a concentration of 175 mg/kg for 10 days. As a result, it was shown that embryo implantation was inhibited. However, there was no teratogenicity in pregnant mothers or fetuses (Nath et al., 1992). In this study, researchers used a 4% radish extract cream containing 40 mcg/ml of methanol. See all previous studies. Data indicate its safety and teratogenicity is not conclusive. Raw juice solution is genotoxic compared to 200 mcl of lyophilized extract. Extracts containing other substances such as propylene glycol can enhance the effectiveness of white radish, but there is not yet enough evidence to conclude on their safety.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Study Design

Randomized, Single blinded (Blind to volunteers), Comparative clinical experimental study

This is the study to compare effectiveness between 4% white radish extract cream and 2% alpha arbutin on skin for facial skin whitening.

3.2 Study Population

Volunteers in both genders with Fitzpatrick skin type II-V of aged between 20-50 years old who came to participate for facial skin whitening at Mae Fah Luang Hospital, Bangkok

3.3 Study Location

Mae Fah Luang University Hospital, Bangkok.

3.4 Sample Size Determination

Comparative study of the efficacy and safety of 4% white radish extract cream versus 2% alpha arbutin for facial whitening in parallel groups has never been established. Therefore, the researcher chose a similar article for sample sized calculation. It is about a comparative study of 2% oxidized glutathione cream compared with placebo for facial whitening in 20-50 years old women; a randomized, single-blind, matched-pair, placebo-controlled trial (Fah, 2020).

For glutathione group, the Mexameter ® reading at week 10 showed a significant drop from 272.77± 26.17 at baseline to 243.47± 26.31 compared to placebo group, whose mexameter readings from 274.13± 25.82 at baseline to 265.50± 25.81at 10^{th} week.

Melanin index before Glutathione cream = 272.77± 26.17

Melanin index after Glutathione cream = 243.47± 26.31

From the formula,

$\alpha = 0.05$ (two-tailed) $Z_{0.025} = 1.96$

$\beta = 0.10$ $Z_{0.10} = 1.28$

$n_1 = 30$ $n_2 = 30$

$\sigma_1 = 26.17$ $\sigma_2 = 26.31$

$Sp^2 = [(n_1-1)S_1^2 + (n_2-1)S_2^2] \div (n_1 + n_2 - 2)$

$= [(30-1)(26.17)^2 + (30-1)(26.31)^2] \div (30 + 30 - 2)$

$= 688.54$

$\mu_1 = 272.77$, $\mu_2 = 243.47$

$\mu_d = 272.77 - 243.47 = 29.3$

$N = (Z_{\{\alpha/2\}} + Z_\beta)^2 \times \sigma_d^2 \div \mu_d^2$

$= (1.96 + 1.28)^2 \times 688.54 \div (29.3)^2$

$= 8.41$ or 9 subjects

Note

n=sample size

σ = standard deviation

μd = mean difference

The approximate drop out for follow-up visits is 20%, in that case, n = 9 / (1-0.20) = 12 volunteers were registered for each group. So, the investigator called for 24 subjects who voluntarily wanted to help in the research study.

3.5 Criteria for Selection

3.5.1 Inclusion Criteria

1. Healthy male and female volunteers aged between 20-50 years old
2. Fitzpatrick skin phototype II-V
3. Participants who voluntarily wanted to help in the research study and able to come for follow up once a month for three successive months.
4. Participants who can give informed consents for feasible possible complications and danger of both treatment process and publication of the pictures for thesis purpose.
5. Volunteers are well-being and have no history of problems with whitening agents.
6. Volunteers who acknowledge not to apply any whitening cream during 12 weeks of study
7. Volunteers who agree not to do any whitening injection, chemical peeling, IPL or any laser treatment over the face during the study.

3.5.2 Exclusion Criteria

1. Pregnancy and breastfeeding women
2. People who taken micro-needling, microdermabrasion, IPL (Intense pulse light), chemical peeling, non-ablative laser, and facial whitening treatment before 2 months of thesis
3. People who taking any medication which can influence the melanin synthesis (for example, anticonvulsants, oral contraceptives, and hormonal therapy)
4. People who have underlying medical illness such as uncontrolled diabetes mellitus, hypertension, cardiovascular disease, liver disease, renal disease and using immunosuppressant
5. People who have malignant or premalignant lesion history in facial area
6. People who are taking chemotherapy
7. People who is sensitive to sunlight and cannot avoid sun
8. People who have open wound or active inflammation in the face

9. People who have allergy to chemical compounds of 4% white radish cream ,2% alpha arbutin, sunscreen and/or mild soap

3.5.3 Withdrawal Criteria

1. Subject who using facial whitening agent other than 4% white radish cream or 2% alpha arbutin cream

2. Subject who suffers from serious side effect or allergy from the treatment

3. Subject who got injury from the medical disease, accident, or death

4. Subject who got pregnant during trial period

5. Subject who willing to leave the trial with any reasons

6. Subject who fails to cooperate with the protocol or lost follow up more than 2 visits

3.5.4 Early Termination Criteria

1. 30% of participants experience severe allergic reactions

2. Occurrence of unforeseen study cream safety issues during research study

3.6 Variables of the Study

3.6.1 Independent Variable

Using 4% white radish extract cream and 2% alpha arbutin cream

3.6.2 Dependent Variable

1. Melanin index
2. Dermatologist and subject’s satisfaction score
3. Side effects and complications

3.7 Intervention

Total number of subjects are divided into 2 groups: equal numbers in each group by using Random Sequence Generator

4% white radish extract cream is applied to whole face while 2% of alpha arbutin is applied to whole face in another group and follow up once every 4 weeks.

3.8 Equipments

1. 4% white radish extract cream
2. 2% alpha arbutin cream
3. Sunscreen SPF-50, PA+++ (UVA/UVB Defense SPF 50)
4. VISIA® Complexion Analysis System (Canfield, Fairfield, NJ)
5. Mexameter MX 18® (Courage-Khazaka Electronic, Koln, Germany)
6. Finn chamber for patch test
7. Volunteers profile record
8. Mild soap
9. Qualification letter
10. Adverse effect record form
11. Satisfactory questionnaire of the treatment for 3 independent dermatologists and volunteers

Chemical Constituents of 4% White Radish Extract Cream

1. Standard cream base constituents of the White Radish Root Extract Cream

    1) Aqua
    2) Raphanus Sativus Root Extract (สารสกัดหัวไชเท้า Raddish)
    3) Stearyl alcohol
    4) Cyclohexasiloxane
    5) Butylene glycol
    6) Dimethicone
    7) Squalane
    8) Cetyl alcohol
    9) PEG-100 (and) Glycerylstearate
    10) Paraffinum Liquidum
    11) Glycerylglucoside
    12) DMDM Hydantoin
    13) Polysorbate20
    14) Acrylate copolymer

15) PEG-40 Hydrogenated castor oil

16) Sorbitanmonooleate

17) Tetrasodium EDTA - ใบรับจดแจ้งเลขที่ : 12-1-6600041104

Odor - No fragrance, Color – Cream Color

Package -white tube, 30 g for each tube

Factory name-Luxmin factory,Thailand.

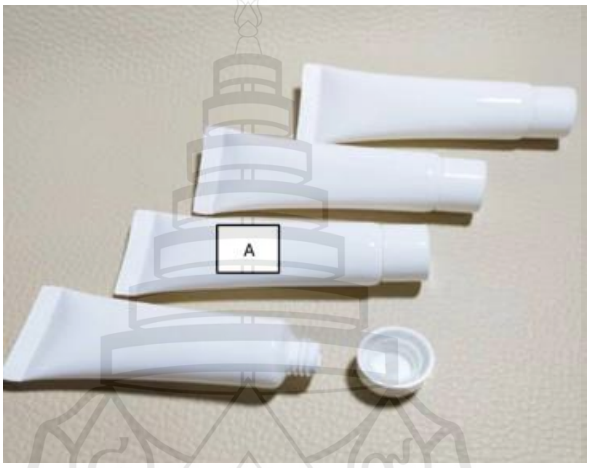


Figure 3.1 4% White radish root extract cream in tube

Preparation Steps:

Step A:

1. Combine Aqua (68.8%), Butylene Glycol (2%), Polysorbate 20 (0.8%), and PEG-40 Hydrogenated Castor Oil (0.5%).

2. Heat this mixture to a temperature of 75-80°C.

Step B:

1. Combine Stearyl Alcohol (2%), Cyclopentasiloxane (2%), Dimethicone (2%), Squalane (1.5%), Cetyl Alcohol (1.5%), PEG-100 andGlyceryl Stearate (1.5%), Liquid Paraffin (1%), and Sorbitan Monooleate (0.3%).

2. Heat this mixture to a temperature of 75-80°C.

Step C:

1. Gradually mix the heated mixture from Step B into the mixture from Step A.

2. Homogenize (blend thoroughly) the combined mixture until it cools down to 45°C.

3. Once at 45°C, add Raphanus Sativus Root Extract (4%), Glyceryl Glucoside (1%), Glydant Liquid (1%), and Tetrasodium EDTA (0.1%).

4. These steps ensure that the cream has the right texture and that all ingredients are evenly distributed in the process of 4% white radish root extract cream. The cream is a colorless, odorless, and thin consistency.

2. Chemical compounds of 2% Alpha Arbutin Cream

1) Aqua
2) Alpha Arbutin
3) Butylene glycol
4) Glyceryl glucoside
5) Polysorbate
6) Sorbitan monooleate
7) Paraffinum Liquidum
8) Dimethicone
9) Cyclopenta & cyclohexasiloxane
10) Squalane
11) Neopentyl Glycol Diheptanoate
12) Isododecane
13) Tocopheryl acetate
14) Tetrasodium EDTA
15) Sodium metabisulfite
16) Glyceryl monostearate
17) Cetyl alcohol
18) PEG-100
19) Stearyl alcohol
20) DMDM Hydantoin

Odor - No fragrance, Color – Cream Color

Package -white tube ,30 g for each tube

Factory name-Luxmin factory ,Thailand

Figure 3.2 2% Alpha arbutin cream in tube

3. Sunscreen SPF 60, PA+++ refers to the broad-spectrum sunscreen that has SPF 60, PA+++. Ingredients inside sunscreen cream are as follow;

1) Titanium dioxide
2) Oxybenzone
3) Zinc oxide
4) Octocrylene
5) Octyl methoxycinnamate
6) Behenyl alcohol
7) Propylene glycol
8) Propylparaben
9) Stearyl alcohol
10) Carbomer
11) Cetyl alcohol
12) Gltcerol monostearate
13) Hydrogenated polydecene

3.9 Study Procedure

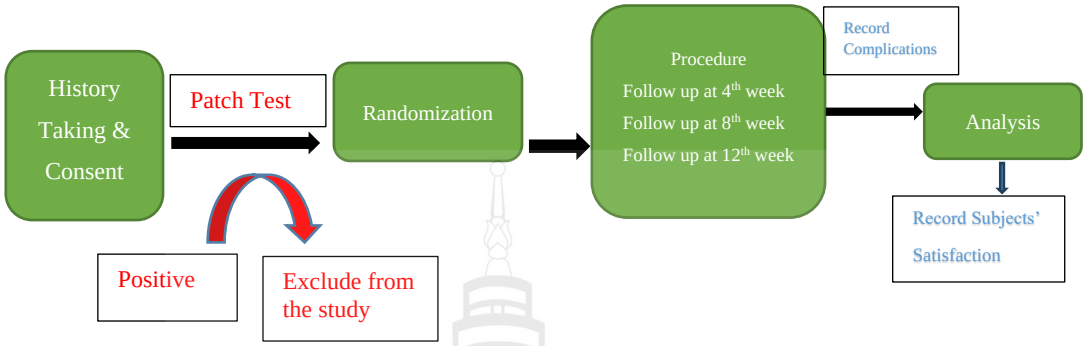


Figure 3.3 Study procedure

If volunteers who do not follow the protocol during study period, considered as withdrawal and remove from the research trial.

3.9.1 Research Study Process

3.9.1.1 Patient Selection

Participants were chosen based on specific inclusion criteria and were thoroughly informed about the study's aims, potential benefits, and possible drawbacks. After receiving a clear explanation, participants voluntarily provided written consent to participate in the study.

3.9.1.2 History Taking

A complete medical history was taken from each participant.

3.9.1.3 Patch Test Procedure

A patch test was performed by applying 4% white radish extract cream and 2% alpha arbutin cream to the volunteers' arms. The creams were left on the skin for 24 hours, with volunteers instructed to avoid sun exposure and excessive sweating. Reactions were examined at 48 and 96 hours post-application. Reactions were scored using the International Contact Dermatitis Research Group System:

+? = Doubtful reaction: mild redness only

+ = Weak positive reaction: redness and slight thickening of skin

++ = Strong positive reaction: red, swollen skin with small water blisters

+++ = Extreme positive reaction: intense redness and swelling with large blisters or spreading reaction

NT = Not tested

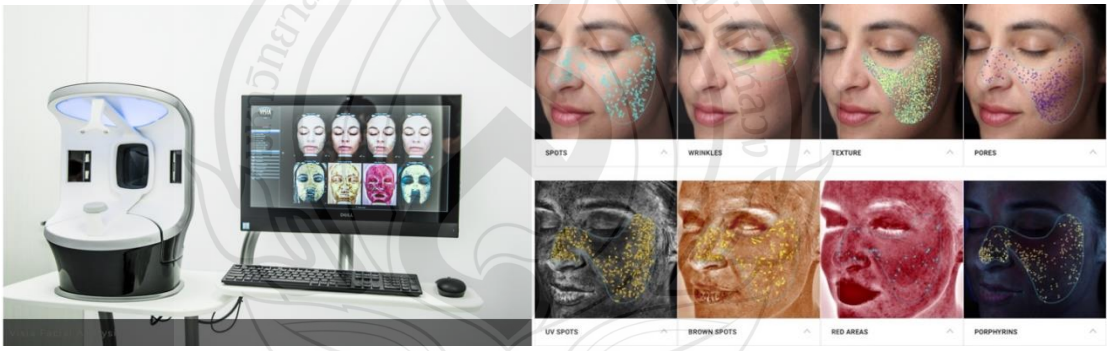
IR = Irritant reaction

Subjects who exhibited a ++ or stronger reaction were excluded from the study.

3.9.1.4 Baseline Skin Condition Assessment

To evaluate the baseline skin condition, photographs were taken using the VISIA® complexion analysis system at the start, 4th, 8th, and 12th weeks. The process for the VISIA® scan included:

1. Explaining the machine and its function to the patient
2. Ensuring room lighting was turned off for optimal image resolution
3. Using a 12-megapixel resolution camera
4. Automatic focus and white balance correction
5. Taking facial images at specific angles: 37° left, 0° center, and 37° right
6. Multi-spectral imaging using standard daylight fluorescent lighting, cross-polarized flash, and ultraviolet lighting.



Source Canfield Scientific (2025)

Figure 3.4 VISIA® complexion analysis system

3.9.1.5 Melanin Index Measurement

The Mexameter® is an electronic device used to measure two components of the skin, melanocytes and erythrocytes, based on light reflection and absorption. It uses two specific wavelengths (660 nm and 880 nm) to calculate a melanin index, which helps assess melanin levels in the skin. For accurate results, the probe's tip must remain in constant contact with the skin.

In this study, the melanin index of the subject's face was measured at baseline and at 4-week intervals (4th, 8th, and 12th weeks). Measurements were taken from two specific facial areas: 1 cm above the eyebrow along the mid-pupillary line and 2 cm below the lower eyelid along the same line. The recorded melanin index was then analyzed at each of these time points.

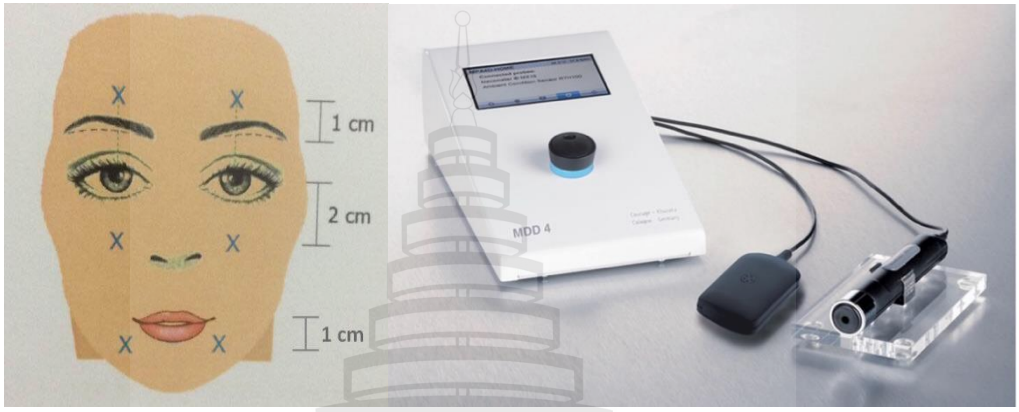


Figure 3.5 Landmarks to measure by Mexameter® MX18 for melanin index

3.9.1.6 Randomization of Subjects

A total of 24 numbers were randomly chosen from the range of 1 to 1000 using a random sequence generator. These 24 numbers were assigned to 24 subjects and then grouped into two categories based on the order of enrollment (first-come, first-served) (http://www.random.org/sequences/).

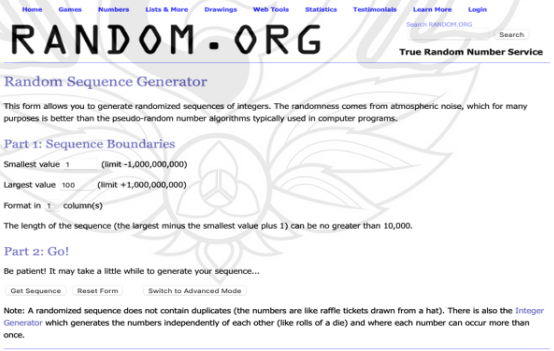


Figure 3.6 Random sequence generator

3.9.1.7 Group Assignment

Even numbers were assigned to Group A, and odd numbers were assigned to Group B.

3.9.2 Usage Instructions

3.9.2.1 Cream Preparation and Safety

In this study, the researcher utilized a properly manufactured 4% white radish root extract cream and a 2% alpha arbutin cream. According to previous studies, no significant or proven adverse effects have been associated with these creams. The 4% white radish root extract cream and 2% alpha arbutin cream used in the research study have received approval from the Thai FDA.

3.9.2.2 Daily Usage Instructions

1. Facial Cleansing (Twice a Day):

1) Cleanse the face with water.

2) Apply a small amount of mild soap to the palm and gently rub it onto the face for 1 minute.

3) Rinse the face thoroughly with water to remove all soap.

4) Pat the face dry using a soft, clean, and dry tissue or towel.

2. Application of Creams A and B (Twice a Day):

1) Squeeze a small amount of cream from the tube (labeled "Cream A" or "Cream B") onto the index finger.

2) Apply the cream evenly to the entire face, using gentle motions.

3) Repeat the process for each skincare session.

Figure 3.7 Fingertip unit measurement

3. Cream A or B group will apply the same cream respectively for the whole study.

4. If the volunteer must go outside or under the sunlight, apply sunscreen 30 minutes beforehand.

The registered volunteers have to follow the instructions which are described in the informed consent like avoid long time contact with sunlight, taking whitening pills and using other skin whitening products. And the volunteers must record the side effects that occurred from the cream on the paper the researcher gave them. If the volunteers experienced any side effects which is mild or severe, must inform to the researcher immediately.

3.10 Follow Up

All volunteers need to visit follow up appointments at every 4 weeks to evaluate the results and access the adverse reactions on the face.

3.11 Outcomes Measurement and Data Collection

3.11.1 At 4th,8th and 12 weeks respectively, dermatologist measure the melanin index on the face with mexameter ® MX 18.

3.11.2 The dermatologist accessed the side effects by asking questionaries at every follow up: the following questions were asked to the subjects for side effects assessment.

1. Pruritus score ranging from 0 to 100
2. Duration (days) of erythema
3. Others such as allergic contact dermatitis, post inflammatory hyperpigmentation and hypopigmentation

3.11.3 To access the efficacy of 4% white radish extract cream and 2% alpha arbutin cream, the volunteers must be taken pictures by using VISIA® Skin Analysis System at 4th,8th and 12th weeks.

3.11.4 Improvement score was taken with global aesthestic satisfaction score that includes -1 to +4

-1 = worse

0 = no improvement

+1 = fair improvement (1-25 %)

+2 = moderate improvement (26-50%)

+3 = good improvement (51-75%)

+4 = excellent improvement (76-100%)

3.12 Data Analysis

3.12.1 Participants' eligibility for this study will be assessed based on the inclusion and exclusion criteria, and their personal information will be kept confidential during the data analysis process.

3.12.2 Medical records and data from this study conducted at the Mae Fah Luang University Dermatology Clinic will be analyzed using SPSS 18 software and Microsoft Excel 2010.

3.12.3 Descriptive statistical analysis will be used to record general demographic data of the participants, providing summary statistics such as means, medians, modes, percentages, ranges, and standard deviations.

3.12.4 The baseline melanin index of the face will be compared for participants using the 4% white radish root extract and 2% alpha arbutin creams at weeks 4, 8, and 12, measured by the MX18 device.

3.12.5 Comparisons between the baseline, 4th, 8th, and 12th weeks will be made between groups using a repeated measures ANOVA.

3.12.6 Satisfaction ratings from three dermatologists will be summarized using descriptive statistics for the 4th, 8th, and 12th weeks.

3.12.7 Patient satisfaction scores from both groups will be compared at week 12 using the Chi-square test, and any side effects will be documented. Descriptive statistics will be used to summarize the data.

3.12.8 The researcher will perform the analysis at a significance level with a p-value of less than 0.05.

3.13 Ethnical Consideration

This study will adhere strictly to the Good Clinical Practice (GCP) guidelines, which provide international ethical and scientific standards for the design, conduct, documentation, and reporting of trials involving human participants. These guidelines are established by the International Conference on Harmonization (ICH).

The GCP guidelines cover the following key considerations:

1. Protection of human rights for individuals participating in clinical trials.
2. Assurance of the safety and effectiveness of newly developed compounds.
3. Standards for how clinical trials should be conducted.
4. Clear definition of roles and responsibilities for clinical trial sponsors, investigators, and monitors.

Participants will have a full understanding of the study's methodology, objectives, and potential side effects. They will voluntarily sign an informed consent form before participating, with the freedom to withdraw from the study at any time without any negative consequences. Participation in this study is completely free of charge, and there is no financial gain for either the research team or the participants. All personal information of the participants will remain confidential and stored in a password-protected file in Microsoft Excel 2010 on a computer in the research room at Mae Fah Luang University Hospital, Bangkok. The VISIA scanned images will also be kept with black censor strips over the participants' eyes to protect their identities.

Both the 4% white radish extract cream and 2% alpha arbutin cream have been approved by the FDA. However, allergic reactions or other side effects may occur depending on the individual. Therefore, patch tests are conducted for all subjects before the study begins. In the event of any issues arising due to participation in the research, the researcher will assume responsibility and provide the best possible care.

3.14 Obstacles and Strategy

Skin color may vary depending upon sunlight intensity and duration. Therefore, volunteers need to follow the instructions that include in the protocol and the researcher must explain them about consequences.

CHAPTER 4

RESULTS

4.1 Participants' Demographic Data

Table 4.1 Demographic data

Demographic data	4% White Radish Root (n=12)	2% Alpha Arbutin (n=12)	P-value
Gender, n(%)			
Male	4 (33.3)	6 (50.0)	0.408[c]
Female	8 (66.7)	6 (50.0)	
Age (years), mean±SD	31.92±5.95	32.67±6.98	0.780[a]
Occupation, n(%)			
Student	7 (58.3)	8 (66.7)	
Employee	4 (33.3)	2 (16.7)	0.714[d]
Housewife	1 (8.3)	2 (16.7)	
Underlying disease, n(%)	0 (0.0)	0 (0.0)	-
Fitzpatrick skin type			
II	1 (8.3)	2 (16.7)	
III	8 (66.7)	7 (58.3)	1.000[d]
IV	3 (25.0)	3 (25.0)	
Exposure to sunlight (minute/day), median (IQR)	15 (10, 30)	20 (10, 30)	0.627[b]
Cosmetics treatment 4 weeks before study, n(%)	0 (0.0)	0 (0.0)	-

Table 4.1 (continued)

Demographic data	4% White Radish Root (n=12)	2% Alpha Arbutin (n=12)	P-value
Food or drug allergy, n(%)	1 (8.3)	1 (8.3)	1.000[d]
Cosmetics allergy, n(%)	0 (0.0)	0 (0.0)	-
Personal medication & supplement, n(%)	3 (25.0)	3 (25.0)	1.000[d]

Note Data were analyzed with Independent t-test[a], Mann-Whitney U test[b], Chi-square test[c], Fisher's exact test[d]

* Statistically significant at the 0.05 level

According to Table 4.1, the demographic data of participants shows that, among those who applied the 4% White Radish Root cream, 8 were female and 4 were male, with a mean age of 31.92±5.95 years. Most participants were students (n=7), employees (n=4), and housewives (n=1). None of the participants had any underlying disease. The Fitzpatrick skin types of the participants were Type III (n=8), Type IV (n=3), and Type II (n=1). The median of sunlight exposure was 15 (IQR 10, 30) minutes/day. None of the participants had received cosmetic treatments in the 4 weeks prior to the study. One participant had a history of drug and food allergies, but no participant had a history of cosmetic allergies. Three participants were using personal medications and supplements.

Among the participants who applied the 2% Alpha Arbutin cream, 6 were female and 6 were male, with a mean age of 32.67±6.98 years. Most participants were students (n=8), employees (n=2), and housewives (n=2). None had chronic illnesses. The Fitzpatrick skin types of the participants were mostly Type III (n=7), Type IV (n=3), and Type II (n=2). The median exposure to sunlight was 20 (IQR 10, 30) minutes per day. None had received cosmetic treatments in the 4 weeks prior to the study. One participant had a history of drug and food allergies, but no participant had a history of

cosmetic allergies. Three participants were using personal medications and supplements.

When comparing the demographic data between the groups that received the 4% White Radish Root cream and the 2% Alpha Arbutin cream, no statistically significant differences were found between the two groups (P>0.05).

4.2 Mean Melanin Index

Table 4.2 Comparison of mean melanin index for 4% white radish root cream and 2% alpha arbutin cream across follow-up times

Follow-up times	4% White Radish Root, mean±SD	2% Alpha Arbutin, mean±SD	Mean difference (95%CI)	P-value[a]
Forehead				
Baseline	299.58±42.55	318.42±35.68	-18.83 (-52.08, 14.41)	0.253
4 weeks	293.92±44.94	308.17±37.37	-14.25 (-49.24, 20.74)	0.407
8 weeks	280.08±47.11	293.67±38.97	-13.58 (-50.18, 23.02)	0.450
12 weeks	272.67±46.16	283.33±34.32	-10.67 (-45.10, 23.77)	0.527
P-value[b]	**<0.001***	**<0.001***		
Cheek				
Baseline	261.5±48.46	280.17±35.95	-18.67 (-54.79, 17.46)	0.296
4 weeks	250.92±49.34	264.50±35.0	-13.58 (-49.80, 22.63)	0.445
8 weeks	238.92±51.88	251.83±37.49	-12.92 (-51.24, 25.40)	0.492
12 weeks	233.42±49.92	245.08±36.33	-11.67 (-48.63, 25.29)	0.520
P-value[b]	**<0.001***	**<0.001***		

Note Data were analyzed with Independent t-test[a], Repeated measure ANOVA[b]

* Statistically significant at the 0.05 level

According to Table 4.2, the comparison of the mean melanin index in the forehead and cheek areas reveals that the group using the 4% White Radish Root cream showed mean melanin index values for the forehead at baseline, 4, 8, and 12 weeks of 299.58±42.55, 293.92±44.94, 280.08±47.11, and 272.67±46.16, respectively. These values showed a statistically significant decrease at the 0.05 level (P<0.001), with a partial η^2 of 0.841. This indicates that the 4% White Radish Root cream was effective in changing the mean melanin index in the forehead area to 84.1%. On the other hand,

the 2% Alpha Arbutin group had average melanin index values for the forehead at baseline, 4, 8, and 12 weeks of 318.42±35.68, 308.17±37.37, 293.67±38.97, and 283.33±34.32, respectively. These values also showed a statistically significant decrease at the 0.05 level ($P<0.001$). This indicates that the 2% Alpha Arbutin cream was effective in changing the mean melanin index in the forehead area to 90.2%. However, when comparing the mean melanin index in the forehead area between the two groups at each follow-up time point, no statistically significant differences were found ($P>0.05$).

For the cheek area, the 4% White Radish Root cream group showed average melanin index values at baseline, 4, 8, and 12 weeks of 261.5±48.46, 250.92±49.34, 238.92±51.88, and 233.42±49.92, respectively. These values showed a statistically significant decrease at the 0.05 level ($P<0.001$), with a partial η^2 of 0.886, indicating that the 4% White Radish Root cream was effective in changing the mean melanin index in the cheek area to 88.6%. Meanwhile, the 2% Alpha Arbutin cream group showed mean melanin index values at baseline, 4, 8, and 12 weeks of 280.17±35.95, 264.50±35.0, 251.83 ±37.49, and 245.08±36.33, respectively. These values also demonstrated a statistically significant decrease at the 0.05 level ($P<0.001$) meaning the 2% Alpha Arbutin cream was effective in changing the mean melanin index in the cheek area to 90.3%. However, when comparing the mean melanin index in the cheek area between the two groups at each follow-up time point, no statistically significant differences were found ($P>0.05$).

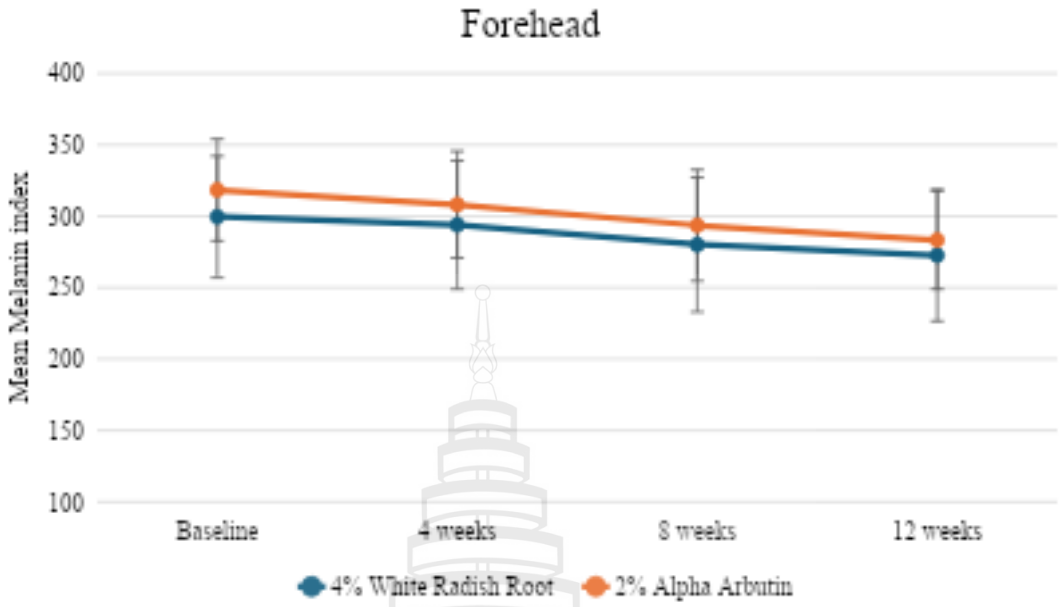


Figure 4.1 Line graph showing mean melanin index on the forehead for 4% white radish root cream and 2% alpha arbutin cream at baseline, 4, 8, and 12 weeks

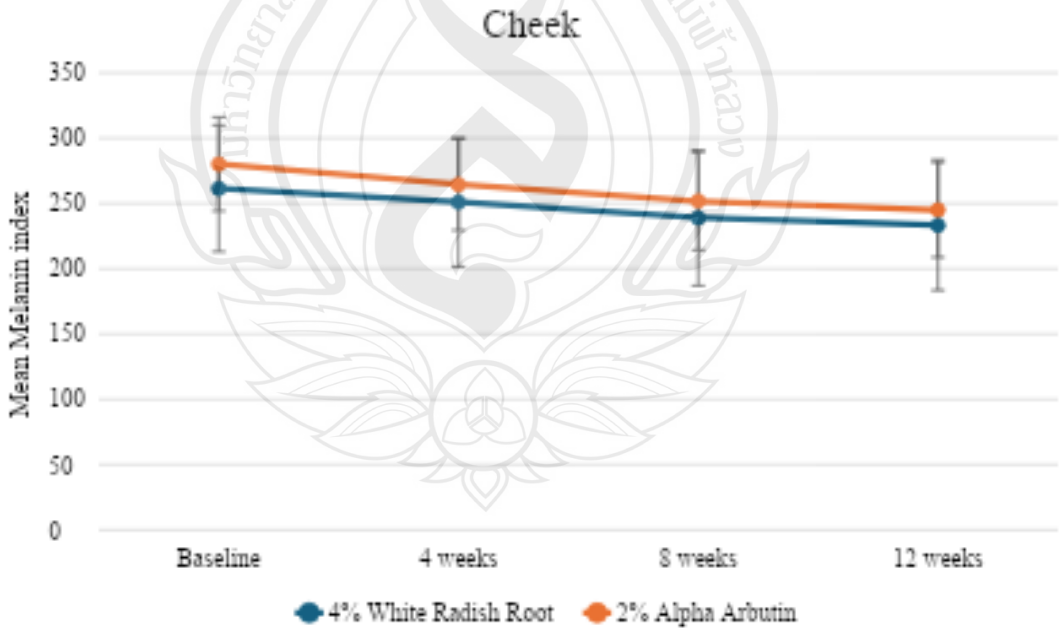


Figure 4.2 Line graph showing mean melanin index on the cheek for 4% white radish root cream and 2% alpha arbutin cream at baseline, 4, 8, and 12 weeks

Table 4.3 Multiple comparison analysis (post-hoc test) of mean melanin index

Pairwise	4% White Radish Root, mean difference (P-value)	2% Alpha Arbutin, mean difference (P-value)
Forehead		
Baseline - 4 weeks	-5.67 (P=0.091)	-10.25 (P<0.001*)
Baseline - 8 weeks	-19.50 (P<0.001*)	-24.75 (P<0.001*)
Baseline - 12 weeks	-26.92 (P<0.001*)	-35.08 (P<0.001*)
4 weeks – 8 weeks	-13.83 (P<0.001*)	-14.50 (P<0.001*)
4 weeks – 12 weeks	-21.25 (P<0.001*)	-24.83 (P<0.001*)
8 weeks – 12 weeks	-7.42 (P=0.073)	-10.33 (P=0.020*)
Cheek		
Baseline - 4 weeks	-10.58 (P<0.001*)	-15.67 (P<0.001*)
Baseline - 8 weeks	-22.58 (P<0.001*)	-28.33 (P<0.001*)
Baseline - 12 weeks	-28.08 (P<0.001*)	-35.08 (P<0.001*)
4 weeks – 8 weeks	-12.00 (P=0.001*)	-12.67 (P<0.001*)
4 weeks – 12 weeks	-17.50 (P<0.001*)	-19.42 (P<0.001*)
8 weeks – 12 weeks	-5.50 (P=0.164)	-6.75 (P=0.078)

Note Adjustment for multiple comparisons by Bonferroni method

* The mean difference is significant at the 0.05 level

According to Table 4.3, the multiple comparison analysis of the mean melanin index indicates that in the 4% White Radish Root cream group, the mean melanin index on the forehead at weeks 8 and 12 was lower than at baseline by 19.50 and 26.92, respectively. Additionally, the values at weeks 8 and 12 were lower than week 4 by 13.83 and 21.25, respectively, all comparisons showed statistical significance at the 0.05 level (P<0.05). In the 2% Alpha Arbutin cream group, the mean melanin index on the forehead at weeks 4, 8, and 12 was lower than at baseline by 10.25, 24.75, and 35.08, respectively. The values at weeks 8 and 12 were lower than week 4 by 14.50 and 24.83, respectively, and the value at week 12 was lower than week 8 by 10.33. All changes were statistical significance at the 0.05 level (P<0.05).

For the cheek area, in the 4% White Radish Root cream group, the mean melanin index at weeks 4, 8, and 12 was lower than baseline by 10.58, 22.58, and 28.08, respectively. The values at weeks 8 and 12 were lower than week 4 by 12.00 and 17.50,

respectively, all with statistical significance at the 0.05 level (P<0.05). In the 2% Alpha Arbutin cream group, the mean melanin index at weeks 4, 8, and 12 was lower than baseline by 15.67, 28.33, and 35.08, respectively. The values at weeks 8 and 12 were lower than week 4 by 12.67 and 19.42, respectively, all with statistical significance at the 0.05 level (P<0.05).

4.3 Dermatologists' Evaluation Score

Table 4.4 Dermatologists' evaluation scores for 4% white radish root cream and 2% alpha arbutin cream across follow-up times

Follow-up times	4% White Radish Root	2% Alpha Arbutin	P-value
4 weeks			
No change (0)	4	3	
Fair satisfaction (1)	7	9	
Moderate satisfaction (2)	1	0	
Median (IQR)	1 (0,1)	1 (0.25,1)	0.916
8 weeks			
Fair satisfaction (1)	5	2	
Moderate satisfaction (2)	7	10	
Median (IQR)	2 (1,2)	2 (2,2)	0.187
12 weeks			
Moderate satisfaction (2)	9	3	
Good satisfaction (3)	3	9	
Median (IQR)	2 (2,2.75)	3 (2.25,3)	0.016*

Note IQR: Interquartile range; Data were analyzed with Mann Whitney U test

* Statistically significant at the 0.05 level

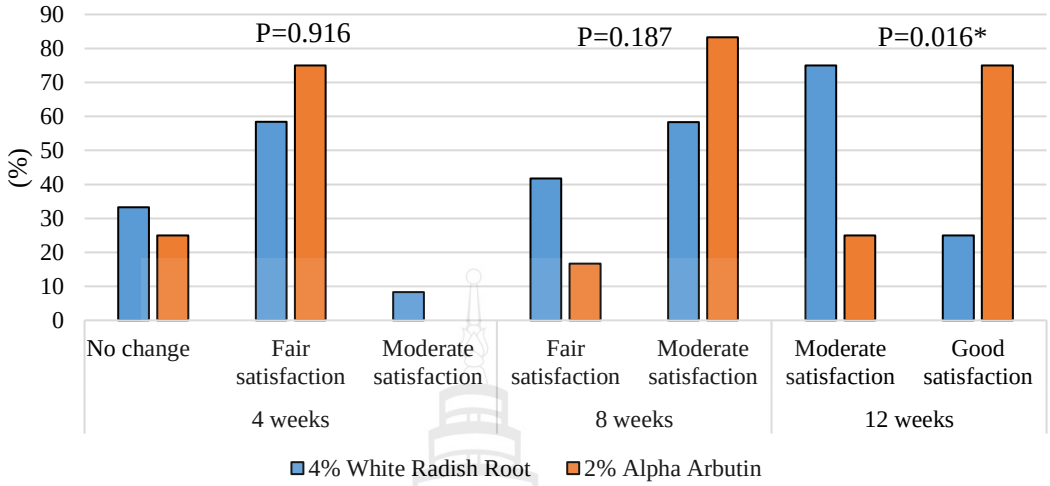


Figure 4.3 Bar chart showing proportion of dermatologists' evaluation scale for 4% white radish root cream and 2% alpha arbutin cream

Table 4.4 summarizes dermatologists' evaluation scores for patients treated with 4% White Radish Root cream and 2% Alpha Arbutin cream over 4, 8, and 12 weeks, analyzed using the Mann–Whitney U test. At the 4-week assessment, no statistically significant difference was found between the two treatments ($p = 0.916$). Both groups had a median score of 1 (Fair satisfaction), with interquartile ranges indicating low variability in early outcomes.

At 8 weeks, improvements were observed in both groups. The 2% Alpha Arbutin group had a median score of 2 with a narrow IQR (2–2), indicating consistent moderate satisfaction among evaluators, whereas the 4% White Radish Root group also had a median of 2 but with a wider IQR (1–2), reflecting more variability. However, the difference remained statistically non-significant ($p = 0.187$).

By 12 weeks, a statistically significant difference emerged ($p = 0.016$), with dermatologists rating the 2% Alpha Arbutin cream more favorably. The Alpha Arbutin group had a higher median score of 3 (Good satisfaction) compared to 2 (Moderate satisfaction) for the White Radish Root group. The interquartile range also shifted upward in the Alpha Arbutin group (2.25–3), suggesting more consistently positive evaluations. These findings indicate that, from a clinical perspective, the 2% Alpha Arbutin cream provided superior skin-whitening efficacy over time compared to the 4% White Radish Root cream.

4.4 Participants' Satisfaction Score

Table 4.5 Participants' satisfaction score for 4% white radish root cream and 2% alpha arbutin cream at 12 weeks

Satisfaction levels	4% White Radish Root	2% Alpha Arbutin	P-value
Moderate Satisfaction (2)	5	1	
Good Satisfaction (3)	6	8	
Excellent Satisfaction (4)	1	3	
Median (IQR)	3 (2,3)	3 (3,3.75)	0.058

Note IQR: Interquartile range; Data were analyzed with Mann Whitney U test

* Statistically significant at the 0.05 level

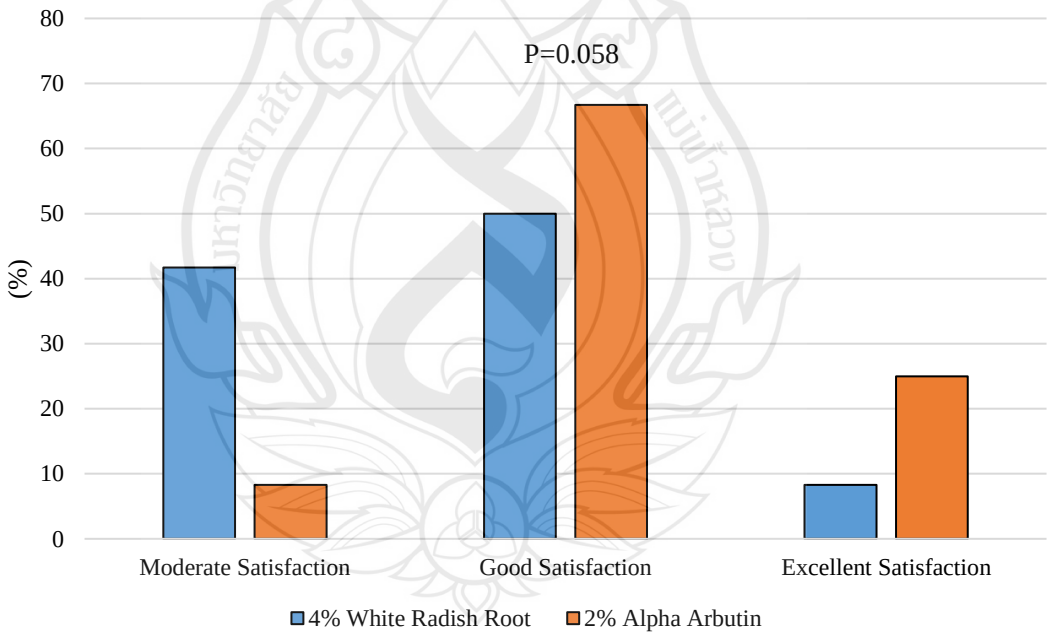


Figure 4.4 Bar chart showing proportion of participant's satisfaction scale for 4% white radish root cream and 2% alpha arbutin cream

At the 12-week follow-up, participants' satisfaction scores for the 4% White Radish Root cream and 2% Alpha Arbutin cream were compared. The satisfaction

levels for both treatments were categorized as Moderate (2), Good (3), and Excellent (4).

For the 4% White Radish Root cream, 5 participants reported "Moderate satisfaction," 6 reported "Good satisfaction," and 1 reported "Excellent satisfaction." In contrast, for the 2% Alpha Arbutin cream, 1 participant reported "Moderate satisfaction," 8 reported "Good satisfaction," and 3 reported "Excellent satisfaction." The median satisfaction scores for both treatments were 3 (Good satisfaction), with the interquartile range (IQR) for both treatments also being similar. The p-value was 0.058, indicating that there was no statistically significant difference between the two treatments at the 0.05 significance level. These findings suggest that, while both treatments achieved similar satisfaction levels, the difference between the two groups was not statistically significant at 12 weeks.

4.5 Adverse Effects

No adverse effects were observed in any participants during the treatment with 4% white radish root extract cream and 2% alpha arbutin cream.

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 Discussion

In today's world, cosmetics incorporating herbal and botanical ingredients are increasingly regarded as safer alternatives to those containing synthetic chemicals, attracting significant consumer interest. However, larger studies with more extensive sample sizes are necessary to validate the safety and clinical efficacy of herbal medicines with high therapeutic indices. As public awareness of the potential risks of synthetic chemicals grows, the cosmetic industry has shifted its focus towards natural, plant-based products, making herbal remedies for skin whitening a growing global trend.

To the best of our knowledge, this is the comparative, single-blind, randomized, controlled clinical trial to evaluate the efficacy of 4% white radish root extract cream and 2% alpha arbutin cream for facial whitening in males and females aged 20-50.

In this study, 24 participants (both male and female) with the Fitzpatrick skin type II to type V, were joined. 14 female and 10 male subjects were registered in this study. The mean age of the subject was 31.92±5.95 for 4% white radish root cream and 32.67±6.98 for 2% alpha arbutin cream ranging from 20-50 years. There were 15 students, 6 employers and 3 housewives. All volunteers had history of cosmetic usage before but no history of facial skin whitening treatment recently. Average sun exposure time between 10 am to 4 pm which was the main aggravating factor for melanogenesis was 20 (IQR 10,30) minutes per day. None had received cosmetic treatments in the 4 weeks prior to the study. Two participants had a history of drug and food allergies, but no participant had a history of cosmetic allergies. Six participants were using personal medications and supplements. Hence, the researcher instructed to stop taking supplements temporarily till the end of this study. All the volunteers had sun exposure which is an aggravating factor of melanogenesis.

A statistically significant reduction in melanin concentration from the baseline period was observed in the study's results following a 12-week application of 4% white radish root extract cream and 2% alpha arbutin cream. Recent studies proved that anti-tyrosinase properties of 4% white radish root extract cream and 2% alpha arbutin cream take part in reduction of melanin index, which is key enzyme for inhibiting melanogenesis (Jakmatakul et al., 2019).

Dermatologists' evaluations at 4 and 8 weeks showed no significant difference in satisfaction between the 4% White Radish Root cream and 2% Alpha Arbutin cream, with both treatments having identical median scores (1 at week 4 and 2 at week 8). However, by week 12, the 2% Alpha Arbutin cream showed significantly higher satisfaction (median = 3) compared to the White Radish cream (median = 2), suggesting improved dermatological outcomes with Alpha Arbutin over time. For participants' satisfaction scores, at the 12-week both the 4% White Radish Root cream and the 2% Alpha Arbutin cream were similar, with median scores of 3 (Good satisfaction) and comparable interquartile ranges. Although more participants reported higher satisfaction with the Alpha Arbutin cream, the difference between the two groups was not statistically significant ($p = 0.058$). Regarding side effects, No side effects, such as redness, rashes, or other skin problems, were observed with either the 4% white radish root extract cream or the 2% alpha arbutin cream. The 4% white radish root extract cream was well tolerated and considered safe for longer use. However, further research is needed to confirm its safety for extended use.

5.2 Conclusion

Although 2% Alpha Arbutin cream showed a slightly better reduction in melanin levels than 4% White Radish Root extract cream, the difference was minimal. This indicates that the 4% White Radish Root extract cream is almost as effective as the 2% Alpha Arbutin cream in reducing melanin. Significant skin lightening was observed after just 4 weeks of use. The 4% White Radish Root extract cream caused no side effects, and volunteers were generally satisfied with the results. Therefore, it is a promising, safe, and cost-effective option for facial whitening. However, further

research is needed to determine how long it takes for the 4% White Radish Root extract cream to achieve its maximum whitening effect and to assess any potential side effects from prolonged use.

5.3 Limitation

The study period may limit the depth of the results, with a longer study potentially providing more definitive outcomes. Moreover, there was no strict control over factors such as sun exposure, sleep routines, health habits, age, and stress. These uncontrolled variables might lead to more prominent effects on the study's results.

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APPENDIX A

INFORMED CONSENT FORM

หนังสือแสดงเจตนายินยอมเข้าร่วมในโครงการวิจัย สำหรับอาสาสมัคร

(Informed Consent)

ข้าพเจ้า _____ตัดสินใจเข้าร่วมการวิจัยเรื่อง “การศึกษาเปรียบเทียบประสิทธิภาพของครีมสารสกัดหัวไชเท้า 4%กับครีมอัลฟ่าอาร์บูติน 2% ในการบำรุงผิวหน้าให้ขาวใส” ซึ่งข้าพเจ้าได้รับข้อมูลและคำอธิบายเกี่ยวกับการวิจัยนี้แล้ว และได้มีโอกาสซักถามและได้รับคำตอบเป็นที่พอใจแล้ว ข้าพเจ้ามีเวลาเพียงพอในการอ่านและทำความเข้าใจข้อมูลในเอกสารให้ข้อมูลสำหรับผู้เข้าร่วมการวิจัยอย่างถี่ถ้วน และได้รับเวลาเพียงพอในการตัดสินใจว่าจะเข้าร่วมการวิจัยนี้

ข้าพเจ้ารับทราบว่าข้าพเจ้าสามารถปฏิเสธการเข้าร่วมการวิจัยนี้ได้โดยอิสระ และระหว่างการเข้าร่วมการวิจัย ข้าพเจ้ายังสามารถถอนตัวออกจากการวิจัยได้ทุกเมื่อ โดยไม่ส่งผลกระทบต่อการดูแลรักษา หรือสิทธิที่ข้าพเจ้าพึงมี

โดยการลงนามนี้ ข้าพเจ้าไม่ได้สละสิทธิใดๆที่ข้าพเจ้าพึงมีตามกฎหมาย และหลังจากลงนามแล้ว ข้าพเจ้าจะได้รับเอกสารข้อมูลและเอกสารขอความยินยอมไว้จำนวน ชุด

ลายมือชื่อผู้เข้าร่วมการวิจัย _____ วัน-เดือน-ปี _____

(_____)

..... (กรณีที่ผู้เข้าร่วมการวิจัยอ่านหนังสือไม่ออกแต่ฟังเข้าใจ) .....

ข้าพเจ้าไม่สามารถอ่านหนังสือได้ แต่ผู้วิจัยได้อ่านข้อความในเอกสารข้อมูลและขอความยินยอมนี้ให้แก่ข้าพเจ้าฟังจนเข้าใจดีแล้ว ข้าพเจ้าจึงลงนามหรือพิมพ์ลายนิ้วมือของข้าพเจ้าในหนังสือนี้ด้วยความสมัครใจ

ลงนาม/พิมพ์ลายนิ้วมือผู้เข้าร่วมการวิจัย _____ วัน-เดือน-ปี_____

(_____)

ลายมือชื่อผู้ขอความยินยอม _____ วัน-เดือน-ปี _____

คำรับรองของพยานผู้มิได้มีส่วนได้เสียกับการวิจัย (กรณีที่ผู้เข้าร่วมการวิจัยอ่านหนังสือไม่ออกแต่ฟัง เข้าใจ)

ข้าพเจ้าได้อยู่ร่วมในกระบวนการขอความยินยอมและยืนยันว่า ผู้ขอความยินยอมได้อ่าน/อธิบายเอกสารข้อมูลให้แก่ _____ ซึ่งผู้มีชื่อข้างต้นมีโอกาสซักถามข้อสงสัยต่าง ๆ และได้ให้ความยินยอมเข้าร่วมการวิจัยโดยอิสระ หลังจากรับทราบข้อมูลที่มีอยู่ตรงตามที่ปรากฏในเอกสารนี้แล้ว

ลายมือชื่อพยาน _____ วัน-เดือน-ปี _____

(_____)

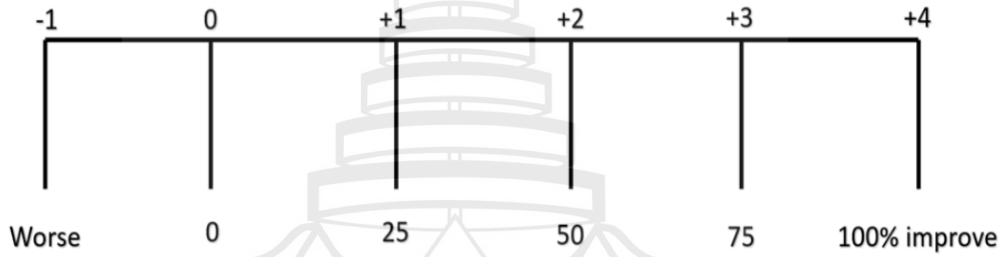
APPENDIX B

SKIN BRIGHTENING SATISFACTION QUESTIONARIES

การศึกษาเปรียบเทียบประสิทธิภาพของครีมสารสกัดหัวไชเท้า 4% กับครีมออัลฟาอาร์บูติน 2% ในการบำรุงผิวหน้าให้ขาวใส

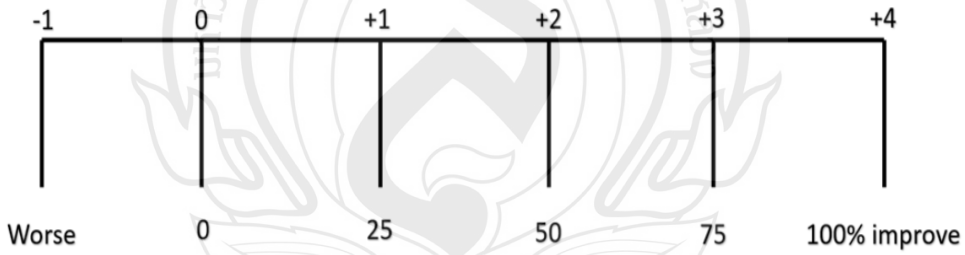
Overall Satisfactory Score (ความพึงพอใจโดยรวม)

Satisfaction by Dermatologist (Please draw the circle)



Satisfaction by volunteers at the 12th week (Please draw the circle)

ความพึงพอใจของอาสาสมัครสัปดาห์ที่ 12 (โปรดวาดวงกลม)



Score range from -1 to +4

-1 = Worse

0 = No changes

+1= Improved -25% (fair)

+2 = Improved 26-50% (moderate)

+3 = Improved 51-75% (good)

+4 = Improved 76-100% (excellent)

ช่วงคะแนนตั้งแต่ -1 ถึง +4

-1 = แย่ลง

0 = ไม่มีการเปลี่ยนแปลง

+1= อาการดีขึ้น-25% (พอใช้)

+2 = อาการดีขึ้น 26-50% (ปานกลาง)

+3 = อาการดีขึ้น 51-75% (ดี)

+4 = อาการดีขึ้น 76-100% (ดีเยี่ยม)

APPENDIX C

SIDE EFFECT RECORD FORM (PHYSICIAN EVALUATION)

Adverse Effects	**4% white radish cream**				**2%alpha arbutin cream**			
	No	**Mild**	**Mod**	**Severe**	**No**	**Mild**	**Mod**	**Severe**
Erythema								
Scaling								
Edema								
Itchy								
Dry Skin								

Others……..

APPENDIX D

RESEARCH PROFILE (CONFIDENTIAL)

Volunteer number.....

Patient Record Form

General Information

1. Date_ _/_ _/_ _
2. Gender a. Male b. Female

   Pregnancy or lactation 1. Yes 2. No
3. Occupation
   1) Government officer
   2) business owner
   3) Housewife
   4) Student
   5) Employee
   6) Others
   7) Specify _
4. Underlying disease _
5. Photosensitivity or Drug Induced Hypersensitivity 1. Yes 2. No
6. Personal medication and supplement
   1) Chemotherapy
   2) Active inflammatory skin disease, open wound in the treatment area
   3) History of malignant or premalignant lesions in the treatment area
7. History of food or drug allergy 1. Yes 2. No

   If Yes, specify _
8. Current facial product allergy 1. Yes 2. No

   If Yes, specify _

9. History of the following treatment before this study? 1. Yes 2. No

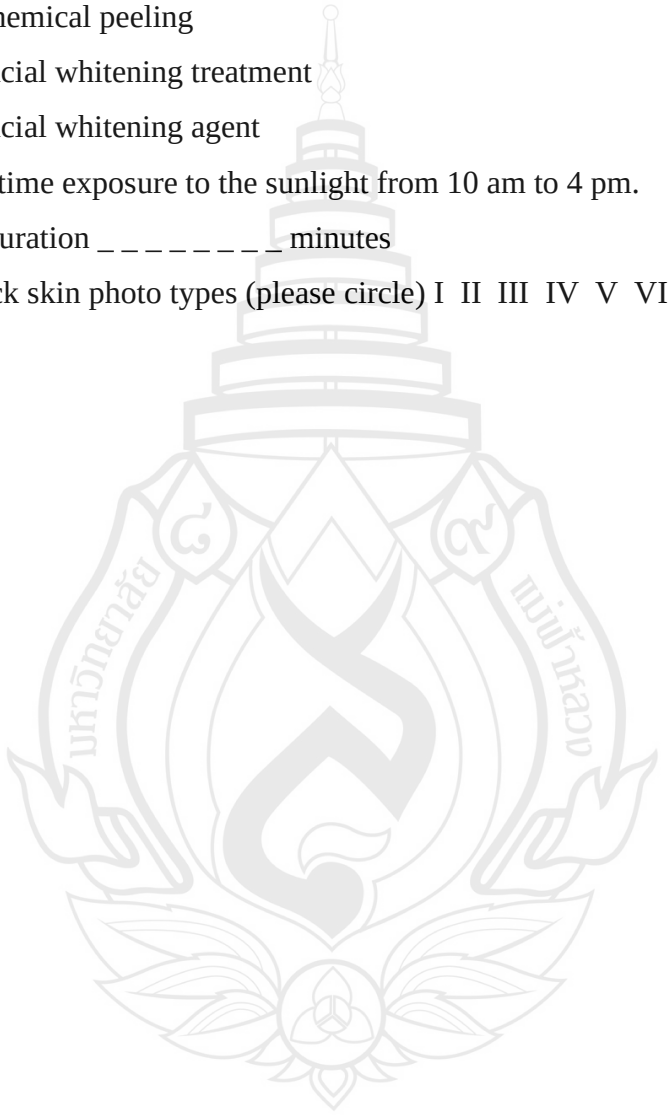
   If Yes, ablative and non-ablative laser

   - ❖ Intense pulse light
   - ❖ Microdermabrasion
   - ❖ Skin needling
   - ❖ Chemical peeling
   - ❖ Facial whitening treatment
   - ❖ Facial whitening agent

10. Average time exposure to the sunlight from 10 am to 4 pm. 1. Yes 2. No

    If Yes, Duration _ _ _ _ _ _ _ _ minutes

11. Fitzpatrick skin photo types (please circle) I II III IV V VI



APPENDIX E

CLINICAL EVALUATION

Table E1 Mean melanin index scores with 4% White Radish Root Extract Cream or 2% Alpha Arbutin Cream on each visit

Number of Subjects	Mean melanin index (n=24)			
	4% White Radish Root Extract Cream (or) 2% Alpha Arbutin Cream			
	Baseline	4th week	8th week	12th week
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				

Table E2 Dermatologists evaluation scores 4% White Radish Root Extract Cream (or) 2% Alpha Arbutin Cream on 12th week

Dermatologist Satisfaction Scores Number of Patients (N)
4% White Radish Root Extract Cream (or) 2% Alpha Arbutin Cream
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19

Table E3 Patient satisfaction scores on 12th week with 4% White Radish Root Extract Cream (or) 2% Alpha Arbutin Cream

Patient Satisfaction Scores	**Number of patients (n)**
	4% White Radish Root Extract Cream (or) 2% Alpha Arbutin Cream
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	

APPENDIX F

DOCTOR RECORD FORM

Melanin Index (MI) by Mexameter MX 18

Melanin Index (White Radish Root Extract Cream)

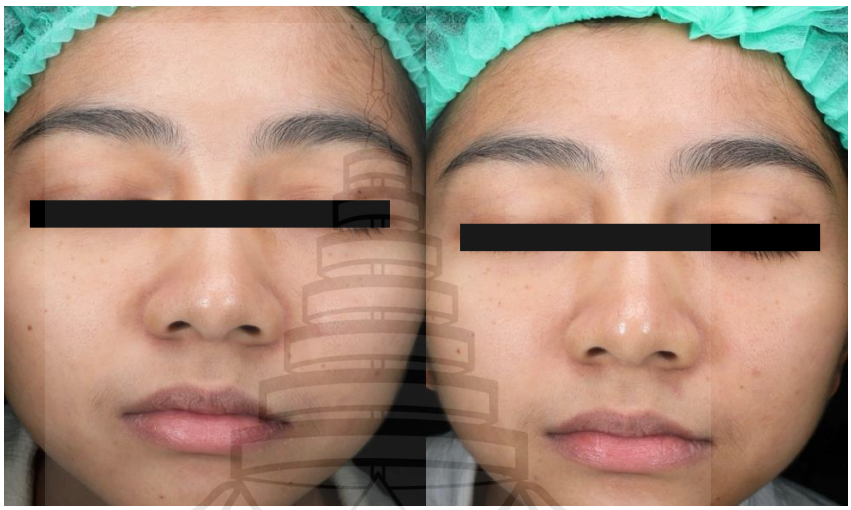
Baseline	4th Week	8th Week	12th Week

Melanin Index (Alpha Arbutin Cream)

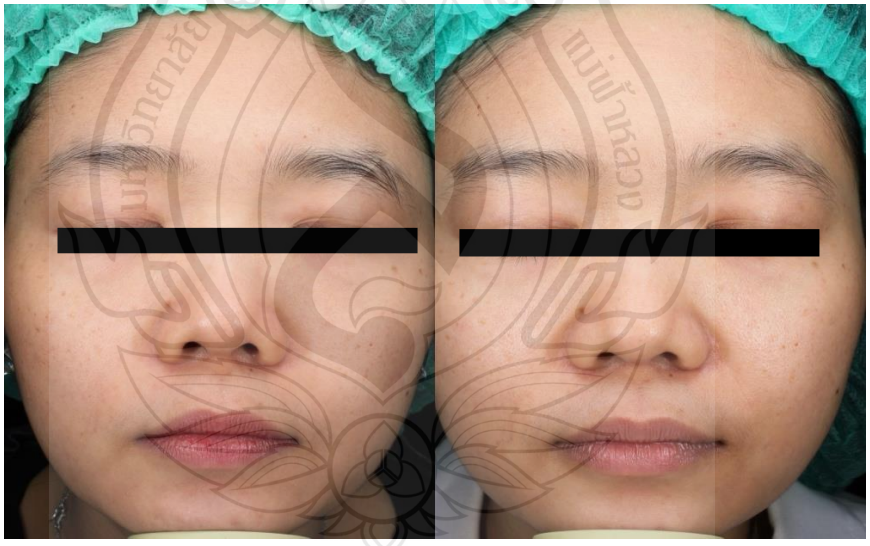
Baseline	4th Week	8th Week	12th Week

APPENDIX G

STANDARDIZED PHOTOGRAPHS OF SUBJECTS

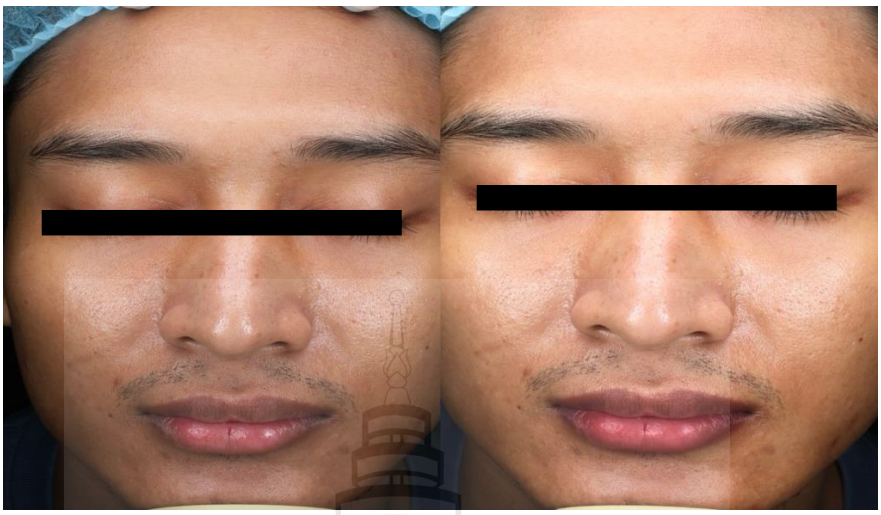


Before **After**

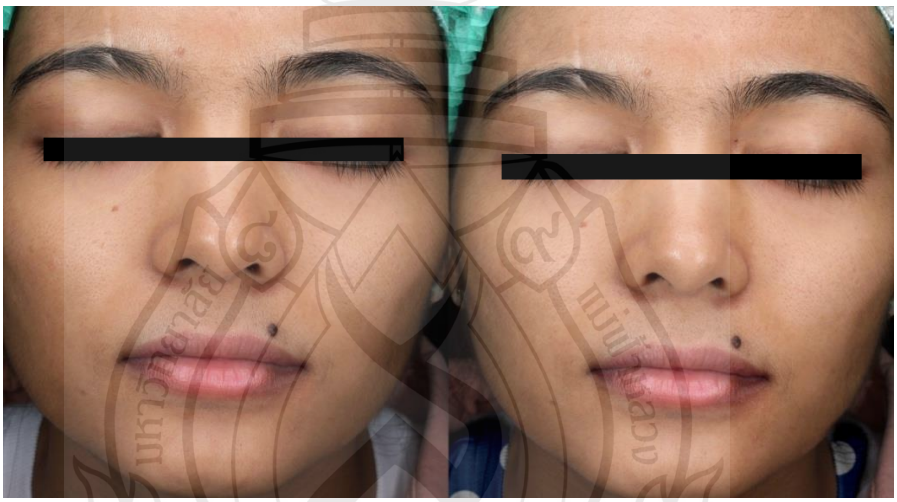


Before **After**

Figure G1 Photos of subjects applying 4% white radish root extract cream before and after 12th week result



Before **After**



Before **After**

Figure G2 Photos of subjects applying 2%Alpha Arbutin cream before and after 12th week result

APPENDIX H

CLINICAL EVALUATION (RESEARCH QUESTIONS)

Research Questions

To compare the efficacy of 4% white radish root extract cream and 2% alpha arbutin cream in facial whitening.

Table H1 Participants' demographic data

Vol No	Gender	Age	Work	Underlying diseases	Fitzpatrick Skin Type	Exposure to sunlight Per day	Cosmetics Treatment 4 weeks Before study	Food or drug allergy	Cosmetics allergy	Personal Medication & supplement
W1	F	30	Student	No	III	30 mins	No	No	No	Supplement
W2	F	30	Student	No	III	15 mins	No	No	No	No
W3	F	29	Student	No	III	15 mins	No	No	No	No
W4	F	28	Student	No	III	30 mins	No	No	No	No
W5	F	33	Employee	No	IV	10 mins	No	No	No	No
W6	M	24	Student	No	III	10 mins	No	No	No	No
W7	M	26	Student	No	IV	20 mins	No	No	No	No
W8	M	35	Employee	No	II	30 mins	No	No	No	No
W9	F	34	Employee	No	III	30 mins	No	No	No	No
W10	F	45	Housewife	No	III	10 mins	No	No	No	Multivitamins

Table H1 (continued)

Vol No	Gender	Age	Work	Underlying diseases	Fitzpatrick Skin Type	Exposure to sunlight Per day	Cosmetics Treatment 4 weeks Before study	Food or drug allergy	Cosmetics allergy	Personal Medication & supplement
W11	F	29	Student	No	III	10 mins	No	Seafood Allergy	No	No
W12	M	40	Employee	No	IV	10 mins	No	No	No	Multivitamins
W13	M	36	Employee	No	IV	10 mins	No	No	No	No
W14	F	44	Housewife	No	III	30 mins	No	No	No	No
W15	F	47	Housewife	No	III	10 mins	No	No	No	Supplement
W16	F	35	Student	No	III	20 mins	No	No	No	Supplement
W17	F	32	Student	No	III	10 mins	No	No	No	No
W18	M	31	Student	No	II	10 mins	No	No	No	No
W19	M	31	Student	No	II	30 mins	No	No	No	No
W20	F	32	Employee	No	III	20 mins	No	Seafood Allergy	No	No
W21	F	26	Student	No	III	30 mins	No	No	No	Supplement
W22	M	26	Student	No	IV	20 mins	No	No	No	No
W23	M	27	Student	No	IV	30 mins	No	No	No	No
W24	M	25	Student	No	III	20 mins	No	No	No	No

Table H2 Mean Melanin index of the face that applied with 4% white radish root extract cream

Mean melanin index (n=12)								
4% White Radish Root Extract Cream								
Vol	**Baseline**		**4th week**		**8th week**		**12th week**	
No	**Forehead**	**cheek**	**forehead**	**cheek**	**forehead**	**cheek**	**forehead**	**cheek**
1	265	186	258	180	243	165	234	155
2	324	295	318	288	295	270	290	264
3	307	275	315	267	300	257	295	248
4	325	290	320	277	311	271	307	267
5	330	285	335	273	328	268	304	265
6	270	238	268	225	255	220	252	214
7	254	232	240	225	220	194	216	205
8	240	197	225	184	215	177	207	168
9	394	367	385	360	378	355	365	340
10	321	278	310	269	295	255	307	250
11	287	254	281	240	268	225	253	210
12	278	241	272	223	253	210	242	215

Table H3 Mean Melanin index of the face that applied with 2% alpha arbutin cream

Mean melanin index (n=12)								
2% Alpha Arbutin Cream								
Vol	**Before Treatment**		**4th week**		**8th week**		**12th week**	
No	**Forehead**	**cheek**	**forehead**	**cheek**	**forehead**	**Forehead**	**cheek**	**forehead**
1	340	285	335	267	1	340	285	335
2	326	282	315	269	2	326	282	315
3	387	353	382	340	3	387	353	382
4	257	219	243	195	4	257	219	243
5	284	250	267	239	5	284	250	267
6	313	284	310	268	6	313	284	310
7	328	296	315	284	7	328	296	315
8	341	317	326	292	8	341	317	326
9	335	288	327	273	9	335	288	327
10	265	230	260	235	10	265	230	260
11	319	275	300	252	11	319	275	300
12	326	283	318	260	12	326	283	318

Table H4 Satisfaction Score by Volunteers at 12th week

Volunteer No	4% white radish root extract cream	Volunteer No	2% alpha arbutin cream
	Score		Score
1	2	1	4
2	3	2	3
3	2	3	4
4	3	4	3
5	2	5	2
6	3	6	3
7	3	7	3
8	2	8	3
9	4	9	3
10	2	10	3
11	3	11	3
12	3	12	4

Score -1 = Worse

Score 0 = No Changes

Score 1 = Fair Satisfaction (1-25% improve)

Score 2 = Moderate Satisfaction (>25-50% improve)

Score 3 = Good Satisfaction (>50-75% improve)

Score 4 = Excellent Satisfaction(>75-100% improve)

Table H5 Dermatologists' evaluation score of 4% white radish root extract cream for facial whitening on 4th ,8th, 12th week

Volunteer	4th week			8th week			12th week		
	Dr 1	**Dr 2**	**Dr 3**	**Dr 1**	**Dr 2**	**Dr 3**	**Dr 1**	**Dr 2**	**Dr 3**
1	1	0	1	1	1	2	2	2	3
2	1	1	1	2	1	2	2	3	3
3	1	-1	0	2	2	1	2	3	2
4	1	0	0	2	2	1	2	3	3
5	0	-1	0	1	2	1	2	2	1
6	0	0	1	1	2	1	2	2	3
7	2	1	2	1	2	2	2	2	3
8	2	1	1	2	2	1	2	3	3
9	1	1	0	1	1	1	2	2	2
10	1	0	1	2	1	1	1	2	2
11	1	0	1	2	2	1	2	2	3
12	1	1	2	2	1	2	2	2	3

Score -1 = Worse

Score 0 = No Changes

Score 1 = Fair Satisfaction (1-25% improve)

Score 2 = Moderate Satisfaction (>25-50% improve)

Score 3 = Good Satisfaction (>50-75% improve)

Score 4 = Excellent Satisfaction(>75-100% improve)

Table C6 Dermatologists' evaluation score of 2% alpha arbutin cream for facial whitening on 4th, 8th, 12th week

Volunteer	4th week			8th week			12th week		
	Dr 1	Dr 2	Dr 3	Dr 1	Dr 2	Dr 3	Dr 1	Dr 2	Dr 3
1	1	1	1	2	2	3	2	3	3
2	1	1	2	2	2	2	2	3	3
3	0	1	1	2	1	2	3	2	3
4	1	1	1	1	2	3	2	2	3
5	1	0	0	1	2	2	2	2	2
6	1	1	1	2	2	2	2	3	3
7	0	0	1	1	1	2	2	2	2
8	1	1	1	2	1	3	2	3	3
9	1	1	1	2	1	2	3	3	3
10	1	1	0	2	2	2	2	3	3
11	1	1	0	2	2	1	2	3	3
12	0	0	1	1	1	2	2	3	3

Score -1= Worse

Score 0 = No Changes

Score 1 = Fair Satisfaction (1-25% improve)

Score 2 = Moderate Satisfaction (>25-50% improve)

Score 3 = Good Satisfaction (>50-75% improve)

Score 4 = Excellent Satisfaction(>75-100% improve)

CURRICULUM VITAE

NAME Wint Nandar Thein

EDUCATIONAL BACKGROUND

2020 Bachelor of Medicine and Bachelor of Surgery,
University of Medicine 1, Mandalay (M.B.B.S)

WORK EXPERIENCE

2018-2019 Internship
Mandalay General Hospital
Mandalay Children Hospital,
Central Women Hospital Mandalay.

2020-2021 Medical Officer
Pun Hlaing Silom Hospital, Mandalay, Myanmar.