PRELIMINARY CLINICAL STUDY, EFFICACY AND SAFETY EVALUATION OF HERBAL PREPARATIONS ADDED WITH CANNABIS IN THE TREATMENT OF PSORIASIS PATIENTS

BY

KAMOLRAK LOMWONG

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การศึกษาทางคลินิกเบื้องต้น การประเมินประสิทธิผลและความปลอดภัยของยาทาสมุนไพรที่มีส่วนผสมของกัญชาในการรักษาผู้ป่วยโรคสะเก็ดเงิน

โดย
กมลรักษ์ ล้อมวงษ์

วิทยานิพนธ์ฉบับนี้เป็นส่วนหนึ่งของการศึกษาตาม
หลักสูตรวิทยาศาสตรมหาบัณฑิต สาขาวิชาวิทยาศาสตร์ชีวการแพทย์
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Thesis entitled

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วิทยานิพนธ์ฉบับนี้สำเร็จได้เป็นอย่างดีเนื่องมาจากได้รับความอนุเคราะห์และการให้คำปรึกษาอย่างดีจากหลายท่าน ขอขอบพระคุณอาจารย์ที่ปรึกษาวิทยานิพนธ์ ผศ. รตท. หญิง ดร. อัจฉราวรรณ ทองมี และ อาจารย์ที่ปรึกษาร่วม ดร. วันทิกา เครือน้ำคำ ได้ประสิทธิประสาทความรู้และคำแนะนำในการทำวิจัย ตลอดจนให้ความช่วยเหลือในการเขียนและตรวจสอบวิทยานิพนธ์จนประสบความสำเร็จเป็นอย่างดี ผู้วิจัยขอขอบพระคุณเป็นอย่างสูง

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งานวิจัยนี้สำเร็จได้เป็นอย่างดีเนื่องมาจากได้รับการสนับสนุนจาก บริษัท เอ็มพาวเวอร์ไลฟ์ จำกัด ที่ให้ทุนสนับสนุนการวิจัยและครีมทาสูตรปรับปรุงจากน้ำมันกัญชา “GPOCE (THC:CBD 1:1)” และ ครีมทาสูตร “ไทย-ไบโอ®” + “GPOCE (THC:CBD 1:1)” ที่ใช้ในงานวิจัยนี้ ผู้วิจัยขอขอบพระคุณเป็นอย่างสูง

สุดท้ายนี้ขอขอบพระคุณครอบครัวและเพื่อน ๆ ทุกคนที่ให้การสนับสนุนตลอดระยะเวลาในการทำงานวิจัยนี้

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Abstract

The objectives of this study were 1) to investigate the efficacy and safety of a traditional sublingual oil drop product named "GPOCE THC:CBD 1:1" when used at 5% concentration as a cream base, 2) to compare its effectiveness with an improved formulation of topical cream called "Thai Bio®" combined with "GPOCE THC:CBD 1:1" at 5% concentration (with a ratio of 95% "Thai Bio®" to 5% "GPOCE THC:CBD 1:1"); and thirdly, to develop a Cannabis-containing topical dosage form tailored for psoriasis patients. Both formulations were administered to a group of 20 voluntary psoriasis patients who participated in the study for 8 weeks. The severity of the disease was assessed using the PASI score, while the quality of life of the subjects was investigated through the administration of the Psoriasis Disability Index (PDI) and the Dermatology Life Quality Index (DLQI) questionnaires. Additionally, the study analyzed the changes in biochemical levels in the blood before and after the treatment.

The results of the study indicated a significant reduction in PASI scores after 4 weeks of cream application in both the "GPOCE THC:CBD 1:1" cream formula group and the "Thai Bio®" cream group. By incorporating the formula "GPOCE THC:CBD 1:1," the cream's effectiveness can be enhanced, leading to a reduction in the severity of the disease and an improvement in the quality of life for patients. These results demonstrate the safety and efficacy of both topical creams for the treatment of psoriasis. The ointment formulated with a combination of "Thai Bio®" and "GPOCE THC:CBD 1:1" was found to be more potent than the ointment formulated with "GPOCE THC:CBD 1:1" alone.

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การวิจัยในครั้งนี้มีวัตถุประสงค์ เพื่อศึกษาประสิทธิผลและความปลอดภัยของผลิตภัณฑ์จากน้ำมันรูปแบบดั้งเดิมแบบหยดใต้ลิ้น “GPOCE THC:CBD 1:1” ที่ใช้น้ำมัน “GPOCE THC:CBD 1:1” 5% เพียงอย่างเดียวในครีมเบส เปรียบเทียบกับสูตรปรับปรุงของครีมยาทา “Thai Bio®” ผสมตำรับ “GPOCE THC:CBD 1:1” 5 % (“Thai Bio®” 95%:“GPO THC:CBD 1:1” 5 %) และเพื่อพัฒนารูปแบบยาใช้ภายนอกที่มีส่วนผสมของกัญชาสำหรับผู้ป่วยโรคสะเก็ดเงิน ในอาสาสมัครเป็นผู้ป่วยโรคสะเก็ดเงินจำนวน 20 ราย โดยอาสาสมัครได้รับผลิตภัณฑ์ทั้ง 2 สูตรใช้ต่อเนื่องกันเป็นเวลา 8 สัปดาห์ โดยผลการศึกษาทำการเปรียบเทียบความความรุนแรงของโรคด้วย PASI score และคุณภาพชีวิตของอาสาสมัครด้วยแบบสอบถาม Psoriasis Disability Index (PDI), Dermatology Life Quality Index (DLQI) และ ตรวจวัดระดับสารชีวเคมีในเลือด ก่อนและหลังการรักษา

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คำสำคัญ: กัญชา, ครีมยาทา, โรคสะเก็ดเงิน

ลายมือชื่อนักศึกษา ..... ลายมือชื่ออาจารย์ที่ปรึกษา .....

ลายมือชื่ออาจารย์ที่ปรึกษาร่วม .....

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CHAPTER 1

INTRODUCTION

1.1 Background and Rationale

Psoriasis is a chronic skin condition caused by various factors such as food, weather, diabetes mellitus, stress, and other individual variations. Patients with psoriasis have a wide range of impacts on their physical health, mental health, families, society, economy, and quality of life (World Health Organization, 2016). Regarding the treatment of psoriasis, the available topical drugs are considered.

For the standard treatment of psoriasis, patients need to take the drug for a long time and may experience some side effects. The conceptual development of the skin cream drug will be a formula that consists of various herbal medicines. Generally, the drug characteristics are to reduce itching and inflammation of the skin and provide moisture to the skin. The selection of suitable herbs, involved a comprehensive review of Thai traditional medicine, modern medical knowledge, and relevant literature to create effective and safe formulas for users. Notably, ingredients like clove oil, false lime merlimau, mangosteen peel, false daisy, turmeric, common rhinacanthus, licorice, sea holly, snow lotus, and zinc are commonly found in the skin creams designed for psoriasis treatments.

This study focuses on the development of herbal medicines as an alternative the treatment of psoriasis, which is a disease that cannot be cured entirely. In addition, this research aims to develop a new formula for topical medications by incorporating added cannabis extract. Therefore, in this study, the cannabis oil was added to a formula registered as a skincare product named “Thai-Bio®”, FDA certificate No. 10-1-6100052062 under clinical trial research (CITE) and registered a petty patent, application number 2003002601. The efficacy of this formulated cream was assessed

by determining the psoriasis treat and Severity Index (PASI) score and by evaluating quality of life of the volunteers using the Psoriasis Disability Index (PDI) and Dermatology Life Quality Index (DLQI) before and after treatment with this cream. In addition, the effectiveness of the original sublingual oil “GPO THC: CBD 1:1”, referred to as CBD cream, was compared with the combination of Thai-Bio® formula enriched with cannabis oil in the treatment of Psoriasis.

1.2 Research Objectives

This study aims to evaluate and compare the efficacy of the two formulations:

1) The original sublingual oil “GPO THC: CBD 1:1” which uses only 5% of “GPO THC: CBD 1:1” oil in a cream base.

2) The new formulation of “Thai-Bio®” topical cream mixed with “GPO THC: CBD 1:1” 5 % (“Thai Bio®” 95%: “GPO THC: CBD 1:1” 5 %).

The PASI, PDI and DLQI scores are utilized to assess the severity and quality of life for psoriasis patients.

1.3 Research Questions

It is interesting to investigate whether the combination of Thai-Bio® with cannabis oil can provide belter relief from psoriasis compared to CBD cream.

1.4 Research Hypothesis

The combination of Thai-Bio® with cannabis oil has demonstrated greater efficacy for psoriasis compare to the CBD cream.

1.5 Scope of the research

The study examining short-term relief of signs and symptoms of psoriasis is structured as follows:

Research Design: The randomized crossover trial, a longitudinal study in which subjects receive a sequence of different treatments, will be conducted.

Control: CBD cream

Treatment: The combination of Thai-Bio® with cannabis oil

Subjects: There are 20 volunteers, aged between 18 and 69 years, who have mild psoriasis rash (PASI score≥3). The subjects are divided into two groups, 10 subjects per group.

Duration: This study will take 18 weeks to assess the efficacy of the treatment and the observation will be periodically made.

Evaluation: The criteria and evaluation schedule are given as follows:

PASI will be evaluated every two weeks.

PDI will be assessed every four weeks.

DLQI will be measured every week.

1.6 Expected Benefits

An alternative treatment for psoriasis will be developed. Guidelines for conducting further studies on a larger number of patients will be established.

CHAPTER 2

LITERATURE REVIEWS

2.1 Psoriasis

Psoriasis is a prevalent chronic inflammatory skin disease affecting approximately with 1-3 percent of the global population (Christophers, 2001). Psoriasis is associated with various body systems, including inflammatory bowel disease and psoriatic arthritis. Psoriasis arises from an immune system malfunction that accelerates the skin's natural shedding process, leading to rapid turnover and resulting in symptoms such as in scaly skin, red spots, itching, and Inflammation. The developments of psoriasis are influenced by a combination of factors, including genetics and environment triggers, which can exacerbate the discuss and its symptoms.

2.2 Types of Psoriasis

2.2.1 Plaque Psoriasis

Plaque Psoriasis is the most prevalent type of psoriasis, accounting for 80% of cases. The appearance of the lesion is characterized by thick scabs and red rashes, clear boundaries, and approximately 1 centimeter or more in size. This type of psoriasis is most commonly observed on the elbows, scalp, trunk, and buttocks, with lesions severity reaching approximately 20% (Fry, 1992). (Figure 2.1)

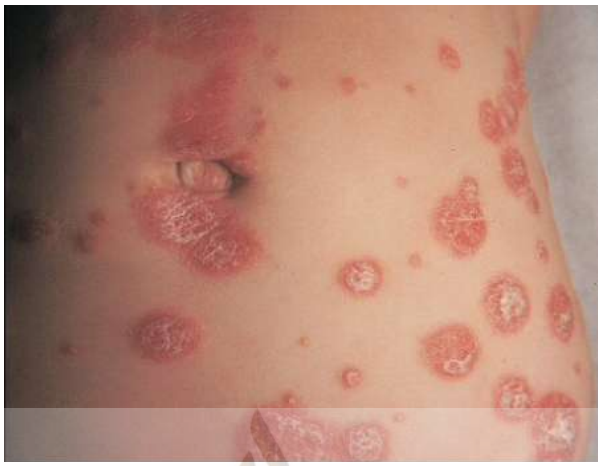


Figure 2.1 Character of Plaque Psoriasis

Source: Fry, 1992

2.2.2 Guttate Psoriasis

Guttate Psoriasis is rarely found, occurring in around 20% of all patients. A psoriasis lesion is a red and flaky blister whose size does not exceed 1 cm. Guttate Psoriasis is commonly found on the thighs, upper arms, and torso. In patients younger than 30 years, it is often associated with an episode of group A Beta-hemolytic streptococci infection occurring 2-3 weeks prior (Fry, 1992). (Figure 2.2)

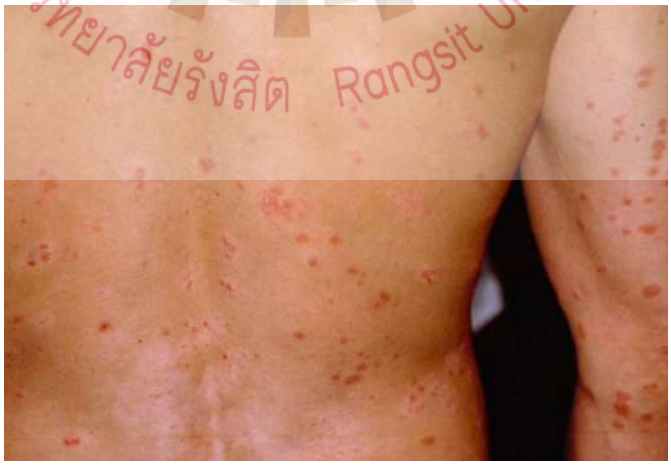


Figure 2.2 Character of Guttate Psoriasis

Source: Fry, 1992

2.2.3 Pustular Psoriasis

The lesion of Pustular Psoriasis resembles pustules characterized by the presence of pustules throughout and can be categorized into two types. Type1 is the generalized pustular variant, found in pustules in the area where the rash is red and inflamed area of the whole body. Type2 is a localized pustular variant, primarily found on the palms and soles of the feet, sometimes accompanied by plaque psoriasis (Fry, 1992). (Figure 2.3)

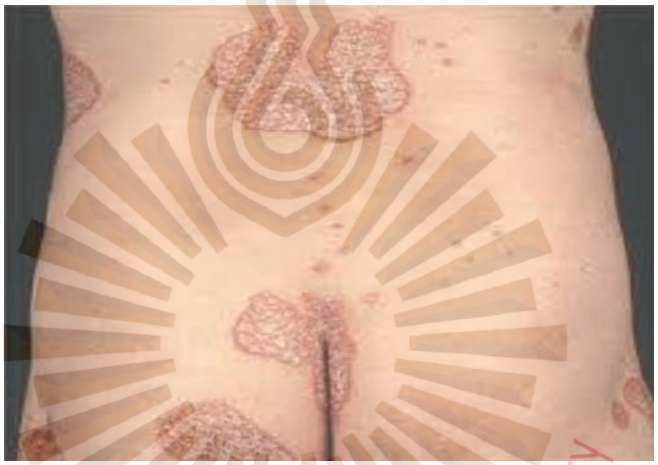


Figure 2.3 Character of Pustular Psoriasis
Source: Fry, 1992

2.2.4 Erythrodermic Psoriasis

Erythrodermic Psoriasis is a rapidly developing condition characterized by an extensive red rash covering the entire body. Patients may also experience high fever, fatigue, and chills, and may also have a loss of water and protein (Leading to dehydration and hypoalbuminemia) (Fry, 1992). (Figure 2.4)

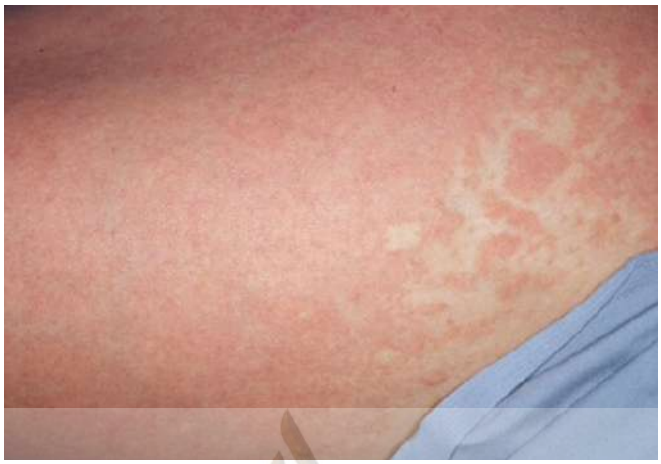


Figure 2.4 Character of Erythrodermic Psoriasis

Source: Fry, 1992

2.2.5 Inverse Psoriasis

Inverse psoriasis lesions typically appear in the body is skin, including the armpits, genitals, groin. The lesions are generally less scaly due to the high moisture levels in this area (Fry, 1992). (Figure 2.5)

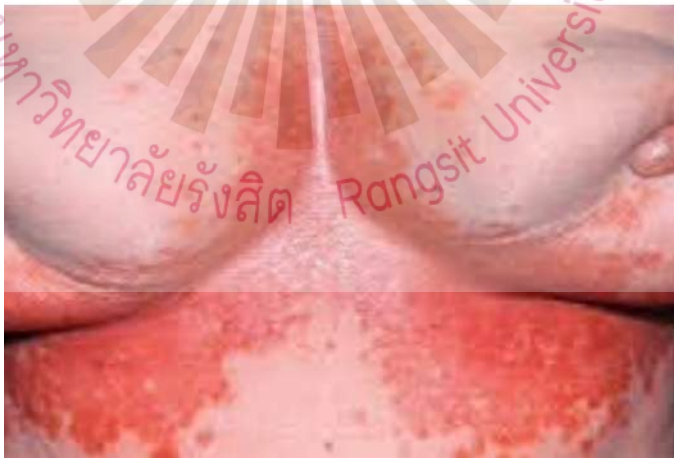


Figure 2.5 Character of Inverse Psoriasis

Source: Fry, 1992

2.2.6 Psoriatic Nails

Psoriasis nails is a condition that can affect both fingers (50%) and toes (35%). In all patients, the most common nail changes include pitting, onycholysis, and hyperkeratosis. 90% of patients with psoriatic are nail psoriasis (Fry, 1992). (Figure 2.6)

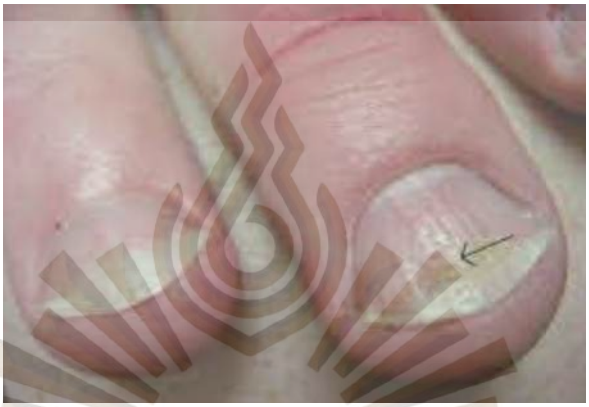


Figure 2.6 Character of Psoriatic Nails

Source: Fry, 1992

2.2.7 Psoriatic Arthritis

Psoriatic Arthritis affects approximately 40 percent of patients with psoriasis. It causes inflammation of the joints and may cause joint deformities (Fry, 1992). (Figure 2.7)

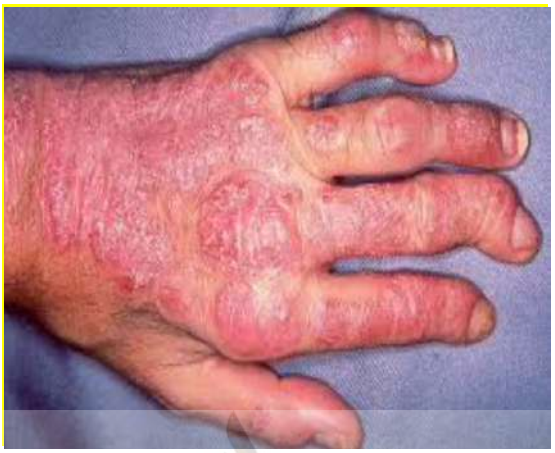


Figure 2.7 Character of Psoriatic Arthritis

Source: Fry, 1992

2.3 Diseases Associated with Psoriasis

2.3.1 Metabolic Syndrome

It has been found that patients with psoriasis are more likely to develop metabolic syndrome than non-psoriasis patients which can increase the risk of cardiovascular disease. In addition, obesity, Diabetes mellitus, Dyslipidemia, and Hypertension are more prevalent among patients with psoriasis compared to non-psoriasis patients (Peralta, Hamid, Batool, Achkar, & Maximus, 2019).

2.3.2 Autoimmune Disease

Psoriasis patients are more likely to develop Crohn's disease and ulcerative colitis compared to individuals without psoriasis 3.8-7.5 times. In addition, Multiple sclerosis is more likely found in families with people with psoriasis, suggesting that there was a genetic relationship between these conditions (Sticherling, 2016).

2.3.3 Lymphoma

In England, the incidence of lymphoma in patients with psoriasis was 3 times higher than in populations of similar age and sex (Gelfand, et al., 2006).

2.4 Assessment of the severity of the disease

The severity of the Psoriasis disease can be assessed by several parameters, such as;

2.4.1 Psoriasis Area and Severity Index (PASI)

PASI assesses severity of the rash by considering factors such as redness, stiffness, and thickening, and involvement of various body areas affected by the discase.

PASI Calculation (Complete all sections in table below)

Patient name					
Date					
Plaque Characteristic	Rating Score	Body region and weighting factor: Head	Upper Limbs	Trunk	Lower Limbs
Erythema	0 = None				
Thickness	1 = Slight 2 = Moderate				
Scaling	3 = Severe 4 = Very Severe				
Totals		0	0	0	0
Weighting Factor		x 0.1	x 0.2	x 0.3	x 0.4
Surface area totals		0	0	0	0
Degree of involvement as % for each body region affected (score each region between 0 and 6)	0 = None 1 = 1-9% 2 = 10-29% 3 = 30-49% 4 = 50-69% 5 = 70-89% 6 = 90-100%				
Surface area totals x % involvement t		0	0	0	0
				Sum Scores above = PASI Score	0

Ref: Fredriksson T, Pettersson U. Severe psoriasis: oral therapy with a new retinoid. Dermatologica. 1978;157(4):238-244

Figure 2.8 Calculation of PASI score

Source: Fredriksson & Pettersson, 1978

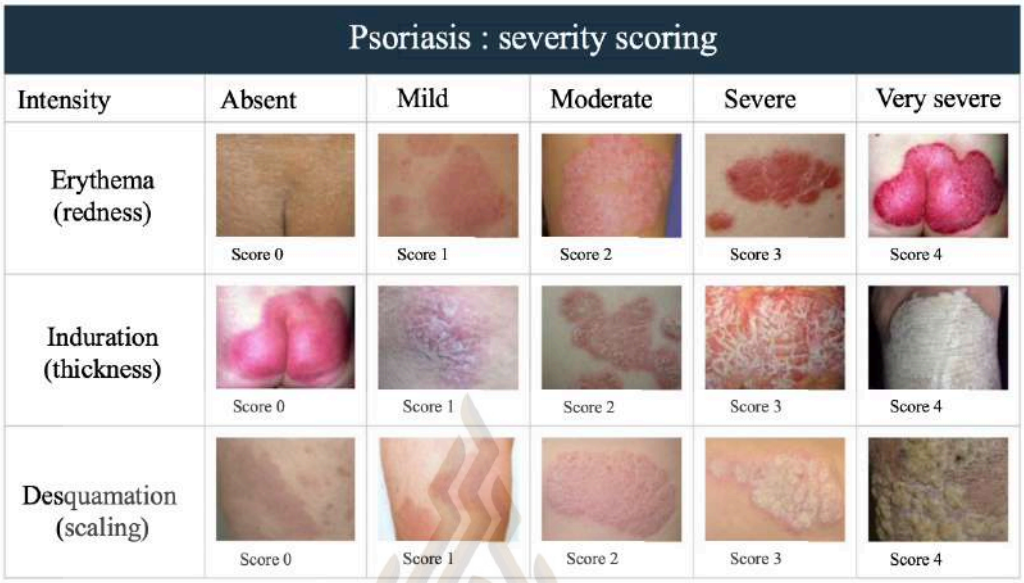


Figure 2.9 Score assessment of redness, thickness, and scaling of psoriasis

Source: DermNet, 2023

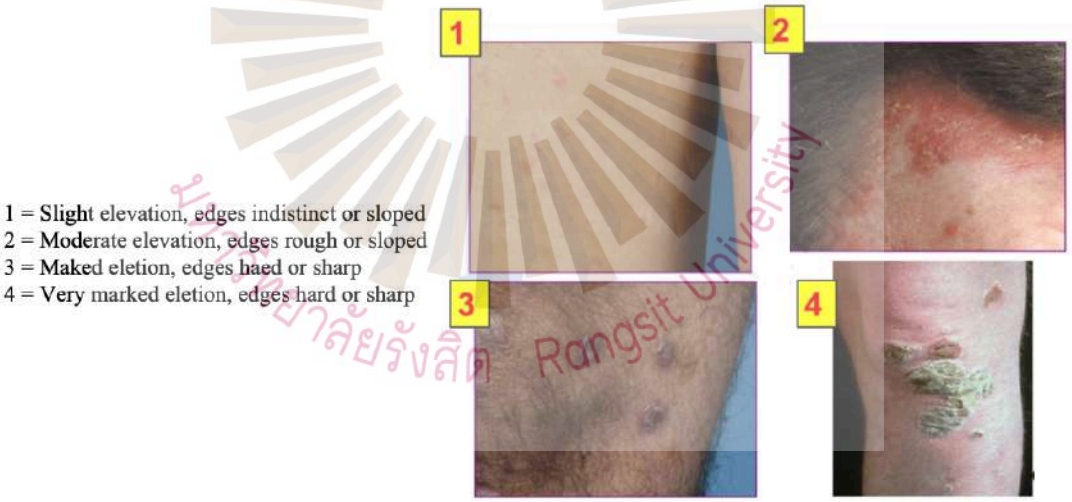


Figure 2.10 Assessing the severity of the thickness of the psoriasis lesions

Source: DermNet, 2023

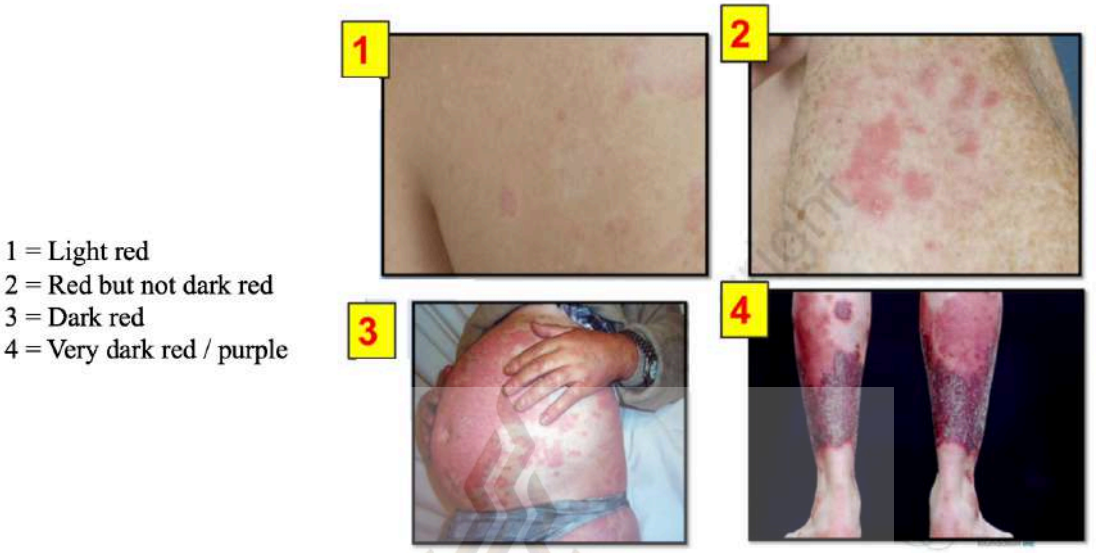


Figure 2.11 Assessing the severity of the redness of the psoriasis lesions

Source: DermNet, 2023

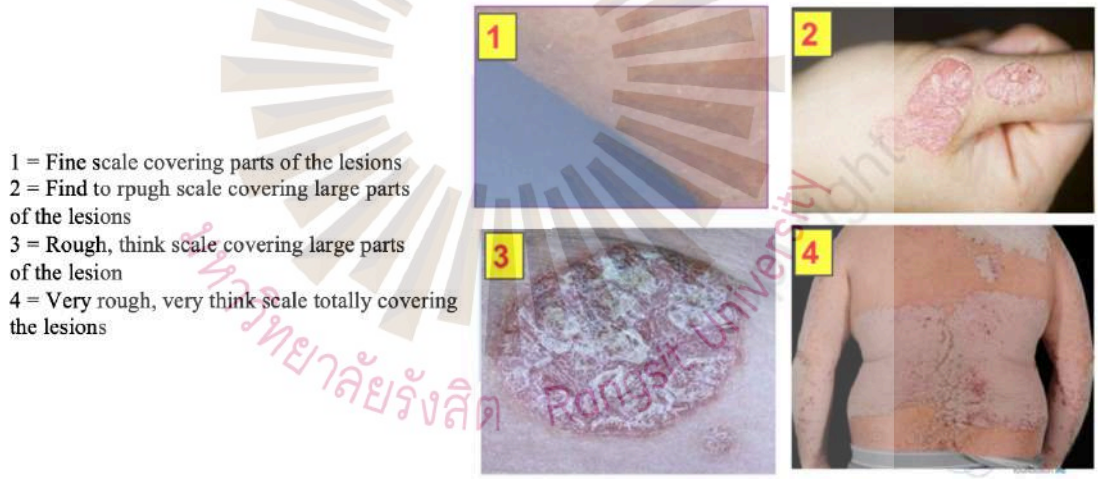


Figure 2.12 Assessing the severity of the scaling of the psoriasis lesions

Source: DermNet, 2023

2.4.2 Body Surface Area (BSA)

BSA is the evaluation of the skin of psoriasis patients usually on the patient's palm. One palm of the patient's palm accounts for one percent of the total surface area. (Figure 2.13)

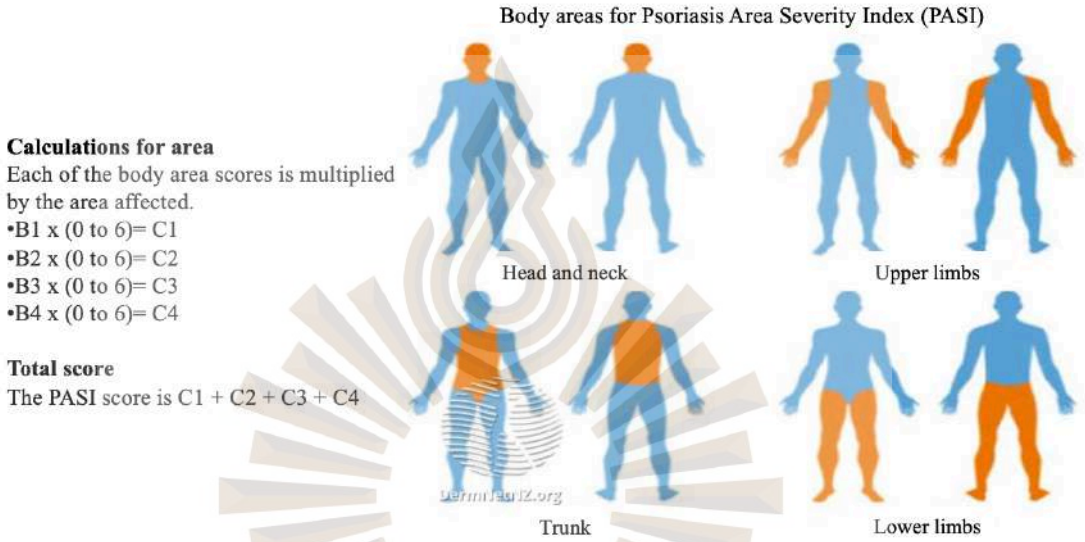


Figure 2.13 Skin lesions in different areas

Source: DermNet, 2023

2.4.3 Dermatology Life Quality Index (DLQI)

DLQI is a Thai version of the questionnaire designed to assess the quality of life of dermatology patients. It was developed from the Dermatology Life Quality Index (DLQI) of Professor AY Finlay and Dr. GK Khan. This questionnaire comprehensive by addresses various aspects of an individual's quality of life. Due to its simplicity, respondents can complete it independently in 15 minutes.

2.4.4 Psoriasis disability index (PDI)

Assess the quality of life of psoriasis patients they were asked to complete a psoriasis assessment questionnaire reflecting their experiences over the past 4 weeks.

The severity of the disease can be categorized into 3 levels.

1) Mild psoriasis: characterized by lesion area covering less than 10% of body surface area (BSA), and a PASI score below 10.

2) Moderate to severe psoriasis: indicated by a lesion area greater than 10% BSA, and a PASI score exceeding 10, and a DLQI score above 10.

3) Psoriasis affecting the face, hands, and feet, and genitals. In case where the lesion area is less than 10%, it is classified as moderate to severe psoriasis.

2.5 Psoriasis Treatment

A topical treatment for psoriasis that is commonly used includes the following;

1) Topical corticosteroids: These drugs are highly effective in psoriasis treatment and is inexpensive. However, prolong use at high concentrations can lead to skin thinning and cracking. Additionally, there is a risk of developing drug resistance and suppression the function of the adrenal glands (Faculty of Medicine Siriraj Hospital, 2017).

2) Tar: Tar is known to reduce the division of abnormal skin shells, but the tar is brown and has a foul smell. When applied it may stain clothing. Adverse effects can induce inflammation of the hair follicles and skin irritation (Faculty of Medicine Siriraj Hospital, 2017).

3) Calcipotriol: Calcipotriol promotes the normalization of skin cell growth, and exhibits good efficacy. However, it can be irritating when applied to area with thin skin, and the drug is quite expensive (Faculty of Medicine Siriraj Hospital, 2017).

4) Calcineurin inhibitor topical: In areas with thin psoriasis, these drugs can help reduce inflammation on the face or crevices and avoid the side effects of corticosteroids, such as skin thinning. These drugs are not widely used because they are expensive (Faculty of Medicine Siriraj Hospital, 2017).

Oral medication for psoriasis is considered in cases of moderate to severe psoriasis. Three types of oral medication are commonly used in Thailand including:

1) Methotrexate:

Methotrexate is a very effective drug. It not only inhibits the abnormal division of skin cells but also suppress the body's immune system. Possible side effects include nausea and vomiting, and prolong usage can increase the risk of cirrhosis. Therefore, the physician regularly monitors the patient's blood cells and count liver values (Faculty of Medicine Siriraj Hospital, 2017).

2) Acitretin:

Acitretin is an oral medication classified within the vitamin A group and is very effective for pustular psoriasis. Possible side effects include dry and peeling mouth, skin dryness, peeling of hands and feet, elevated blood lipid levels, and the risk of hepatitis. Patients receiving this drug should avoid pregnancy because it can lead to birth defects in the fetus. In addition, patients receiving this drug must use birth control and must continue contraception for a minimum 2 years after stopping this drug (Faculty of Medicine Siriraj Hospital, 2017).

3) Cyclosporin:

Cyclosporin has the effect of reducing inflammation and suppressing the immune system of the body and is a good effective treatment. It is used in moderate to severe psoriasis. However, it is important to be aware of potential side effects on the kidneys and high blood pressure. Consequently, while patient is on this medication, the doctor must regularly perform blood test to monitor kidney function and measure blood pressure periodically (Faculty of Medicine Siriraj Hospital, 2017).

Phototherapy

Phototherapy is another effective and safe way to treat psoriasis. Currently, there are two types of light used to treat psoriasis: ultraviolet A light and ultraviolet B light. Patients must be hospitalized for 2-3 sessions per a week for a minimum of 3 months to achieve favorable results, often exceeding 70-80% success rates with minimal side effect. Some patients may experience itching and redness on the irradiated skin after treatment (Faculty of Medicine Siriraj Hospital, 2017).

Biological agents

The biological agent is a new drug that has an altered effect on the body's immune system by subcutaneous injection. It is a very effective treatment, but it necessitates continuous injections. The disadvantage is high cost of this drug. Since these drugs are new, there is still un certainty regarding potential long-term side effects (Faculty of Medicine Siriraj Hospital, 2017).

2.6 Complementary and Alternative Medicine

Psoriasis is a chronic disease that is difficult to cure. Most individual receive modern medical treatment through symptomatic support, such as anti-itching with steroid creams, which will have side effects when used continuously for a long time. Light therapy may irritate the skin. Therefore, alternative medicine is an alternative psoriasis treatment. There are several alternative medicine treatments, including psoriasis diet therapy, psoriasis phytotherapy, psoriasis acupuncture, and psoriasis homeopathy. Thai traditional herbal medicine, which is topical and has fewer side effects, can be a promising alternative for psoriasis patients.

2.7 Herbs related to research

Turmeric

Figure 2.14 Turmeric

Source: Schell, 2009

Common name: Turmeric, Curcuma

Binomial name: *Curcuma longa* Linnaeus

Family: Zingiberaceae

Properties: Turmeric contains curcuminoids and is also used as an ingredient in many cosmetic products. Turmeric has an effect on anti-acne, protects the skin, reduces wrinkles, inhibits tyrosinase enzymes, reduces melanin pigment production, and has the ability of antioxidants (Khatun, Eguchi, Yamaguchi, Takamura, & Matoba, 2006). One study showed that feeding rats turmeric extract at a dosage of 1,000 mg/kg twice a day for 19 weeks, while exposing them to ultraviolet B radiation, resulted in a reduction of skin wrinkling in the rats. Turmeric can inhibit the enzyme matrix metalloproteinase2 (MMP-2), which is involved in tissues degradation (Moongkarndi, 2006). A study on the anti-inflammatory activity of turmeric in postoperative patients showed that after these patients took 400 mg of turmeric 3 times a day for 5 days the inflammation in these patients reduced.

In addition, after 18 rheumatoid arthritis patients took turmeric at a dosage of 1,200 mg 4 times a day for 2 weeks, these patients' symptoms improved significantly. Another study found that taking turmeric at a dosage of 375 mg 3 times a day

improved symptom of chronic conjunctivitis (Herbal Information Office, Faculty of Pharmacy, Mahidol University, 2009). In addition, turmeric has antibacterial activity against *Staphylococcus aureus*. The petroleum ether extract, benzene extract, chloroform extract, methanol extract, and aqueous extract from turmeric rhizome were tested for antibacterial activity by using the disc diffusion method. Two types of bacteria used for testing were the standard strains *S. aureus* ATCC 6571 and the clinically isolated *S. aureus*. The results showed that extracts of petroleum ether, benzene, chloroform, methanol, and water were able to inhibit *S.aureus* ATCC 6571 with MIC values of 73, 84, 42, 100 and 73%, respectively, and inhibit clinically isolated *S. aureus* 85, 107, 71, 42 and 85%. In conclusion, methanol extract was the most effective in inhibiting standardized *S. aureus* ATCC 6571 and benzene extract showed similar activity. Both works best in inhibiting clinically isolated *S. aureus* (Tong, Davis, Eichenberger, Holland, & Fowler Jr, 2015).

False lime merlimau

Figure 2.15 False lime merlimau

Source: Plantthaiorc, 2008

Common name: False lime merlimau

Binomial name: *Suregada multiflora (A.Juss) Baill*

Family: Euphorbiaceae

Properties: In vitro anti-inflammatory study showed that hexane and dichloromethane extracts from trunk bark of the false lime suppressed the inflammation induce by lipopolysaccharide (LPS). These extracts were also observed to inhibit nitric oxide (NO), production, leading to the reduction of NO and prostaglandins which are involved in the inflammatory process (Tewtrakul, Subhadhirasakul, Tansakul, Cheenpracha, & Karalai, 2011). In addition, the extract of dichloromethane from the bark of the false lime merlimau was also studied. Each substance was tested for allergic reactions in vitro to see the effect of inhibiting β-hexosaminidase enzyme secretion. The results showed that the extract inhibited β-hexosaminidase enzyme secretion, which is released during the activation process of RBL-2H3 cells, indicative of allergic reactions. The results revealed that the extract outperformed ketotifen fumarate in inhibiting β-hexosaminidase enzyme secretion (Cheenpracha et al., 2006).

A study of the antibacterial activity test by disk diffusion method showed that the extract from the bark of the false lime merlimau had no antibacterial activity. However, the aqueous solution inhibited *Staphylococcus aureus* and *Staphylococcus epidermidis* proliferation with a value of MIC at 7.8 mg/ml, and MBC at 15.62 mg/ml. Moreover, the effect of the extract can inhibit the growth of liver cancer cells and cervical cancer cells. Based on this research, it can be concluded that water extracts from the bark of the false lime merlimau processes biologically active in reducing the effects of cancer treatment as an antioxidant and inhibiting the growth of cancer cells (Phoomphong, Devakul Na Ayutthaya, Wanakachornkri, Sukplang, & Thongmee, 2017).

Mangosteen peel

Figure 2.16 Mangosteen peel
Source: Zen Biotech, 2018

Common name: Mangosteen

Binomial name: *Garcinia mangostana Linn.*

Family: Clusiaceae

Properties: Mangosteen is a plant that has been studied for its biological activity. It was found that mangosteen peel contains tannin, which has astringent properties, and xanthone, which can reduce inflammation and also has antibacterial and fungal properties. In addition, studies have also found that mangosteen extract can inhibit infection of *Propionibacterium acnes* (Chomnawang, Surassmo, Nukoolkarn, & Gritsanapan, 2005). The anti-psoriasis effect of mangosteen peel extract was also studied in rats induced psoriasis-like skin lesions induced by Imiquimod. The treatment with garcinol (YDIS), isolated from mangosteen rind at a dose of 100 mg/kg once daily for 7 days was compared to 50 mg/kg of cyclosporine A (CsA) in rats. Abnormal changes in the skin cells of YDIS-treated mice were reduced and also found a decrease in Interleukin-23 (IL-23) / T-helper 17 (Th17) axis, Tumor necrosis factor-α (TNF-α), IL-2, and Interferon (IFN-γ). In addition, YDIS also inhibited abnormal T cell secretion and inhibited the conversion of CD4+ T cells to Th 17 cells in the spleens of mice treated with imiquimod. When tested in serum, YDIS increased IL-10 and decreased IL-17, indicating that YDIS had anti-inflammatory activity and caused

less liver and kidney damage than CsA. In vitro studies have shown that YDIS can induce HaCaT keratinocytes. It was more lethal than CsA and was able to reduce inflammation caused by lipopolysaccharide (LPS) in cells. The results concluded that isogarcinol derived from mangosteen peel was effective in treating psoriasis (Chen et al., 2017). Traditional Thai medicine suggests that the bark has a bitter taste and can be boiled or brewed to relieve diarrhea. It is effective as an astringent to cure dysentery and can be applied to rotting wounds, purulent wounds, healing wounds caused by infection, and reducing inflammation (Herbal Information Office, Faculty of Pharmacy, Mahidol University, 2009).

Coconut oil

Figure 2.17 Coconut oil
Source: Summit Vanuatu, 2013

Common name: Coconut
Binomial name: *Cocos nucifera L.*
Family: Arecaceae
Properties: Coconut oil contains saturated fatty acids, and exposure to lower temperature can lead to the structure change in coconut oil through the action of lipase. This structural modification enhances its antimicrobial and antioxidant properties. The structurally modified coconut oil at a concentration of 6.25% could inhibit *S.aureus* and *E. coli* tested by the disk diffusion method (Sungpud, C.,

Sungpud, J., & Sujarit, 2015). It destroys the bacteria with a lipid cell membrane (Sittitunyakit & Pradubwate, 2005). In addition, lauric acid from cold-pressed coconut oil at a concentration of 20 mg/ml inhibited the growth of *Streptococcus mutants* (Atritthirong et al., 2017). Coconut oil also plays a role in killing viruses. Consumed coconut oil goes to the follicles under the skin, resulting the skin look younger, moisturized, and smooth. Coconut oil will penetrate into the inner layer of the skin, making the tissues strong. Coconut oil makes the skin more beautiful. Since coconut oil contains mostly saturated fatty acids, it is difficult to oxidize oxygen and it also has antioxidant activity that resists the addition of oxygen. Coconut oil penetrates well into the subcutaneous layer, giving it the ability to add moisture to the skin. It has also been found that the lauric acid in coconut oil can kill germs that cause melasma, freckles, spots, or dimples. Coconut oil also helps treat skin diseases such as dermatitis, encompasses different types such as red and inflamed itching skin lesions with lymph and scabs (eczema) as well as other infectious skin conditions (Chomchalow, 2010).

White crane flower

Figure 2.18 White crane flower

Source: บ้านคุณหมอ, 2558

Common name: White crane flower

Binomial name: *Rhinacanthus nasutus Kurz*

Family: Acanthaceae

Properties: White crane flower (*Rhinacanthus nasutus (L.) Kurz*) has a history of being used in the treatment of cancer, hepatitis, skin diseases, and ringworm (Zubaid, Abdullah, Khan, & Noor, 2004; Nascimento, Locatelli, Freitas, & Silva, 2000). It inhibits the growth of some bacteria (Cowan, 1999; Nascimento et al., 2000). The active substances from white crane flowers are Rhinacanthin, Lupeol, and Umbelliferone, which can inhibit the growth of cancer cells (Cai, Luo, Sun, & Corke, 2004; Siripong et al., 2006; Wu, Tien, Yeh, & Lee, 1998), and reduce the adhesion of bacteria on the skin include *Staphylococcus aureus*, *S.epidermidis*, *Pseudomonas aeruginosa*, etc (Tewtrakul et al., 2011). Rhinacathin-C, rhinacathin-D and rhinacathin-N separated from the golden leaves were found to be effective against fungi that cause skin disease (Panichayupakaranant & Kongchai, 2003). Rhinacathin-C extracted from white crane flowers can be used as a shampoo for use in people with fungal infections on the scalp or body. Rhinacathin-C has antimicrobial activity against many bacteria, such as *Streptococcus mutans*, *Propionibacterium acnes*, *Helicobacter pylori*, *Staphylococcus aureus*, *S. epidermidis* and *Candida albicans*, determined by the microdilution assay (Puttarak, Charoonratana, & Panichayapakaranant, 2010).

Sea holly

Figure 2.19 Sea holly

Source: Wikipedia, 2020

Common name: Sea holly

Binomial name: *Acanthus ebracteatus Vahl*

Family: Acanthaceae

Properties: Sea holly is effective in treating blisters, lymphatic drainage, treating various pains, treating skin diseases, and skin rashes (Potjanee, 1994). The study of D'Souza L showed that ethanol extract (90%) from dried Sea holly was not effective against *Staphylococcus aureus*. However, when testing with the seeds of sea holly, it was found to be effective against *S. aureus* while also demonstrated the anti-inflammatory properties (DeSouza & Wahidullah, 1996). Sea holly are used in many types of skin disinfectants to inhibit the growth of *S.aureus* and *S.epidermidis.* It is also known for wound-healing properties and its ability to support the body's immune system (Chaiyasit, Niamsa, & Puangpronp, 2009).

Sesame oil

Figure 2.20 Sesame oil

Source: Indiamart, 2017

Common name: Sesame

Binomial name: *Sesamum indicum L.*

Family: Pedaliaceae

Properties: Sesame oil is obtained by extracting the seeds of *Sesamin indicum*, which are rich in fats, proteins, carbohydrates, and many other important minerals. They are

used as the anti-oxidant, especially substances in the group of lignans and tocopherols. Mechanism of anti-oxidation action of sesame oil and extracts from sesame with methanol and hexane in black sesame, white sesame, and red sesame were found to have the ability to eliminate free radicals and inhibit lipid peroxidation by DPPH, FRAP, and TBARS assay, respectively (Srisayam, 2014). It helps the immune system and can reduce the risk of developing many types of cancer (Akaboshi, Tanaka, Sumono, Takada, & Kawai, 1998). Sesame contains lignans, sesamin, sesamol, and vitamin E (Budowski, 1950; Sirirat & Naruethai, 2006). The lignans in sesame seeds are pro-oxidant effects when the concentration is 100 mM (Hou et al., 2004). Sesamin has two methy-lenedioxy bridges and 4OH, thus inhibiting reactive oxygen species (ROS) in normal conditions better than OH2-containing sesamin (Nakano et al., 2006). Lignan has been shown to combat the effects of aging and reduce the level of cholesterol in the blood in both human and animal studies (Yamashita, Kagaya, Higuti, & Kiso, 2000).

Snow lotus

Figure 2.21 Snow lotus

Source: Pobpad, 2022

Properties: Snow lotus used as a mixture of “Thai-Bio Cream” is a pearly white cream. This cream is known as “Bao Fu Ling”, but the ingredient does not contain lotus or plants called snow lotus. The cream called snow lotus contains pearl powder, wild

ginseng, bovine gallstone, musk wipes, aloe vera, camphor, and vaseline. Wild ginseng has properties to heal various wounds, especially burns.

False daisy

Figure 2.22 False daisy

Source: Wikipedia, 2023

Common name: False daisy, White-head

Binomial name: *Eclipta prostrata L.*

Family: Asteraceae

Properties: False daisy is used to cure premature gray hair and make hair black. In addition, according to Thai traditional medicine, the leaves and roots are used as laxatives to induce vomiting. Roots cure fainting from childbirth, cure indigestion, nourish the liver, and spleen, and nourish the blood. The whole plant cures cancer, asthma, bronchitis, colic, ringworm. as an astringent. The juice from the plant treats jaundice (Wongsathit, 1995). The above-ground part of the false daisy tree can inhibit bacteria. Hexane extract of the false daisy has a strong antimicrobial effect against *Staphyllococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella typhi*, *Klebsiella pneumonia*, *S. pyogenes*, and *Pseudomonas aeruginosa* (MIC < 100 mcg/ml) which similar to antimicrobial agents ciprofloxacin 25 mcg/ml. Ethyl acetate extract from the false daisy inhibited *B. subtilis*, *S. aureus*, *Proteus mirabilis*, *B. cereus*, *E.coli*, *S.typhi*, *P.aeruginosa*, *S.epidermidis*, and *Candida albicans*. Petroleum

ether extracts inhibited fungal pathogens *Micosporum* and *Trichophyton*, as well as saponins isolated from the leaves of the false daisy can inhibit bacteria and fungi as well (Khanna & Kannabiran, 2009).

Skin care cream “Thai-Bio®”

Figure 2.23 Skin care cream “Thai-Bio®”

Source: Empowerlife, 2012

Skin cream “Thai-Bio®” is an external cream with the main components from many plants and herbs such as coconut oil, sesame oil, clove oil, snow lotus, false lime merlimau, mangosteen peel, false daisy, turmeric, white crane flower, licorice, sea holly, and other ingredients, such as Lecithin, Zinc, Camphor, Menthol, Glycerin, Keratin, Polysorbate 60 and Water. The drug contains a mixture of plants and herbs, many of which are used in the textbooks of Thai traditional medicine and Chinese medicine to treat or relieve skin diseases. The application of “Thai-Bio®” cream, alongside the guidance of healthcare professionals, has demonstrated significant improvements in patient symptoms. Within 1-2 weeks of using the cream, most patients experienced reductions in white flakes and redness, inflammation and itching.

Cannabis

Figure 2.24 Cannabis sativa
Source: Sciencephotogallery, 2023

Common name: Cannabis

Binomial name: *Cannabis sativa L.*

Family: Cannabaceae

Properties: Cannabinoids have anti-inflammatory effects and can help slow epidermal keratinocyte differentiation and inhibits epidermal keratinocyte differentiation (Wilkinson & Williamson, 2007). The researchers concluded that cannabinoids can play an important role in the treatment of psoriasis. It has also been reported that the major compounds in cannabis, both Cannabidiol (CBD) and Tetrahydrocannabinol (THC) suppress the immune system, especially THC which is present in large proportions in Thai cannabis strains (*Cannabis sativa* L.) exerts its suppressive effect. Cannabis may be an effective treatment for psoriasis because psoriasis is caused by a highly active T-lymphocyte abnormality. Many studies have been reported that cannabis has the potential to treat conditions such as psoriasis, lupus, nail-patella syndrome, severe pain, acne, dermatitis, itching, wound healing, and skin cancer (Eagleston et al., 2018; Marks & Friedman, 2018; Mounessa, Siegel, Dunnick, & Dellavalle, 2017; Sheriff, Lin, Dubin, & Khorasani, 2020).

CHAPTER 3

MATERIALS AND METHODS

This section illustrates experimental design, subject recruitment, formulations, trial design, dosage regimen to investigate the efficacy and safety of the two formula creams.

3.1 Experimental Design

The crossover study design was selected for comparison the effectiveness of the two different formulations by evaluating the responsiveness of subjects to both treatments. In a cross-over study, the subjects were randomly divided into two groups.

Group 1 Received Agent A: The cannabis extract GPOCE (THC: CBD 1:1)

Group 2 Received Agent B: Combining a GPOCE with a polyherbal formulation (ThaiBio®) (ThaiBio® 95% : GPOCE 5%)

Participants in either Group 1 or Group 2 were treated with one cream formulation (either Formula A or Formula B) for 8 weeks. After 8 week of treatment, the participants have no treatment for 2 weeks, called stop washout period. Following this washout period, the regimen was resume by switched to the other formulation as shown in Figure 3.1

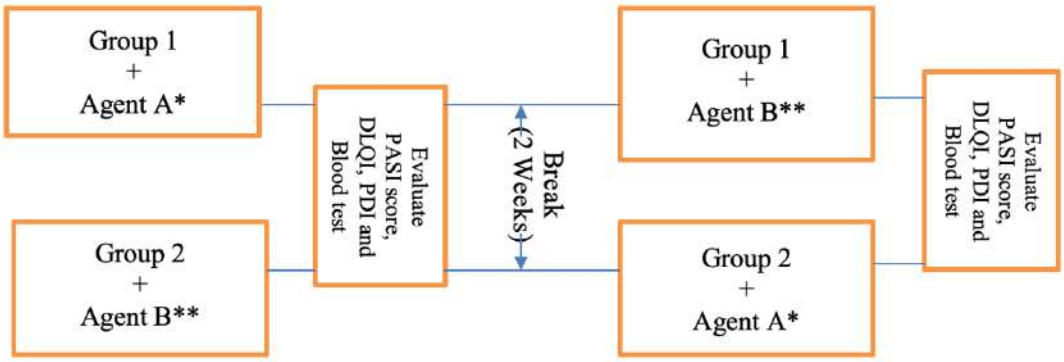


Figure 3.1 Cross-over study

* Agent A: The cannabis extract GPOCE (THC: CBD 1:1)

** Agent B: Combining a GPOCE with a polyherbal formulation (ThaiBio®)

Ethical considerations:

The research received approval from the Ethics Committee at Rangsit University, COA. No. RSUERB2021-043, as well as the Pathum Thani Provincial Public Health Office in Thailand. The investigation was carried out in compliance with the principles outlined in the Helsinki Declaration.

3.2 Subject Recruitment

Before starting research, there will be publicity and recruitment of volunteers through online channels. If the volunteers meet the criteria of the research project (patients with mild psoriasis rash (PASI score ≥ 3), both males and females 20 people, aged 18-69 years) will be able to join this project.

Inclusion Criteria:

1) Positive control group: patients aged 18-69 years using the corticosteroids at the time of enrollment, assessed a PASI score of greater than or equal to 3, participated in voluntary treatment and consented to the investigator collecting treatment data corticosteroids for 8 weeks, 2 weeks off, and 8 weeks on trial, 2 weeks off, and then 8 weeks on again.

2) Patients aged 18-69 years old when entering the program must agree to stop treatment with modern medicine and other herbs for at least 2 weeks and have a PASI score greater than or equal to 3 participate in voluntary treatment and sign a letter agreeing to participate in the project.

Exclusion criteria:

1) Individuals with a history of allergy to products derived from cannabis extraction which may be attributed to other components/or the solvent used in the extraction process.

2) Individuals with severe, unstable cardio-pulmonary condition such as angina, peripheral vascular disease, cerebrovascular disease, and arrhythmia or those with risk factors for coronary artery disease.

3) Individuals with preexisting psychosis or ongoing mood or anxiety disorder.

4) Individuals with a medical history that necessitates additional laboratory tests posing a risk of using cannabis extract products as determined by the physician.

5) Individuals taking specific medications that may potentially interact with cannabis products, thereby placing project volunteers at risk giving reports of cannabinoids affecting.

6) Pregnant or lactating women, as well as those planning to conceive, preterm and low-weight birth including the presence of cannabinoids in breast milk.

7) Volunteers who missed more than 2 scheduled appointments and assessments, as well as participants who withdrew from the program.

8) Subjects experiencing severe adverse drug reactions, leading the physicians to decide to discontinue their participation in the trial in their discretion.

9) Any other reasons at the physician's discretion that are deemed appropriate for withdrawing from participation in the research project.

Withdrawal criteria for individual participants:

1) Patients experiencing side effects or increased redness, scaling, itching inflammation or other lesions, and physicians at their discretion may be dangerous and recommend that participants should avoid participating in the study.

2) The participant did not cooperate with the treatment or was unable to monitor the results of the treatment.

3) The participant received treatment other than the one prescribed.

4) Research participants can withdraw at any time without affecting the research participants.

Termination criteria for the whole research project:

1) Patients have side effects or have a rash, inflammation, or severe complications in some patients. The doctor commented that the research should be discontinued.

2) More than half of the total number of participants refused or requested to withdraw from the program.

3.3 Formulations

Agent A: The cannabis extract GPOCE (THC: CBD 1:1) was procured from the Government Pharmaceutical Organization (GPO) and contained 27 mg/ml and 25 mg/ml of THC and CBD, respectively. The final concentration of THC and CBD in agent A was 1.35 mg/g and 1.25 mg/g.

Agent B: Combining a GPOCE with a polyherbal formulation (ThaiBio®) (ThaiBio® 95% : GPOCE 5%) The herbal formulation contained botanical extracts and 0.1% zinc carbonate ($ZnCO_3$) as active ingredients. The main botanical extract ingredients included coconut oil, clove oil, sesame oil, *Suregada multiflorum* bark extract, *Eclipta prostrata* leaf powder, *Acanthus ebracteatu* leaf powder, *Rhinacanthus nasutus* leaf powder, licorice root extract, turmeric rhizome powder, and mangosteen peel extract. The ingredients of ThaiBio® and GPOCE were mixed with the final

concentrations of THC and CBD were equal to agent A, i.e., ConcTHC1.35 mg/g: ConcCBD1.25 mg/g in the product.

3.4 Evaluations

There were four main research testing tools in this study including biodata, Psoriasis Area and Severity Index (PASI) form, Dermatological Life Quality Index (DLQI) form, and Psoriasis Disability Index (PDI) form. Each testing tool is described as follows.

3.4.1 Biodata

It consists of general personal information, age, gender, marital status, educational level, congenital disease, regular medication, herbal medicine/supplement, lifestyle, history of smoking, drinking alcohol, health behavior and diet information, daily exposure to chemicals, and history of stress. History of how long the scab has lasted and how to treat it. General physical examination, vital signs, and classification of types of psoriasis were recorded.

The severity of lesions and quality of life were evaluated using Psoriasis Area and Severity Index (PASI), Dermatological Life Quality Index (DLQI) and Psoriasis Disability Index (PDI) Quality of Life Questionnaire.

3.4.2 Psoriasis Area and Severity Index (PASI)

PASI is the gold standard for assessing the symptoms of psoriasis (Feldman & Krueger, 2005), categorized as mild (PASI score <7), moderate (PASI score=7-12), and severe (PASI score>12). A PASI score evaluates the area affected by psoriasis and its redness, thickness and scaliness in each of four zones: the head and neck, upper arms, trunk, and lower limbs.

The score scale ranges from Most (3), Very (2), Slightly (1), and None (0) for 15 items, including scores from all items. The highest total score was 45 and the lowest was 0. Patients with high scores implied that psoriasis had a significant impact on quality of life in order of the total scores.

3.4.3 Questionnaire to measure the quality of life of dermatology patients (Dermatological Life Quality Index: DLQI)

The DLQI is a standardized questionnaire in the Psoriasis Patient Care Guidelines. It was designed to assess the health-related quality of life of adult patients with skin disease (Smith et al., 2017).

The volunteers answered the assessment questionnaire, indicating how much their skin rash has affected their quality of life in the past week.

The scores were from high (3), medium (2), little (1), and none (0) for 10 items, including scores from all items.

A score of 0-1 did not affect the patient's life.

Scores 2-5 had a small effect on patients' life.

Scores 6-10 have a moderate effect on patients' life.

A score of 11-20 has a very large effect on a patient's life.

A score of 21-30 has a large effect on a patient's quality of life (extremely large effect on a patient's life).

3.4.4 Psoriasis Disability Index (PDI) Quality of Life Questionnaire.

PDI is a simple and reliable standardized questionnaire have used for evaluation psoriasis (Kent & al-Abadie, 1993). It assesses whether the symptoms had an impact on the patient's quality of life during the past four weeks. Across five dimensions:

1) Daily activities (5 items)

2) Work or school (3 items)

3) Personal relationships (2 items)

4) The use of leisure time (leisure) (4 items)

5) Treatment (treatment) (1 item)

The score scale for the PDI questionnaire include ratings of Most (3), Very (2), Slightly (1), and None (0) for each of the 15 items. The total score, which can range from 0 (no impact) to 45 (significant impact), reflects the degree to which psoriasis affects the patient's quality of life. Higher total scores indicate a greater impact of psoriasis on the patient's quality of life.

3.4.5 Blood Test

Complete blood count (red blood cell count, white blood cell count, platelets), urinalysis, kidney function (BUN, Creatinine) and liver function tests (AST, ALT, and alkaline phosphatase) were measured at weeks 0 (before study) and 8 (after treatment) and other tests that the doctor considers ordering additional tests on a case-by-case basis.

3.5 Data Collection

For evaluation the efficacy of the two formulations, skin lesion by PASI score was evaluated in weeks 0, 2, 4, 6 and 8. Evaluating quality of life DLQI and PDI questionnaires were assessed by the self-reported. The DLQI score was evaluated every week while the PDI score was evaluated only in weeks 0, 4 and 8. Based on the crossover randomized controlled trial, each participant needed to complete the clinical trials in the total study period of 18 weeks.

For the first time, volunteers will be appointed to explain about details and requirements of research participation. All volunteers must sign the research consent form and the researcher must explain the details completely before signing this document.

Then volunteers had a physical examination and history taking by a doctor to look at the appearance of psoriasis lesions. Itching, location and size of the rash, scaly rash, and a photograph of the rash's appearance, scaly, and scaly lesions were evaluated using the Psoriasis Area and Severity Index (PASI).

When the assessment is completed, all volunteers will receive 2 tubes of the product for use at home by participants for 2 weeks. The method, dosage, and time of use of the product will be explained by the researcher. Issue appointments for volunteers to return for product evaluation using the Psoriasis Area and Severity Index (PASI) and the Dermatology Life Quality Index (DLQI) Questionnaire every 1 week (weeks 1-8) and quality of life was assessed before the trial and every 4 weeks (weeks 4 and 8) using the PDI (Psoriasis Disability Index) questionnaire.

Cream was applied to the skin twice a day after taking a shower in the morning and evening. The amount of cream depends on the size of the area of the skin where the psoriasis is by applying a thin layer of the cream/product to the area that is approximately the Fingertips Unit (FTU). One FTU is equal to 1 knuckle of the finger of the person using the cream, measured from the first point to the fingertips. The amount of cream was 0.5 g compared to adult male fingers, or 0.4 g. compared to adult female fingers were applied over the affected area and avoid the exposure to sunlight. The duration for participants to use the cream was 8 weeks.

3.6 Statistical Data Analysis

In this investigation, a significance threshold of 0.05 was employed.

3.6.1 PASI score

Shapiro-Wilk test was used to analyze the distribution of PASI scores collected every couple of weeks. For additional statistical data analysis, the non-parametric test was used since the PASI values were not regularly distributed. Subsequently, the study

investigated the differences and estimated how the PASI score changes over time using pairwise comparisons with the Fisher's exact test.

3.6.2 DLQI score

The DLQI score for each formula combined with eight weeks of treatment were analyzed both linear regression and the Friedman test.

3.6.3 PDI

The assessment of the quality of life before and after treatment was conducted using linear regression and Friedman test for one-way repeated measure.

3.6.4 Blood test

A paired difference Wilcoxon signed-rank test was used to compare blood tests results from weeks 0 to 8.

CHAPTER 4

RESULTS

4.1 Population Distribution

The study included 20 psoriasis patients, with 13 (65%) men and 7 (35%) women, as indicated by the participant demographics. The participants ages ranged from 18 to 69, with a mean age of 38.94 years (Table 4.1). In the crossover research design, all participants received both medications, which consisted of THC and CBD from ThaiBio® medical plants. Participants were first given one product for eight weeks of treatment (either Agent A or Agent B). Participants were switched to receive the other medication after a 2-week wash-out period following the initial treatment.

Table 4.1 Show Population Distribution

Demographics		Amount	Percentage (%)
Gender	Male	13	65
	Female	7	35
Total		20	100
Age (Year)			
Mean± SD		38.94 ± 14.58	
Minimum age		18	
Maximum age		69	

4.2 Psoriasis Area and Severity Index

For all patients receiving medication with Agent A, the Psoriasis Area and Severity Index (PASI scores) were assessed every two weeks. During the duration of the 8-week trial, the results revealed a substantial decline in PASI score for the treatment group, with a considerable decline seen after four weeks of product use. The PASI score was specifically 21.93±14.41, 18.10±12.13, 15.34±11.22, and 16.66±12.15 at weeks 2, 4, 6, and 8, respectively. A picture of a patient's psoriasis lesions before and after treatment was also included in the research (Figure 4.1).

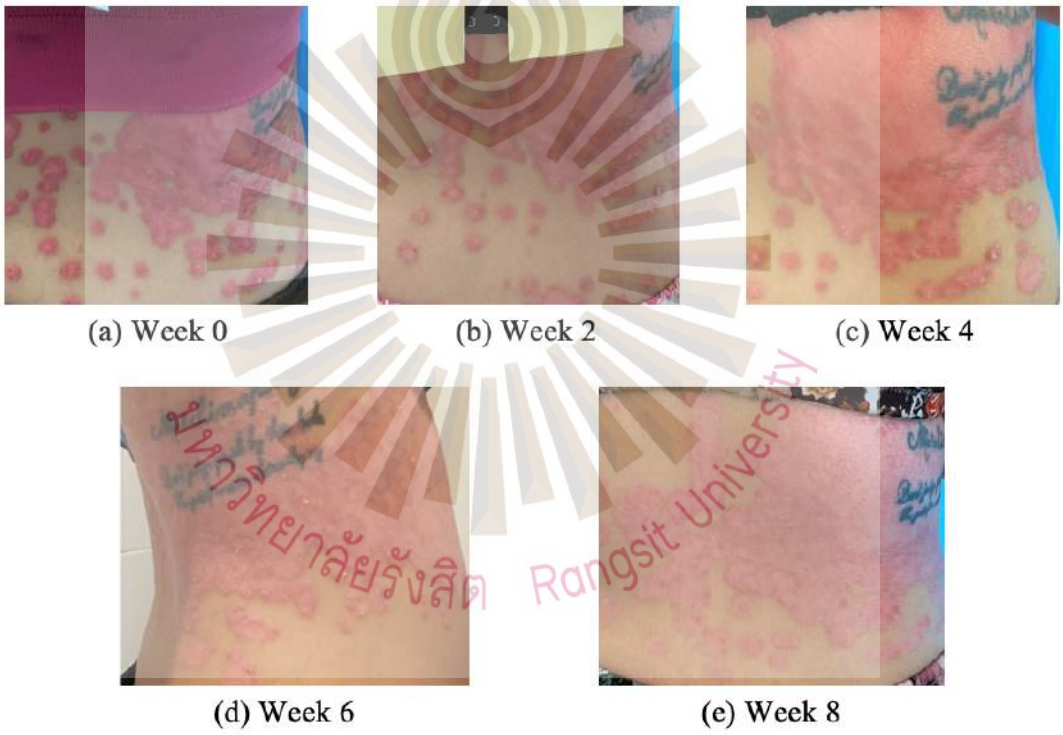


Figure 4.1 The figures illustrate the reduction of psoriasis lesions in a single patient after treatment with the cream agent containing cannabis alone over the course of 8 weeks.

Throughout the 8-week study, the results demonstrated a substantial decline in the PASI score of the treatment group following the administration of Agent B. At weeks 2, 4, 6, and 8, the treatment group's PASI score was specifically 19.79±14.28, 17.88±12.68, 14.34±10.58, and 13.06±11.29.

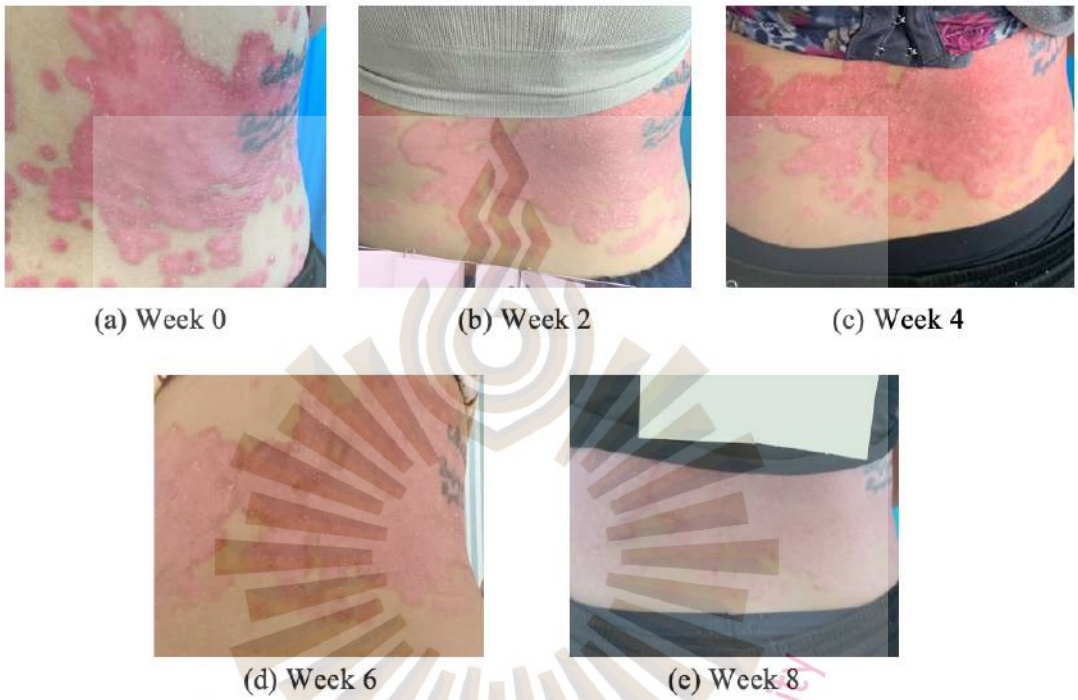


Figure 4.2 The figures illustrate the reduction of psoriasis lesions in a single patient after treatment with the cream containing cannabis and the herbal formulation (ThaiBio®) over the course of 8 weeks.

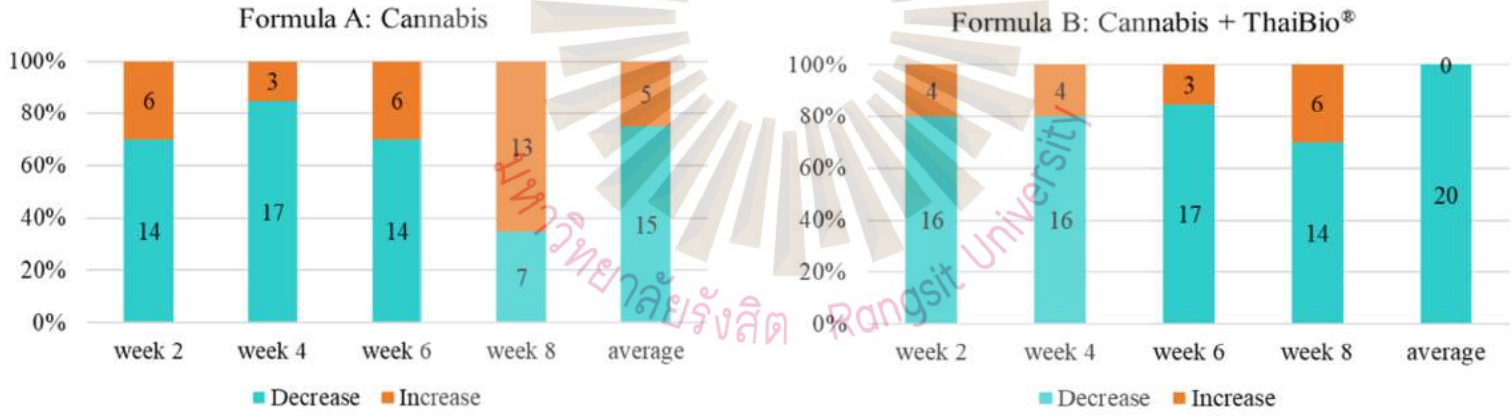
The baseline illness severity, as indicated by the PASI scores before medication (week 0), was 24.32±11.81, and 26.03±17.78 for the two participant groups, respectively. Table 4.2 provides descriptive data regarding the PASI scores during the 8 weeks of treatment. The Shapiro-Wilk test revealed that PASI scores were non-normally distributed for practically every week based on the distribution of the scores and a significance threshold of 0.05; as a result, non-parametric statistics were recommended for further analysis.

The number of patients with decreasing PASI scores was assessed in weeks 2, 4, 6, and 8 to evaluate the effectiveness of each agent, as shown in Figure 4.3

Fisher's exact test with a significance level of 0.05, revealed a statistically significant association between the agents and the percentage of patients with decreasing PASI scores ($p = 0.024$). Binary logistic regression, analysis indicated that patients using Agent B were more likely to experience a decrease in PASI score, compared to those using Agent A with odds being 2.333 (95% CI: lower = 1.592, upper = 3.421) times larger ($p = 0.033$).

Table 4.2 Descriptive statistics for PASI scores from different weeks

	Agent A: Cannabis ($N = 20$)				Agent B: Cannabis+ (ThaiBio®) ($N = 20$)			
	Min	Max	Median	Mean ± S.D.	Min	Max	Median	Mean ± SD.
Week 0	6.60	48.80	23.65	24.32 ± 11.81	3.00	56.30	25.55	26.03 ± 17.78
Week 2	5.20	58.00	19.10	21.93 ± 14.41	3.00	46.10	15.40	19.79 ± 14.28
Week 4	4.60	47.20	12.85	18.10 ± 12.13	3.00	43.20	15.20	17.88 ± 12.68
Week 6	5.50	44.10	11.90	15.34 ± 11.22	2.00	38.40	12.80	14.34 ± 10.58
Week 8	4.40	46.20	10.40	16.66 ± 12.15	1.20	40.70	11.30	13.06 ± 11.29



(a) (b)

Figure 4.3 The figures depict the proportion of patients with decreasing PASI scores in weeks 2, 4, 6, and 8 for Agent A and Agent B.

4.3 Dermatology Life Quality Index

The Dermatology Life Quality Index (DLQI) questionnaire was used to evaluate the 20 participants' quality of life. Figure 4.4 shows the profiles of DLQI scores from the two agents employing different formulations. In the first three weeks, Agent A's DLQI score was lower than that of Agent B's, but in the final four weeks, it was higher. The DLQI score showed a slight overall decrease for Agent A while it steadily decreased for Agent B. Importantly, 20 patients said that after using the Agent B (Cannabis + ThaiBio®) cream, they felt happier.

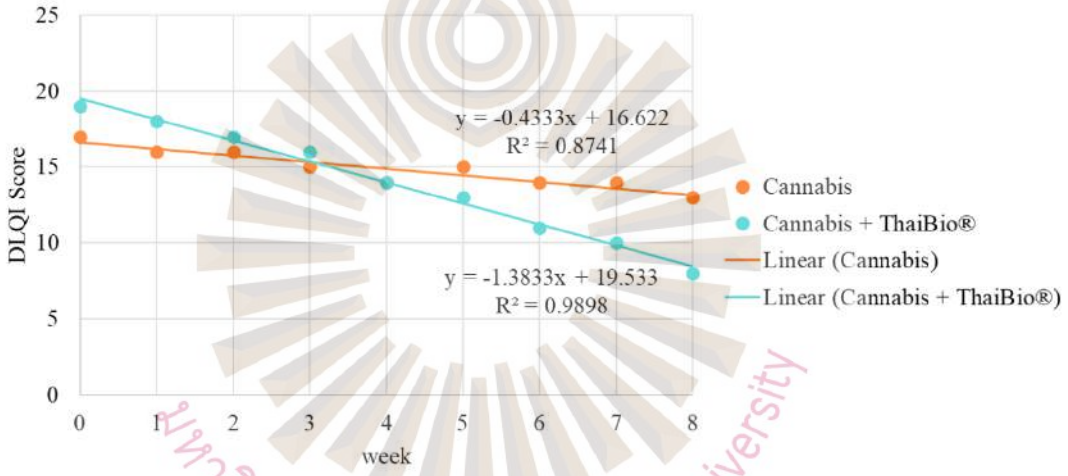


Figure 4.4 The figure shows a comparison of the DLQI scores between the two agents over the course of 8 weeks.

4.4 Psoriasis Disability Index

Participants are assessed for the Psoriasis Disability Index (PDI) at weeks 0, 4, and 8. The quality of life was reportedly impacted by psoriasis before treatment, but it improved during treatments, as demonstrated Table 4.3, following the various subsets of PDI. Both Agent A and Agent B were found to be equally effective in addressing PDI. When analyzing the impact of each formula on the PDI score, the Friedman test (one-way repeated measurements) confirmed a significant decrease at the significant level = 0.05 over the course of weeks 0, 4, and 8. The lower PDI score suggests the

person's psoriasis-related physical functional limitations are less severe. This may mean fewer disruptions to everyday tasks and improved overall functioning abilities. However, because it was difficult to conduct such self-evaluations, the mean PDI ratings for personal relationships, leisure, and medication practically remained the same for both formulations. The 20 patients who are measuring the effects of psoriasis report that Agent B makes them feel better and more at ease than Agent A. The severity of the disease, the location of the psoriatic lesions, and comorbidities can all affect each person's level of disability, which can be used to measure the effect of psoriasis on physical functioning and evaluate changes in impairment over time.

Table 4.3 Comparison of the PDI scores for six different aspects. (*N*=20)

6 different aspects	Agent A: Cannabis			Agent B: ThaiBio®+Cannabis		
	Week 0	Week 4	Week 8	Week 0	Week 4	Week 8
Daliy activities	8.45	6.15	5.25	8.55	7.65	6.80
Work and School	3.65	2.47	2.00	3.35	2.88	2.41
Neither Work and School	4.00	1.60	1.60	5.00	4.67	3.33
Personal relationship	2.15	1.40	1.35	1.55	1.60	1.55
Leisure activities	4.75	4.45	4.10	4.65	4.45	4.00
Medication usage	1.75	1.35	1.30	1.70	1.50	1.45

4.5 Blood Test

The results of a comparison test of the total blood count between weeks 0 and 8 are shown in Table 4.4. There was insufficient evidence to establish that there were any variations in the WBC count, RBC count, hemoglobin, hematocrit, neutrophil, lymphocyte, monocyte, eosinophil, and basophil between the two weeks using a Wilcoxon signed-rank test with a significance level of = 0.05 for each agent. As a result, the total blood count tests for both agents did not demonstrate any significant differences between weeks 0 and 8.

The kidney and liver function tests were compared from week 0 to week 8 as demonstrated in Tables 4.5 and 4.6. Wilcoxon signed-rank test at = 0.05 revealed no significant variations in BUN and creatinine levels between the two weeks for both drugs administered with different agents. Similarly, no significant alterations in three liver function tests, AST, ALT, and alkaline phosphatase were reported between weeks 0 and 8. Throughout the trial, participants' safety was evaluated for any adverse responses. Slight increases in redness and itching at the lesion site were recorded but symptoms disappeared after a few days and did not warrant termination of cream use. There were no serious adverse effects observed.

Table 4.4 Comparison between the complete blood count before and after medication (*N*=20)

Complete Blood Count	Agent A: Cannabis			Agent B: Cannabis+ ThaiBio®		
	Week 0 (Mean ± SD)	Week 8 (Mean ± SD)	P-value 0.05	Week 0 (Mean ± SD)	Week 8 (Mean ± SD)	P-value 0.05
WBC Count	5.67 ±1.70	5.56 ± 1.66	0.8713	6.28 ± 1.64	5.57 ± 1.49	0.2220
RBC Count	4.92 ± 0.49	4.85 ± 0.47	0.7191	5.08 ± 0.54	4.89 ± 0.49	0.3187
Hemoglobin	13.89 ± 1.31	13.23 ± 0.90	0.1724	13.97 ± 1.09	13.79 ± 1.39	0.6845
Hematocrit	42.29 ± 4.37	40.53 ± 2.26	0.2186	43.06 ± 3.64	42.12 ± 4.86	0.5360
Neutrophil	60.35 ± 9.46	59.50 ± 8.66	0.8182	61.56 ± 6.23	57.62 ± 9.25	0.1593
Lymphocyte	29.88 ± 9.02	29.90 ± 9.10	0.9956	28.08 ± 6.60	32.23 ± 9.35	0.1506
Monocyte	6.29 ± 1.40	5.90 ± 1.45	0.4965	6.20 ± 1.19	6.38 ± 1.39	0.6974
Eosinophil	2.59 ± 1.33	2.70 ± 1.70	0.8530	2.61 ± 1.25	2.85 ± 1.41	0.6162
Basophil	0.88 ± 0.49	1.00 ± 0.47	0.5386	1.03 ± 0.42	0.92 ± 0.28	0.4158

* The mean difference is significant at the 0.05 level.

Table 4.5 Comparison between kidney function test before and after medication (*N*=20)

Kidney Function Test	Agent A: Cannabis			Agent B: Cannabis+ ThaiBio®		
	Week 0 (Mean ± SD)	Week 8 (Mean ± SD)	P-value 0.05	Week 0 (Mean ± SD)	Week 8 (Mean ± SD)	P-value 0.05
BUN	11.69 ± 3.41	11.05 ± 4.46	0.6779	11.19 ± 4.73	10.54 ± 2.27	0.6496
Creatinine	0.79 ± 0.20	0.70 ± 0.20	0.2695	0.78 ± 0.20	0.78 ± 0.21	0.9998

* The mean difference is significant at the 0.05 level.

Table 4.6 Comparison between liver function test before and after medication (*N*=20)

Liver Function Test	Agent A: Cannabis			Agent B: Cannabis+ ThaiBio®		
	Week 0 (Mean ± SD)	Week 8 (Mean ± SD)	P-value 0.05	Week 0 (Mean ± SD)	Week 8 (Mean ± SD)	P-value 0.05
AST	23.56 ± 8.45	22.87 ± 9.46	0.8461	24.64 ± 10.49	23.28 ± 8.99	0.7059
ALT	23.37 ± 17.62	20.62 ± 17.96	0.7006	28.07 ± 26.06	23.01 ± 20.16	0.5604
Alkaline phosphatase	70.29 ± 25.50	63.30 ± 20.43	0.4680	70.94 ± 30.13	61.23 ± 17.46	0.3044

* The mean difference is significant at the 0.05 level.

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 Discussion

Psoriasis is a chronic skin disease characterized by inflammation and thickening of the epidermis layer. It typically presents as a red bump or plaques with flaky, white flakes, white scales and is influenced by various factors, such as genetics and environment. It has been reported to have a prevalence of about 1-3 percent of the world's population (Christophers, 2001). The cause of Psoriasis is an abnormality of the body's immune system, which is a T-cell lymphocyte that is more active than normal. T-cell lymphocytes enter the epidermis and divide. More than normal, T-cell lymphocytes will produce cytokines that cause inflammation under the skin layer, resulting in the skin dividing faster than usual. This causes the skin to appear scaly or have red spots (Deci & Ryan, 2008).

The treatment for psoriasis will depend on the severity of the disease. Less severe cases are treated with topical ointments to reduce inflammation, such as triamcinolone acetonide cream or coal tar ointment, recommended and supervised by a specialist doctor. If the rash is thick and large, it will be treated by using oral medication together with topical medication, or treated with other methods, including artificial sunlight. In cases where psoriasis does not respond to standard treatment, alternative methods like biological injections may be employed (Lebwohl, Ting, & Koo, 2005). If it lasts for a long time, it can lead to other diseases such as psoriatic arthritis, metabolic syndrome, cardiovascular disease, diabetes, high blood pressure, liver disease (non-alcoholic fatty liver), colitis (inflammatory bowel disease) (Hauptman, Bruccoleri, & Woolf, 2017), Osteoporosis and fracture incidence through lesions (Osteoporosis and Pathologic Fractures) (Munoz-Torres, Aguado, Dauden, Carrascosa, & Rivera, 2019), etc.

If there are joint symptoms and they are not getting the right treatment, it can cause deformities and disabilities. Psoriasis has also been found to be associated with smoking, alcohol use, anxiety, and mental illness (Psychological and Psychiatric Disorder) (Dhana, Yen, H., Yen, H., & Cho, 2019; Oliveira, Rocha, & Duarte, 2015).

A preliminary clinical study was conducted to evaluate the cannabis extract GPOCE (THC: CBD 1:1) (Agent A) and the combining a GPOCE with a polyherbal formulation (ThaiBio®) (Agent B), formulation for symptom relief and quality improvement. This life for psoriasis patients has a purpose. To develop a topical cannabis-containing drug for patients with topical psoriasis, which is believed to be the route of drug administration. They are safer than the sublingual drops and is the drug delivered directly to the lesion location; and to study the effectiveness and safety of products based on the traditional sublingual oil drop form of "GPOCE THC:CBD 1:1" using 5% "GPO THC:CBD 1:1" oil alone in the cream base. Compared with the improved formulation of topical cream "Thai Bio®" 95% combined with "GPOCE THC:CBD 1:1" using 5%), the effectiveness of Thai Bio® in relieving symptoms and improving quality of life in patients with psoriasis was evaluated by PASI score, PDI, DLQI, adverse reaction assessment, and biochemical examination for diagnosis.

The skin endocannabinoid system (ECS) plays a crucial role in the regulation of various physiological processes, including inflammation and immune response (Shao, Stewart, & Grant-Kels, 2021). The ECS has been shown to regulate the proliferation and differentiation of keratinocytes, the cells that make up the outer layer of skin, suggesting that modulating the ECS could be a potential therapeutic target for psoriasis (Ständer, Schmelz, Metze, Luger, & Rukwied, 2005). The ECS has been implicated in the pathogenesis of psoriasis, and both THC and CBD, the key compounds found in cannabis, are believed to modulate the ECS, leading to the inhibition of proinflammatory cytokines and the reduction of inflammation in the skin. THC has been found to have anti-inflammatory properties and has been shown to inhibit the production of inflammatory cytokines, which are involved in the development of psoriasis (Ständer et al., 2005). A study conducted by Palmieri et al. (2019) found that a CBD-enriched ointment was effective in reducing symptoms of inflammatory skin

diseases, including psoriasis (Palmieri et al., 2019). Recent studies have shown that cannabis-based treatments, both natural and synthetic cannabinoids, have been found to have immunomodulatory effects and can reduce inflammation in psoriasis lesions (Martins, Gomes, Boas, Marto, & Ribeiro, 2022).

5.2 Conclusion

The current research supports earlier studies that suggest psoriasis sufferers may benefit from cannabis-based therapies, particularly those that contain THC and CBD. A promising therapy option for people with psoriasis involves combining cannabis with other medicinal plant extracts. Based on the crossover randomized controlled trial over 8 weeks with the washout period of 2 weeks, the two separate topical creams, including cannabis alone and cannabis in addition ThaiBio® formulas, demonstrated their potential therapeutic advantages in the treatment of psoriasis. Lower PASI, DLQI, and PDI scores show that the cannabis plus ThaiBio® combine produced better outcomes than the cannabis alone formula in terms of efficacy.

These results indicates that the combined of ThaiBio® and cannabis exhibited superior efficacy in the treatment of psoriasis compared to ThaiBio® or Cannabis alone. In terms of safety, the functions of the liver, kidneys, and complete blood count were unaffected by either formula. However, greater study is required to assess the mechanisms of action and potential hazards of these treatments because the long-term effectiveness and safety of these therapies are not yet fully established. To address the intricate mechanisms underlying psoriasis, a combination of cannabis, which primarily target the skin's endocannabinoid system, and other non-cannabis plants with distinct targets, can employed. Utilizing the possible synergistic effects of these many plant chemicals could result in a more thorough therapy strategy and possibly better results for psoriasis patients.

To study the specific synergies and improve the formulation for maximum effectiveness, more research is required in this area. In some areas, people with psoriasis may not have access to cannabis-based medicines (CBMs) due to regulatory

and legal restrictions. Despite these drawbacks, cannabis-based psoriasis treatments have the potential to be therapeutically beneficial and a useful supplement to existing therapy alternatives. With further study, it might be able to tailor the usage of CBMs for psoriasis sufferers, relieving symptoms and enhancing quality of life. In conclusion, research into alternative treatments for psoriasis is an important and promising area that may result in new treatments for patients. Despite the lack of enthusiasm for this field of study, it is critical for the scientific community to keep looking into these prospective medicines in the search for more efficient and widely available psoriasis treatments.

5.3 Finding and Benefits

This information can serve as a foundation for further in-depth research studies involving a larger number of inpatients. The products have demonstrated their potential to alleviate symptoms and improve the quality of life for psoriasis patients. The alternative treatment can be especially valuable for individuals experiencing side effects from standard medications. Additionally, there intellectual property protection. This research holds promise for advancing psoriasis treatment options.

5.4 Future Research

The results of this study open up opportunities for further development of externally applied products based on the "Thai-Bio® + THC: CBD 1:1" cream formula. This may include steps such as product registration and commercial production. In the future, it is anticipated that the formula will continue to be refined and researched on larger groups of patients, potentially leading to improved treatment option for psoriasis.

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