

THE CLINICAL EFFICACY OF SODIUM L- ASCORBYL-2PHOSPHATE, RETINOL, AND THEIR COMBINATION APPLICATION IN ACNE TREATMENT

CHONCHANOK RUAMRAK

MASTER OF SCIENCE
IN COSMETIC SCIENCE

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AN INDEPENDENT STUDY SUBMITTED TO MAE FAH LUANG UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN COSMETIC SCIENCE

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Independent Study Title The Clinical Efficacy of Sodium *L*- ascorbyl-2-phosphate,

Retinol, and Their Combination Application in Acne Treatment

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ABSTRACT

This study examines the clinical efficacy of sodium L-ascorbyl-2-phosphate, retinol, and their combination in acne treatment. The period of experiment was 8 weeks.

Acne vulgaris has multifactorial causes and steps of pathogenesis. The previous studies show that Sodium *L*- ascorbyl-2- phosphate (SAP), a stable form of vitamin C, has antimicrobial and anti-lipid peroxidation effects. Retinol also known as retinoic acid precursor has a similar effect to retinoic acid in 10 fold higher concentration. Comparing the efficacy of SAP, retinol, and combination use of SAP and retinol show that SAP reduced inflammatory acne 20.14% at week 4 and 48.82% at week 8, retinol reduced inflammatory acne 21.79% at week 4 and 49.50% at week 8 and the combination use of SAP and retinol reduced inflammatory acne 29.28% at week 4 and 63.10% at week 8. The efficacy when combine SAP and retinol was significantly increased compared with single SAP or retinol at p. value < 0.05 at week 4 and 8.

Keywords: Acne/ Sodium *L*- ascorbyl-2-phosphate/ Retinol/ Clinical Efficacy

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ABBREVIATIONS

SAP Sodium *L*-Ascorbyl-2-phosphate

P. acnes Propionibacterium acnes

BP Benzoyl Peroxide

CRBP cellular retinol binding protein

CRABP Cellular retinoic acid binding protein

Asc Ascorbic acid

VCP-IS-Na Sodium Isostearyl 2-O-L-Ascorbyl Phosphate

HPLC High Performance Liquid Chromatography

TGF transforming growth factor

CHAPTER I

INTRODUCTION

1.1 Background

Acne vulgaris is one of the most common skin inflammations which has been found in teenagers until mid age. Acne is not only a general appearance effect, but also psychological effect since facial skin is the most common affected part. Many acne patients have searched for different treatments to get the best results, such as drugs, lasers, and cosmeceutical products.

Recently, there are many over the counter (OTC) brand and cosmeceutical product claimed for anti acne property. Each product should has action on the steps of pathogenesis of acne, which are sebum hyperexcretion, comedogenesis, *Propionibacterium acne* colonization and inflammation.

Vitamin C, an antioxidant vitamin, has been studied in several years about their antiinflammatory property in acne, but stability problems have been concerned. Sodium *L*-ascorbyl-2-phosphate (SAP), which is a stable water soluble form of vitamin C derivative, has been studied for acne treatment property compare with clindamycin and benzoyl peroxide, and its good result could be use as the effective active ingredient in cosmeccutical products.

Retinol is the precursor of retinoic acid which has been used as an effective treatment of acne vulgaris, but there are not many studies of anti acne property of retinol due to its instability problem. Retinol 10S®, which is a new stable form of retinol from BASF The chemical company, has been selected in this study.

According to the 4 steps in acne pathogenesis we assume that ideal acne treatment products should have an effect on all mechanisms which are sebum control, keratolytic or comedolytic effect, inhibit *P. acnes* colonization, and anti-inflammation. From these properties of both active ingredients, SAP and retinol as well as their combination have been selected for

comparing the clinical efficacy in the treatment of acne in order to investigate the synergistic effects of these compounds as well.

1.2 Objectives

This study has aimed to compare the clinical efficacy of 5% SAP and 0.2% retinol as well as the combination of 5% SAP and 0.2% retinol in the treatment of acne. The clinical adverse reactions will also evaluate.

1.3 Scope and area of research

- 1.3.1 SAP, retinol, and their combination have been selected into this study to evaluate their clinical efficacy.
- 1.3.2 The clinical test was performed with the patients in cosmetic clinic therefore the number of participants depends on the number of patients enrolled in the clinic with the correct criteria of selection. The number of the participants should be at least ten for each group.
 - 1.3.3 The efficacy will be evaluated by lesion counting.
 - 1.3.4 At the end of study, the data was analyzed by one way ANOVA.

1.4 Benefits

- 1.4.1 The higher efficacy cosmeceuticals for acne treatment have been studied
- 1.4.2 Consumers will have an alternative method form treating with drugs
- 1.4.3 The results will be applicable for any other cosmeceutical formulas
- 1.4.4 The efficacy and adverse reaction of the cosmeceuticals from this study will be studied.

CHAPTER II

LITERATURE REVIEWS

2.1 Cosmeceuticals

In the late 1970's, the term 'Cosmeceuticals' was introduced by Dr. Albert Kligman at the Meeting of the Society of Cosmetic Chemists by joining two words; cosmetic and pharmaceutical.

Cosmeceuticals refer to products which have both properties of cosmetics and drugs therefore, properties of cosmeceuticals could be claimed to have medicinal action. Cosmeceutical products have been marketed as cosmetics, but reputedly contain active ingredients. Cosmeceutical materials must have pharmacological actions, but can be used in normal skin. They may have curative properties for mild skin disease with low risk of side effects. In Europe and Japan, cosmeceuticals had been defined as groups of cosmetic while in USA cosmeceuticals had been grouped as drugs. Cosmeceuticals' raw materials must have pharmacological activities but could be used on normal skin with less adverse reactions than drugs. The comparison of cosmetics, cosmeceuticals, and drug is shown in Table 2.1

Table 2.1 The comparison of cosmetics, cosmeceuticals, and drugs.

	Cosmetics	Cosmeceuticals	Drugs
Pharmacological Activity	+	+	+
Intended effect in skin disease	-	(+)	+
Intended effect in mild skin disorder	-	+	(+)
Side effects	-	(+)	+

From the table, the action of cosmetic, cosmeceutical, and drug have been compared. Cosmetics do not have any effect in skin disorder while the cosmeceuticals and drugs do. The products which have effect in skin disease have claimed as drugs and the cosmeceuticals may have effect in mild skin disorder.

2.2 Acne vulgaris

Acne vulgaris is one of the most common skin inflammations which has been found in teenagers until mid age. Acne is not only general appearance effect, but also the psychological effect since facial skin is the most common affected part. Many acne patients have searched for different treatments to get the best results, such as acne drugs, lasers, and cosmeceuticals.

2.2.1 Etiology of acne²

Acne is a disease of pilosebaceous follicles on face and trunk, mostly under androgenic control. From the hormonal cause, acne usually starts in teenagers and reaches the peak at the age of 16-20 year-old in both males and females, and may be in chronic cases until the age of twenties. Some still have acne even when they reach 40-50 years old.

The human follicles have been divided into three types which are beard follicle, vellus follicles which are composed of hair follicle and sebaceous follicle, and sebaceous follicles or pilosebaceous follicle which have an important role in acne formation.

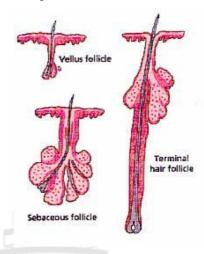


Figure 2.1 The three types of follicle which occur on the face.³

The probable and possible etiological factors in acne vulgaris are familial factor, external factors, drugs, water balance, gastro-intestinal disturbance, infection, stress, and endocrinology imbalance.

2.2.2 Pathogenesis of acne²

The pathogenesis of acne has been divided into four steps which are sebum hyperexcretion, comedogenesis, *Propionibacterium acnes* colonization and inflammation.

1. Sebum hyperexcretion.

The increasing of sebum under androgen control can cause seborrhea. The increasing facial sebum was not found to be the primary cause of acne formation but it is an aggravating condition in acne patients. Increased sebum secretion with follicular obstruction could induce comedogenesis. But the increasing of sebum secretion without follicular obstruction can not incite comedone formation. Active ingredients which affect this mechanism are retinoid and hormone such as cyproterone acetate which decrease androgen activity on the skin.

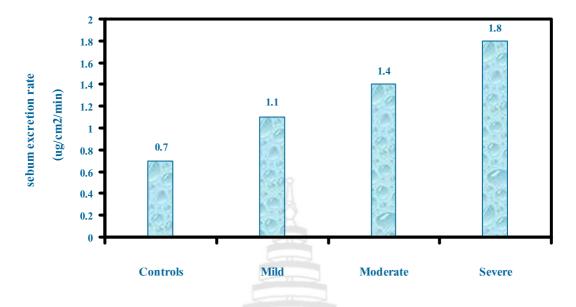


Figure 2.2 The correlation between acne grade and sebum excretion rate² (Modify from : Cotterill, Cunliffe, Strause, Pochi, Chrisot 1969-1990)

The proliferation of the basal sebocytes of sebaceous gland lobules synthesized a numerous of lipid compound. After these cells migrate to the sebaceous duct, they secrete intracellular sebum to the sebaceous ducts and skin.

In most cases of acne patients, there is no sign of abnormal hormonal symptom and therefore it is not necessary to investigate.

Androgen which is produced by adrenal gland and gonad will stimulate sebum secretion from the sebaceous gland. In the sebaceous gland, there is a conversion of testosterone to 5-alpha dihydrotestosterone via the mechanism of 5-alpha reductase type I. For estrogen, it does not have much effect on the sebaceous gland.

2. Comedogenesis^{2,3}

Comedones are formed by the infiltration of ductal corneocytes in the sebaceous ducts which can not move out via duct openings. Ductal hyperproliferation causes comedones formation. There are 2 different types of comedones, black head, and white head comedone which begin with the microcomedones. Comedones are precursor of both inflammatory and non inflammatory lesion. Therefore, the getting rid of microcomedones is necessary for the prevention

of inflammation. White head comedones or closed comedones have very small openings, there are a lot of proinflammatory substances congested in the sebaceous ducts. That is why the white head comedones have a higher risk of inflammation. Black head comedones or opened comedones have bigger openings which have less chance to be inflamed. Comedolytic agents such as retinoid, alpha and beta hydroxy acids play an important role in this step by reducing follicular compaction effects.

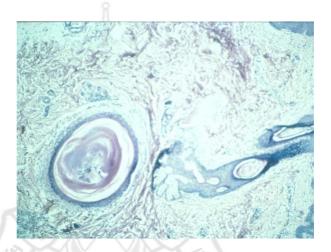


Figure 2.3 Ductal corneccyte accumulating in the ductal lumen²

3 Propionibacterium acnes colonization

The colonization of *Propionibacterium acnes* (*P. acnes*) has been presented in the opening of sebaceous glands. Acne is not an infectious disease. Normally the *P. acnes* are found in a sebaceous rich area of normal skin and the number of *P. acnes* in acne group is not significantly different from the control group. However *P. acnes*, which are lipophilic microorganism, induce inflammation of lesion by colonization in the follicles and secrete proinflammatory mediators. Despite this, the cause of P. acnes colonization is still of a poor understanding. To inhibit *P. acnes* colonization, antiseptics, or antibiotic such as clindamycin, metronidazole, minocycline doxycycline, tetracycline, and erythromycin have to be used for long periods of time.

4 Inflammation

From histology studying in acne patients, at the area of acne papule are presented as the comedones or microcomedones which have been found at the start and follow by duct rupture but this is not found at the beginning of the inflammatory process. T-helper cells which were found in the dermis before the migration of polymorphonuclear leukocytes.

Many studies report that the inflammation of acne is a type IV cell-mediated immune reaction to the antigen which cannot yet be defined. When the infection occurred, CD4 lymphocytes and neutrophils were found at the center. Neutrophiles synthesized hydroxy radicals and singlet oxygen which causes the process of lipid peroxidation, but the mechanism is still not known.

The active ingredients which affect this process are anti-inflammatory agents and anti-oxidants such as anti-oxidant vitamins.

The types of acne lesions have been classified in 5 types which are comedones (white head and blackhead), papules, pustules, nodules, and cysts.

2.2.3 Treatment of acne⁴

There are many recommended methods for acne treatment. The most generally accept methods are topical treatment and systemic treatment.

Steps of acne treatment divided to five steps regarding to the pathogenesis of acne.

- 1. Normalizing keratinization. The products that affect this step are keratolytic agents such as retinoic acid, retinol, and retinol ester.
- 2. *P. acnes* control. The products that affect this step are antibiotics, Benzoyl peroxide
- 3. Remove follicular clogs. The products that affect this step are retinoid and comedolytic agent such as salicylic acid.
 - 4. Anti inflammation. The products that affect this step are antioxidants.
 - 5. Sebum control by using retinoid and hormone such as cyproterone acetate.

2.2.4 Acne grading system⁵

There are several systems for grading the severity of acne currently exist.

1. The acne lesion-counting technique divides the face into five regions. In each region, the numbers of non-inflammatory and inflammatory lesion are counted.

- 2. Global assessment has classified acne severity into the categories of very mild, mild, moderate, severe, or very severe, based on a rater's overall impression. Comedones is classified as mild, papulopustular lesion is moderate, and nodular lesion is severe.
- 3. The Plewig and Kligman system has classified acne into three sub-types, namely comedonal, papulopustular, and conglobate. The right side of the face is considered, and severity of disease is assessed on a I–IV scale according to the number of lesions and the predominant lesion type (inflammatory or noninflammatory).
- 4. The Cunliffe score (Leeds technique) is a photonumeric grading scale. Grading involves comparing the patient's severity of acne to a standard photographic manual and assigning a score from1 (mild) to 10 (very severe).
- 5. Cook's photographic method uses a 0-to-8 severity scale based on photographic standards. The American Academy of Dermatology classification describes acne as mild, moderate, or severe taking into consideration only inflammatory lesions.
- 6. Allen and Smith's classification uses Cook's grading scale as well as lesion counting. Comedoness and papules are counted on the right side of the face, while pustules and overall severity grading are evaluated on both sides of the face.
- 7. Fluorescence photography assesses the severity of comedonal acne. A 0-to-3 scale assigning fluorescence grades of none, mild, moderate, and extensive is used.

Comparison of acne grading system of each method, which has been studied by Amol Doshi, Ahmed Zaheer & Matthew Stiller, has shown in the table below.

Acne grading system	Accurate?	Accurate? Extent of interand intra-rater variability	Time required	Relevant anatomic areas	Special equipment required	Cost	Photographic record of patient?	Applicable to dark skin?	Considers both inflammatory and noninflammatory lesions?	Overall
Lesion counting ²	Yes	Significant	Very slow	Excludes back chest	None	None	No	Yes	Yes	Fair
Global assessment (Ludky, pers. commun.)	2	Moderate	Quick	All-indusive	None	None	°Z	Yes	Yes	Fair
Plewig and Kligman ³	Yes	Significant	Very slow	Right face only, excludes back chest	None	None	No	Yes	Yes	Fair
Cunliffe score (Leeds	2	Moderate	Quick	Excludes back, chest	Photo manual	s	No	Difficult	Yes	Poor
ic method	2	Moderate	Slow	Excludes back, chest	manual	ss :		Difficult	Yes	Poor
AAD classification? Allen and Smiths	s es	Minimal Moderate	Quick	All-Indusive Excludes back, chest	None Photo manual	None	No Yes	Yes Difficult	No Yes	Good
photonumeric system? Fluorescence photography ⁸	Yes	Moderate	Very slow	Excludes back chest	Photography	s	Yes	Difficult	No	Poor
Global Acne Grading System (GAGS)	Yes	Minimal	Quick	All-Indusive	system None	None	o _N	Yes	Yes	Good

2.2.5 Cosmeceuticals for acne treatment

For the treatment of acne vulgaris, cosmeceuticals are alternative choices for the individuals who have denied treatments involving drugs or have adverse reactions from drugs, such as drug resistance or drugs allergy.



Figure 2.4 Skin carriages of antibiotic resistant P. acnes ²

The mechanism of comedogenesis is complicated while each cosmeceutical materials had different benefits. The combination treatment for acne vulgaris might have better benefits than using only one preparation due to the different mechanism of actions and steps of comedogenesis. There are several cosmeceutical ingredients which have been used for acne control such as antioxidant vitamin, hydroxy acid, retinoid, plants extracts, etc.

In this study, vitamin C and retinoid are selected to use for comparing the efficacy of each ingredient and combination in acne treatment from their properties. Vitamin C has effects as an antioxidant and anti-inflammatory but there are some problems with its stability and therefore many cosmetic ingredient companies manufactured several types of vitamin C derivatives to solve the stability problem. Retinoid has defined as a class of vitamin A which has effect on epidermal cell differentiation and renewal. It is a class of retinoid which is allowed to use in cosmetic products but there is also a stability problem. The form of vitamin C derivative which

has been selected into this study is SAP because of its stability property and its previous studies and retinol 10 s has also been selected from its stability property.

2.3 Sodium L-ascorbyl-2-phosphate^{6,7}

Sodium L-ascorbyl-2-phosphate (SAP), a stable water soluble vitamin C derivative, is transform to ascorbic acid after percutaneous absorption.⁶

Figure 2.5 Structure of sodium *L*-ascorbyl-2-phosphate (SAP) ⁶

There are many studies present the biological activity of SAP. The results from those studies conclude as the following.

1. Inhibit growth of *P. acnes* in culture plate by the log reduction 2 at 4 hours and 5 at 8 hours, at 1% concentration. In the figure 9, 0.1% and 1% SAP was added to the culture medium and bacterial counts were statistically calculated at 4 and 8 hours after treatment

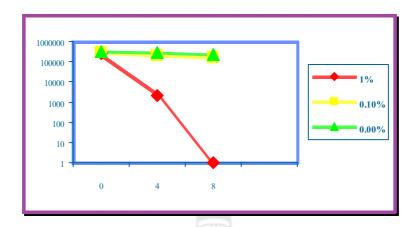


Figure 2.6 Bacterial growth of *P. acnes* analyzed under physiological conditions. (Modify from : J. Knock et al. 2005)

2. At 3% concentration, SAP reduce lipid peroxidation at 40% by scavenged singlet oxygen and hydroxy radical of neutrophils during the inflammatory process ⁷

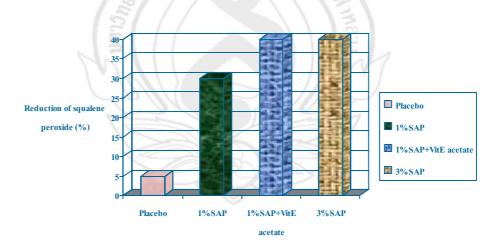


Figure 2.7 The inhibitory effects on lipid peroxidation of placebo, 1%SAP,

1%SAP+1%Vitamin E acetate, and 3%SAP (Modify from J. Knock et al.

2005)

The results from those previous studies showed that SAP inhibits acne formation at the 3rd and 4th steps by inhibit the growth of *P. acnes* colonization and lipid peroxidation respectively. For the clinical studies, there are some studies which had shown the comparison of efficacy between SAP and other anti acne medications such as benzoyl peroxide and clindamycin.

In 2005, Klock et al ⁶ had studied the efficacy of 5% SAP compared with 5% benzoyl peroxide (BP) in acne treatment. The result had presented that the group which had been treated with 5% SAP had the clinical improvement up to 76.9% and in 5% benzoyl peroxide group had the clinical improvement up to 60.9%.

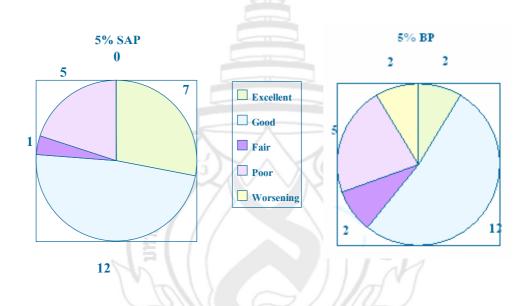


Figure 2.8 Comparison of 5% SAP to 5% Benzoyl peroxide (5%BP) in acne treatment (Modify from : J. Klock et al. 2005)

In 2006, Ikeno et al ⁷ compared the effective of 5% SAP and 1% clindamycin in acne treatment. For the volunteer in 5% SAP group had clinical improvement up to 75.7% while 1% clindamycin improve acne 54.5%. Serious adverse reaction had not found.

The stability of SAP, SAP is a very stable derivative compared with other derivative of vitamin C. The figure 9 shows the study of Shibayama et al 2005 show the stability of SAP compared with ascorbic acid and Sodium Isostearyl 2-O-*L*-Ascorbyl Phosphate (VCP-IS-Na), another derivative, at different pH value. At pH 5 and 7 SAP remaining concentration was at 90%

at after 28 days by HPLC analyzing method. 8 From the graph below, ascorbic acid, SAP and VCP-IS-Na were dissolved in 50 mM citric buffer (pH5.0, graph A) and 50 mM potassium phosphate buffer (pH7.0, graph B) to give 10 mM solution, and then incubated at 50°C for the indicated time. The concentration of test compounds was analyzed by HPLC. Each value represents the mean \pm S.D. of five experiments. 8

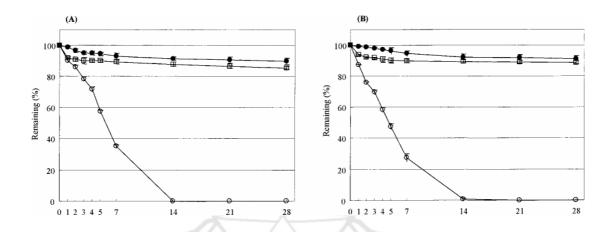


Figure 2.9 Stability of ascorbic derivatives in aqueous solution. ⁸ Ascorbic acid (○), SAP (●), and VCP-IS-Na (□)

In the experiment, ascorbic acid and SAP were applied to a donor cell and stirred for 24 hours at 37°C. The permeation level was expressed as a total amount of ascorbic acid and SAP by HPLC analysis and repeated for three experiments. From the graph, SAP had significant better permeability than ascorbic acid.

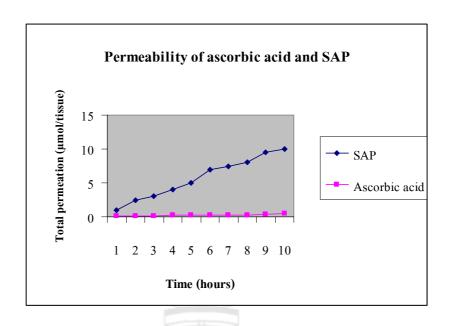


Figure 2.10 The graph compare permeability of ascorbic acid and SAP in an organotype model of human skin. (Modified from Shibayama et al 2005)

The figure 11 shows amount of SAP remain 98.4% while ascorbic acid remain 68.5% at day 100, therefore SAP is more stable that ascorbic acid.



Figure 2.11 Stability of SAP and ascorbic acid (Asc) $\,$ 2% in water, $\,$ 20°C, pH $\,$ 7 13

From all studies above, the use of SAP for acne treatment is effective and safety but the mechanism of action doesn't cover all pathological process of acne formation.

2.4 Retinol

Retinol, a natural form of vitamin A, is an oil soluble vitamin. The natural sources of retinol are fish oil, fruits, and vegetables. In the treatment of acne, many dermatologists have prescribed topical and oral retinoid which is the derivatives of retinol. Retinoids have been accepted as sebum controlling and comedolytic agents, but they are allowed to use as drug. Retinol has been used as an introduction in acne therapy even though the clinical evaluation has not been studied yet but it appears that retinol can induce comedolysis therefore it is interesting to replace of retinoid because it is a precursor of retinoic acid and has been allowed to use as cosmetic.

Retinol is an important ingredient in many cosmetic products. When it has been intaken, it is oxidized to retinoic acid but the concentration is 10 times decreased. Retinol has less skin adverse reaction than retinoic acid. The maximum concentration of retinol which does not have irritation effect is 1.6%

The acne primary lesions are microcomedones, which couldn't be seen with naked eyes. They are precursor lesion of comedones and inflammatory macules, papules or pustules. The pathogenetic factors are hyperseborrhea, ductal hyperproliferation, and abnormal differentiation of ductal epitheliums.

Prevention of microcomedones is important for acne control. Retinol, which has been used in cosmetic as alternative of retinoic acid, has comedolytic effect of in dose dependent by mechanism of gene transcription after conversion to all-*trans* retinoic acid. ¹⁰

In the previous study, many physicians and chemist tried to use systemic retinol to treat the diseases of abnormal keratinization and acne but those studies used high doses of retinol and it caused serious adverse reactions such as hypervitaminnosis A and hepatotoxicity.

In 1960's, AM Kligman and G. Stuttgen had tried to study the effect of topical retinol for acne treatment but unsuccessful because of the instability of retinol. 11

In 2000, LH. Kligman and EH. Gans had compared the efficacy of retinol and retinoic acid on skin. This study showed that retinol and retinoic acid have similar result on epidermis while retinol required higher doses than retinoic acid but more effectively delivered to the skin and less irritation. ¹¹

2.4.1 Mechanism of action of retinol

Retinol and its derivative are important for cell growth and normal differentiation of epithelial tissue. After absorption, it has oxidized to retinoic acid, which has effects of proliferation and differentiation of epithelial cell. Affecting the follicular epithelial turnover lead to an expulsion of comedones and inhibit microcomedones formation. The change of environmental factors in pilosebaceous unit prevents the colonization of P. acnes. Furthermore, inducing desquamation of topical retinoid enhance the penetration of other topical products, with 10 times lower in concentration. The skin adverse reactions from retinol is less than which from retinoic acid and the highest strange which has less irritating effect is 1.6 %. At the concentration up to 1.6 %, retinol may effect to epidermis similar to retinoic acid but less irritation. Retinol has important property as antioxidant. Deficiency of retinol can cause oxidative damage of the liver in rat. Retinol controls sebaceous gland activity and induces desquamation of corneccyte. 13-cisretinoic acid, one of the derivative forms of retinol, is very effective for reduction of sebaceous glands activity. It also reduces cell proliferation and alteration of pattern of keratinization in the follicles. After absorption, retinol transform to retinoic acid which induce the rapid and transient expression of transforming growth factor (TGFB1, TGFB2 and TGFB3). The transforming growth factors inhibit proliferation of keratinocytes and TGFB2, 3 reduce cell proliferation and lipogenesis in sebaceous glands.

There are many studies and experiments which have been performed on the retinoid metabolism but there still not enough information how retinol is metabolized to form active ligands. In vivo study, retinol produces changes in skin, similar to those produced by retinoic acid but less irritation. Inside cells, retinol associated with the protein called cellular retinol binding protein (CRBP). After bind with CRBP retinol metabolized to the different forms depend on cellular retinoid level, if there are enough retinoid level in the cell, cells store retinol in the form of retinyl ester and can be hydrolyzed and converted back to retinol and free fatty acid when necessary. Another form of storage retinol is retinoic acid and retinaldehyde, which is an

intermediate form. This is an enzyme-related conversion reaction. Another study demonstrated that applying topical retinol 0.2% on human skin cause an induction of CRABP-II mRNA similar to retinoic acid 0.025%.

2.4.2 Adverse reactions of topical retinol

- 1. Topical retinol can irritate the skin. Excessive use can cause skin redness and desquamation.
 - 2. Increase sensitivity to the sun's ray lead to increase the chance of sunburn
 - 3. Excessive application of Retinol might sometimes cause itching and scaling.
 - 4. Allergic reaction of retinol

2.4.3 Retinol 10S®

Retinol, as a raw material, is a crystalline solid that is sensitive to oxygen, heat, light, and heavy metal. Retinol 10S® from BASF, Germany has been developed as a stable retinol containing in soy bean oil as its solvent with 1%BHT as its stabilizer system. There are some studies of retino10S® stability show that retinol 10S® is stable to store in different temperature.

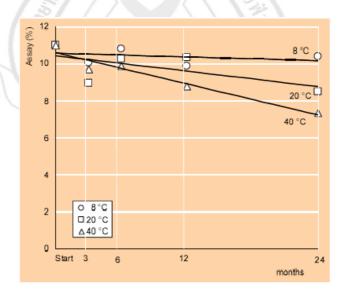


Figure 2.12 Stability of retinol 10S® in storage at different temperatures 13

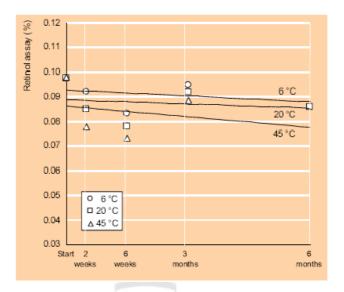


Figure 2.13 Stability of 1% retinol 10S® in formulation in storage at different temperatures 13

From all following reviewed literatures, SAP and retinol 10S® are interesting to study their clinical efficacy in acne treatment due to their mechanism of action and stability. Most studies compare the efficacy of SAP and other acne drugs, but there is not any research compare the clinical efficacy of SAP, retinol, and their combination yet, therefore, this study will be useful for anyone who is interested in the cosmeceutical field.

CHAPTER III

MATERIAL AND METHODS

3.1 Materials

3.1.1 SAP lotion, formulated from the study of J. Klock et.al. ⁶

Water	84.76 %
Propylene glycol	1.83 %
SAP	5.00 %
Ethanol	2.24 %
Glycerin	5.98 %
Methylparaben	0.19 %

- 3.1.2 0.2% retinol cream has been formulated from BASF formulation guideline.
- 3.1.3 Pure lotion base has been formulated.
- 3.1.4 Pure cream base has been formulated.

3.2 Experimental plan

This study had been designed as a cross double blind study. Participants are divided into 3 groups, The first group were indicated to use 5% SAP lotion with cream base, the second group were indicated to use 0.2% retinol cream with lotion base, and the third group were indicated to use 5% SAP lotion with 0.2% retinol cream. Direction of use was that 5% SAP lotion and lotion base should have been applied on the whole face in the morning and in the evening for

8 weeks continuously while retinol cream and cream base should have been applied on the whole face at night time for 8 weeks continuously. Each products amount was 60 grams for each individual for the whole study.

The studying time was 8 weeks and follow up at 4 and 8 weeks to compare the result between each group and statistical analyze by one way ANOVA.

3.3 Selection of Patients

- 3.3.1 The patient age should be 18-40 years old.
- 3.3.2 45 patients with 10-50 inflammatory lesions were enrolled in this study which individuals have 10-50 inflammatory lesions (papules, pustules and nodules).
- 3.3.3 Individuals had not used any other topical anti-acne treatment and antibiotics for 4 weeks before participate in this study.
- 3.3.4 Individuals had not used systemic retinoids for at least 6 weeks before participate in this study.
- 3.3.5 Women must not be pregnant or lactating and stop contraceptive drugs at least 3 months before participate.
- 3.3.6 During study time, the patients must not do any facial skin treatment or operation such as, peeling, iontophoresis, phonophoresis, laser, mesotherapy, dermabrasion, dermaroller, or other procedures which have effect on facial skin.
- 3.3.7 Enrolled patients were randomized to apply both SAP and/or retinol products.All patients had to read the study detail and sign in consent form
 - 3.3.8 All patients had patch test before starting apply the product

3.4 Clinical efficacy investigation

According to the subjects are patients of clinic, therefore each individuals may not start enrolling into the study in the same time.

On the first day of each individual, physician examine their facial skin by counting inflammatory acne lesion and photographs. Acne severity grading has been used in this study is the Lesion counting method which is the most effective method for evaluate the efficacy of the products. The patients will be informed by the physician about the experiment and sign consent form. All patients have known the contacting detail of physician. If there is any adverse reaction occurred during the experiment, physician would have responsible in any case

Patch testing has been tested to all patients. The area of testing was ventral surface of forearm due to patients' convenience because some patients were not comfortable to have a test at their back. Substances for the test were SAP lotion, lotion base, retinol cream and cream base have applied on each individuals. The results have been read in 48 hours.

For the efficacy test, the clinic assistants give 2 products to each patient, one is lotion, and another one is cream. The patients have appointment every 2 weeks with the physician for evaluation. On each appointment, the physician evaluated the severity of acne by counting inflammatory lesions and the photographs had been taken.

3.5 Evaluation

At the end of experiment, the total inflammatory lesions would be counted again for statistic evaluation by one way ANOVA and the result will be discuss and make a conclusion.

CHAPTER IV

RESULT AND DISCUSSION

4.1 Clinical investigation

Forty five patients had enrolled onto this study at the beginning. Fifteen patients discontinued the study. Two of them just discontinue without any reasons. Eight of them were unable to come to the clinic. Two patients wanted to stop for private reasons. Three of them preferred to use other facial treatment procedures. Patch test had been done with 45 patients at the first day. None of them has strong positive patch test. The result could be distributed as shown as in the table 3.

Table 4.1 The result of irritation patch test

No. of patient	Negative	Equivocal	Weak positive	Positive
Sample	3/11/6		Z	
5% SAP lotion	25	9	7	1
Lotion base	27	11	3	2
0.2% retinol cream	21	10	7	3
Cream base	37	4	3	4

There were four patients that did not arrive on patch test assessment day but continued to be present in the study; therefore, we assumed that there was no serious reaction.

4.2 Clinical efficacy evaluation

Efficacy was assessed at the baseline and at 4 and 8 weeks by lesion counting grading system, the inflammatory lesions are counted by the blind investigator. Statistical analysis was performed using one way ANOVA test and the P. values of 0.05 or less were considered statistically significant. All data has been record in the table 4.2 and the comparison of efficacy has been shown in figure 4.1.



Table 4.2 The number of inflammatory lesion comparing between SAP, retinol, and the combination group at week 4 and week 8.

Group/patient	No. of inflammatory lesions		No. of lesion reduction		Percentage of reduction		
	week 1	week 4	Week 8	wk 1- wk4	wk 1- wk8	wk 1- wk4	wk 1- wk8
SAP 1	30	22	16	8	14	26.67	46.67
2	15	12	8	3	7	20.00	46.67
3	18	14	9	4	9	22.22	50.00
4	27	21	15	6	12	22.22	44.44
5	13	11	7	2	6	15.38	46.15
6	33	28	18	5	15	15.15	45.45
7	15	12	7	3	8	20.00	53.53
8	17	13	7	4	10	23.53	58.82
9	26	22	15	4	11	15.38	42.31
10	24	19	11	5	13	20.83	54.17
					average	20.14	48.82
Retinol 1	32	28	17	4	15	12.50	46.88
2	22	17	13	5	9	22.73	40.91
3	25	20	14	5	11	20.00	44.00
4	28	22	13	6	15	21.43	53.57
5	18	15	11	3	7	16.67	38.89
6	14	12	7	2	3	14.29	50.00
7	16	13	8	3	8	18.75	50.00
8	23	16	9	7	14	30.43	60.87
9	27	19	12	8	15	29.63	55.56
10	35	24	16	11	19	31.43	54.29
		1		V	average	21.79	49.50
Combined 1	25	18	9	7	16	28.00	64.00
2	13	10	5	3	8	23.08	61.54
3	22	16	9	6	13	27.27	59.09
4	14	11	5	3	9	21.43	64.29
5	32	26	15	6	17	18.75	53.13
6	12	8	3	4	9	33.33	75.00
7	24	18	10	6	14	25.00	58.33
8	26	16	7	10	19	38.46	73.08
9	16	10	6	6	10	37.50	62.50
10	15	9	6	6	9	40.00	60.00
					average	29.28	63.10

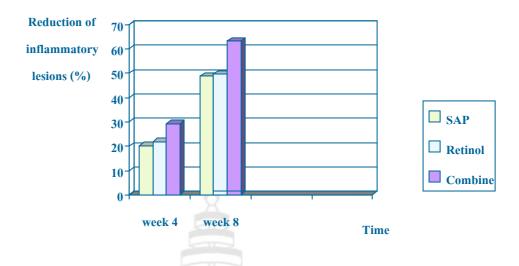


Figure 4.1 Comparing average percentage reduction of inflammatory lesion after 4 weeks and 8 weeks of treatment by SAP, retinol and combination of SAP and retinol

During week 4 of the treatment, SAP group has average inflammatory lesion reduction of 20.14 %. Retinol group has average inflammatory lesion reduction at 21.79 %. Combine group has average inflammatory lesion reduction at 29.28 %

During week 8 of the treatment, SAP group has average inflammatory lesion reduction of 48.82 %. Retinol group has average inflammatory lesion reduction of 49.50 %. Combine group has average inflammatory lesion reduction of 63.10%

The mean percentage reduction of inflammatory lesion counts in SAP treatment group compared with retinol treatment group at week 4 and week 8 were not statistically significant at P value = 0.05 while the mean percentage reduction of inflammatory lesion of combination of SAP and retinol treatment group (29.28%) were statistically significant compared with both of SAP treatment group and retinol treatment group.

During week 8 of the treatment, SAP group has average inflammatory lesion reduction of 48.82 %, retinol group has average inflammatory lesion reduction of 49.50 %., and the combination group has average inflammatory lesion reduction of 63.10%

The mean percentage reduction of inflammatory lesion counts in SAP treatment group compared with retinol treatment group at week 4 and week 8 were not statistically significant at P value = 0.05 while the mean percentage reduction of inflammatory lesion of combination of SAP and retinol treatment group (29.28%) were statistically significant compared with both of SAP treatment group and retinol treatment group.

The comparison of the efficacy of each group at week 4 and week 8 by the student paired t- test, we could see that the efficacy of SAP, retinol and combination formula at week 4 and week 8 were significantly different at P. value = 0.05.

4.3 Other effects

4.3.1 SAP group

None in this group reported unacceptable adverse reactions.

3 patients commented that their skin looked less greasy.

1 patient reported drier skin

4.3.2 Retinol group

2 from 10 patients in this group reported slightly desquamation of the facial skin

7 patients commented that their face looked less greasy.

3 patients reported drier skin

4.3.4 The combination groups

2 patients report an acceptable facial skin desquamation.

Two patients report skin irritation and quit from the experiment within 3 days of use. They had misused the cream (applying cream 3 times per day) and exposed to the sun after use retinol cream without applying sunscreen)

8 of them commented that their face looked less greasy.

4.4 Discussion

From the clinical efficacy evaluation, we could see that SAP and retinol improved acne. Both of them reduce the number of inflammatory lesion. The severity of acne has been measured by lesion counting.

All patients have been randomly selected to enroll in this study. There is no any restriction such as an occupation, cosmetic, dietary, and routine activity. The sample size is small because of the time limitation therefore, the result of treatment were varied within the group.

In each group, the improvement in each individual was varied. The 95% confidence interval for mean in each group were in wide range because the patients in this group varied in occupation and age; a combination of students, officers and outdoor workers. Moreover, some factors were difficult to control such as the routine activities, cosmetic, or environments.

In the SAP treatment group, most patients satisfied the result of treatment from the interview. There were no unacceptable effects that occurred with any patients. Patients with normal skin experienced better effects than those with oily skin.

From the mechanism of action, SAP acts by scavenge singlet oxygen to inhibit inflammatory process therefore SAP improved inflammatory acne which is resulted from lipid peroxidation.

From the result of retinol treatment group, the improvement of acne was significant after 4 and 8 weeks of treatment, although some patients reported adverse reaction from retinol cream such as mild irritation, mild desquamation, and dry skin.

Although retinol has never been claimed as an anti acne active ingredient before and most forms of retinol are not stable, previous studies of retinol metabolites and derivatives have shown that retinol change to tretinoin which has an anti acne property. Furthermore retinol 10S® has been proved of its stability, therefore this study can assume that retinol 10S® can improve acne.

Retinol metabolism in the cell showed that it could change to retinoic acid which has an influence on the sebaceous gland function but the direct action of retinol to sebaceous gland has not been reported yet. The result from this study has not proved retinol function on sebaceous gland and requires further study although some patients in this group reported that their faces look less greasy.

In combine treatment group, there was significantly higher improvement compared with both of SAP and retinol treatment groups after 4 and 8 weeks. Some of the patients in this group were concerned of the irritation effects e.g. One patient experienced a burning reaction from excessive retinol cream application, 3 times per day, and sun exposure when she was suggested to apply it once daily at bed time.

Patient in this group used both of SAP and retinol to treat acne. From the result we could see that the inflammatory lesion dramatically decreased compared with other groups. That should be synergistic effect of retinol and SAP. The desquamation of stratum corneum from retinol may increase SAP permeability to the skin therefore it may have a better treatment effect. Retinol also has keratolytic activity and removed keratin plug, which cause comedogenesis, from pilo-sebaceous units and enhance SAP penetration. Moreover, retinol also has anti oxidative property therefore, it should have anti inflammatory effect.

Regarding the time factor, all treatments in this study are time dependent. Comparing within each group at 4 and 8 weeks of the treatment showed that there is significantly different between week4 and week 8 within each group. At the week 8 of treatment, reduction of inflammatory acne lesion is significantly more than at the week 4 of treatment in all groups.

CHAPTER V

CONCLUSION

5.1 Conclusion from the study

- 5.1.1 The combination treatment of SAP and retinol decrease inflammatory acne lesions significantly better than treating with SAP or retinol alone. The evaluating method is counting lesion method and statistic analysis by ANOVA at p value = 0.05.
- 5.1.2 At the 4th week of study, the reduction of inflamed acne of SAP group and retinol group is not different while there is significantly better effect from the combine group at p. value < 0.05.
- 5.1.3 At the 8th week of study, both SAP and retinol significantly improve inflammatory acne lesions but the result of SAP and retinol is not significantly different.
- 5.1.4 SAP and retinol alone also improved acne but does not provide a significantly different effect from each other. From the interview with patients, SAP had less of an irritation effect than retinol. Meanwhile patients in retinol treatment group reported that there facial skin was less oily.
- 5.1.6 SAP and retinol are effective for acne treatment. When combined using SAP and retinol, the efficacy was increase there for the synergistic effect had been shown.
- 5.1.7 There are no adverse reactions from using SAP lotion in acne patients while there are some non-serious adverse reaction from retinol cream such as slightly desquamation, redness and mild irritation. Excessive applying retinol cream causes serious skin irritation and also the sun exposure afterwards applies.

5.2 The limitations of this study

- 5.2.1 Most patients could not attend the appointment time therefore an evaluated time must be changed from every two weeks to every four weeks.
- 5.2.2 According to all subjects are clients of cosmetic clinic thereby the control cream base and lotion base are not available for use.
- 5.2.3 This IS has a limited studying time. If the longer time was available, the number of participants would increase.
- 5.2.4 Uncontrollable factors such as cosmetic make up, environmental factors or genetic factors can cause the vary result in each individual.

5.3 The recommendations for any further studies

- 5.3.1 The sample size is small to automatically assume that the distribution is normal. It should be at least 25 subjects for each study group.
- 5.3.2 According to the time limitation in this study, further study such as an effect on acne scar or sebum control is recommended.
 - 5.3.3 Volunteers for the control group should have been recruited from other sources.
- 5.3.4 Same age group and occupation should have been selected for controlling hormonal and environmental factors.
- 5.3.5 Varying the concentration of SAP and Retinol should have been tried due to the better cost effectiveness.

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The photos of the volunteers of combined formulation group at week 0, week 4, and week 8 respectively.





The photos of the volunteers of SAP group at week 0, week 4, and week 8 respectively.





The photos of the volunteers of retinol group at week $\boldsymbol{\theta}$, week $\boldsymbol{4}$, and week $\boldsymbol{8}$ respectively.







STATISTICAL ANALYSIS BY SPSS

Table B.1 Statistic analysis by one way ANOVA Comparison of the efficacy of each formula at week4 and week 8

Descriptives

				Std.	Std.	95% Cor	nfidence		
Time	Formulas	N	Mean	Deviation	Error	Interval f	or Mean	Minimum	Maximum
WK4 reduction	SAP	10	20.14	3.85	1.21	17.38	22.89	15.15	26.67
	Retinol	10	21.79	6.76	2.14	16.95	26.62	12.50	31.43
	Combine	10	29.28	7.59	2.40	23.85	34.71	18.75	40.00
	Total	30	23.74	7.28	1.33	21.02	26.45	12.50	40.00
WK8 reduction	SAP	10	48.82	5.18	1.64	45.12	52.53	42.31	58.82
	Retinol	10	49.50	6.91	2.18	44.56	54.44	38.89	60.87
	Combine	10	63.10	6.62	2.09	58.36	67.83	53.13	75.00
	Total	30	53.80	9.03	1.65	50.43	57.17	38.89	75.00

ANOVA

				Sum of		Mean		
				Squares	df	Square	F	Sig.
WK4reduction	Between Groups	(Combined)		475.06	2	237.53	6.03	.007
		Linear Term	Contrast	418.06	1	418.06	10.62	.003
			Deviation	56.99	1	56.99	1.44	.239
	Within Gro	oups		1062.89	27	39.36		
	Total			1537.95	29			
WK8reduction	Between Groups	(Combined)		1297.21	2	648.60	16.44	.000
		Linear Term	Contrast	1018.87	1	1018.87	25.82	.000
			Deviation	278.34	1	278.34	7.05	.013
	Within Gro	oups		1065.05	27	39.44		
	Total			2362.27	29			

Multiple comparisons

			Mean			2-24.5	or 4
			Difference			95% Con:	fidence
Dependent Variable	(I) formula	(J) formula	(I-J)	Std. Error	Sig.	Interv	val
			Lower	Upper		Upper	Lower
			Bound	Bound		Bound	Bound
WK4reduction	SAP	Retinol	-1.65	2.81	.562	-7.41	4.11
		Combined	-9.14	2.81	.003	-14.90	-3.39
	Retinol	SAP	1.65	2.81	.562	-4.11	7.41
		Combined	-7.50	2.81	.013	-13.25	-1.74
	Combined	SAP	9.14	2.81	.003	3.39	14.90
		Retinol	7.50	2.81	.013	1.74	13.25
WK8reduction	SAP	Retinol	68	2.81	.812	-6.44	5.09
		Combined	-14.26	2.81	.000	-20.04	-8.51
	Retinol	SAP	.68	2.81	.812	-5.09	6.44
		Combined	-13.60	2.81	.000	-19.36	-7.84
	Combined	SAP	14.26	2.81	.000	8.51	20.04
		Retinol	13.60	2.809	.000	7.84	19.36

st The mean difference is significant at the 0.05 level.

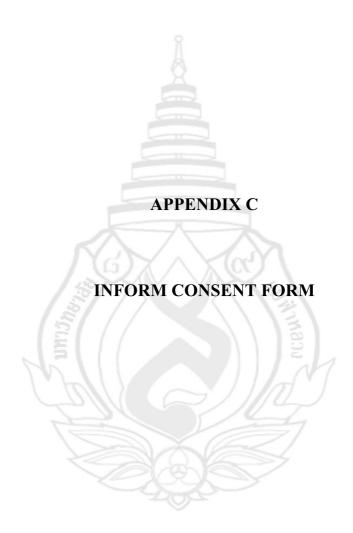
Table B.2 Comparing the efficacy of week 4 and week 8 of each group with pair t-test

Pair sample statistic

		Mean	N	S.D.	SEM
Pair 1	Reduction of SAP wk4	21.04	10	3.81	1.20
	Reduction of SAP wk8	52.44	10	7.11	2.25
Pair 2	Reduction of Retinol wk4	24.54	10	9.37	2.96
	Reduction of Retinol wk8	52.50	10	10.69	3.38
Pair 3	Reduction of combine wk4	25.62	10	7.48	2.36
	Reduction of combine wk8	56.44	10	9.30	2.94

Paired Samples Test

			Paired Differences				
		Mean	S.D.	SEM	95%	% CI	(2-tailed)
Pair 1SAP	Reduction WK4- WK8	-31.40	4.91	1.55	-34.91	-27.88	.000
Pair 2 Retinol	Reduction WK4- WK8	-28.00	6.22	1.97	-32.41	-23.50	.000
Pair 3 Combine	Reduction WK4- WK8	-30.82	7.86	2.49	-36.44	-25.19	.000



ใบยินยอมของประชากรตัวอย่างหรือผู้มีส่วนร่วมในการวิจัย

(Informed Consent Form)

ชื่อโครงการ		
เลขที่ ประชากรตัวอย่างหรือผู้มีส่วน	เร่วมในการวิจัย	
ข้าพเจ้าได้รับทราบจากผู้วิจัย ชื่อ		
ที่อยู่	Ω	
ซึ่งได้ลงนามด้านท้ายของหนังสือนี้	้ ถึงวัตถุประสงค์ ลักษณะ และแนวทางการศึกษาวิจัย รวม	ทั้ง
ทราบถึงผลดี ผลข้างเคียง และคว	ามเสี่ยงที่อาจเกิดขึ้น ข้าพเจ้าได้ซักถาม ทำความเข้าใจเกี่ยวก็	กับ
การศึกษาดังกล่าวนี้ เป็นที่เรียบร้อยเ	เล้ว	
ข้าพเจ้ายินคีเข้าร่วมกา	รศึกษาวิจัยครั้งนี้โดยสมัครใจ และอาจถอนตัวจากการเข้าร่	วม
สึกษานี้เมื่อใดก็ได้ โดยไม่จำเป็นต่	ก้องแจ้งเหตุผล และยอมรับผลข้างเคียง และความเสี่ยงที่อ	าจ
เกิดขึ้น และจะปฏิบัติตัวตามคำแนะ		
ข้าพเจ้าได้รับทราบจา	์ กผู้ทำการวิจัยว่า หากข้าพเจ้าได้รับความผิดปรกติเนื่องจ	าก
	้ ทันทีถึงความผิดปรกติที่เกิดขึ้นได้ จะถือว่าข้าพเจ้าทำให้ก	
้ คุ้มครองความปลอดภัยเป็นโมฆะ (ค		
	า วงข้าพเจ้าแก่คณะผู้วิจัย เพื่อเป็นประโยชน์ในการศึกษาวิจัยค	ร้ำ
นี้		
สุดท้ายนี้ ข้าพเจ้ายินดีเง่	กร่วมการศึกษานี้ ภายใต้เงื่อนไขที่ได้ระบุไว้แล้วในข้างต้น	
สถานที่ / วันที่	ลงนามประชากรตัวอย่างหรือผู้มีส่วนร่วมในการวิ	จัย
	()
สถานที่ / วันที่	ลงนามผู้วิจัยหลัก	
J !	()
สถานที่/วันที่	ลงนามพยาน	



สำนักวิชาวิทยาศาส พร้เครื่องสำอาง เลขที่หนังสือรับ 19 ชา วัน 14 พง. ๑๐ เวลา 1530 น.

บันทึกข้อความ

หน่วยงาน ส่วนบริการงานวิจัย ที่ ศธ 5914(2)/ 0333 โทรศัพท์ 6387, 6389 วันที่ ¹ / พฤศจิกายน 2550

เรื่อง รับรองการเปลี่ยนชื่อเรื่องการศึกษาโดยอิสระ

เรียน คณบดีสำนักวิชาวิทยาศาสตร์เครื่องสำอาง

ตามที่ สำนักวิชาวิทยาศาสตร์เครื่องสำอาง ได้ส่งโครงการการศึกษาโดยอิสระของ นักศึกษาระดับบัณฑิตศึกษา หลักสูตรวิทยาศาสตรมหาบัณฑิต สาขาวิชาวิทยาศาสตร์เครื่องสำอาง เพื่อขอ การรับรองจากคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง จำนวน 17 โครงการ ซึ่ง ผ่านการรับรองจริยธรรมการวิจัยในมนุษย์แล้ว ในคราวประชุมคณะกรรมการฯ ครั้งที่ 3/2550 เมื่อวันที่ 11 ตุลาคม 2550 นั้น

ต่อมา สำนักวิชาวิทยาศาสตร์เครื่องสำอาง ได้มีบันทึกข้อความที่ ศธ 5920/0786 ลงวันที่ 6 พฤศจิกายน 2550 แจ้งขอเปลี่ยนชื่อเรื่องการศึกษาโดยอิสระ จำนวน 10 โครงการ จาก 17 โครงการข้างต้น

ทั้งนี้ คณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวง ในคราวประชุม ครั้งที่ 4/2550 เมื่อวันที่ 7 พฤศจิกายน 2550 ได้พิจารณาเห็นเป็นว่าการเปลี่ยนชื่อเรื่อง โดยมิได้มีการ เปลี่ยนแปลงรายละเอียดเนื้อหาสาระของเรื่องที่ดำเนินการศึกษา ซึ่งผ่านความเห็นชอบของคณะกรรมการ จริยธรรมการวิจัยในมนุษย์ ในคราวประชุมคณะกรรมการฯ ครั้งที่ 3/2550 เมื่อวันที่ 11 ตุลาคม 2550 ไปแล้ว จึงมีมติรับรองการเปลี่ยนชื่อเรื่องการศึกษาโดยอิสระทั้ง 10 หัวข้อ ประกอบด้วย

ที่	ชื่อการศึกษาโดยอิสระเดิม	ชื่อการศึกษาโดยอิสระที่เปลี่ยนแปลง	กรรมการสอบ/บัณฑิตศึกษา
1	การพัฒนาสารสกัดมาตรฐานจากเยื่อหุ้ม	การพัฒนาและประเมินผลทางคลินิกของ	รศ.คร.พรรณวิภา กฤษฎาพงษ์/
	เมล็ดฟักข้าว (The Development of	สารสกัดมาตรฐานผลฟักข้าว (The	นส.วิภัทรา ศุภะจินคา
	Standardized Extract of Momordica	Development of Clinical Evaluation of	
	cochinensis (Lour.) Spreng Seed	Standardized Gac Fruit Extract)	
	Membrane)		

ที่	ชื่อการศึกษาโดยอิสระเดิม	ชื่อการศึกษาโดยอิสระที่เปลี่ยนแปลง	กรรมการสอบ/บัณฑิตศึกษา
2	การพัฒนาเจลโพลีแซคคาไรค์จากสาร	การพัฒนาและประเมินผลทางคลินิกของเจล	รศ.คร.พรรณวิภา กฤษฎาพงษ์/
	สกัคเปลือกทุเรียน (The Development of	โพลีแซคคาไรค์จากสารสกัดเปลือกทุเรียน	นส.บุณธรี ฟูตระกูล
	Polysaccharide Gel from Durian's Fruit-	(The Development and Clinical Evaluation of	
	Hull Extract)	Polysaccharide Gel from Durian's Fruit-Hulls	
		Extract)	
3	การพัฒนาคาร์บอกซีเมทิลกลูแคนใน	การพัฒนาและประเมินผลทางคลินิกของ	รศ.ดร.พรรณวิภา กฤษฎาพงษ์ /
	เครื่องสำอาง (The Development of	คาร์บอนซีเมทิลกลูแคน (The Development	นายวรัฒน์ วัชรปรีชาสกุล
	Carboxymethyl Glucan in Cosmetics)	and Clinical Evaluation of Carboxymethyl	
		Glucan)	
4	ปัจจัยที่มีผลต่อการตัดสินใจเลือกใช้	ปัจจัยที่มีผลต่อการตัดสินใจเลือกใช้ผลิตภัณฑ์	ผศ.คร.สุรพล นธการกิจกุล/
	ผลิตภัณฑ์ให้ความชุ่มชื้นผิวหนังสตรี	ให้ความชุ่มชื้นผิวในสตรี (Factors Affecting	นางชุติมา พบลาภ
	(Decision Factors on Choosing	the Decision on Choosing Skin Moisturizing	
	Moisturizer Products for Women Skin)	Products in Women)	s
5	การศึกษาเปรียบเทียบประสิทธิภาพของ	การศึกษาเปรียบเทียบประสิทธิภาพในการลด	ผศ.คร.สุรพล นธการกิจกุล /
	เลเซอร์ไคโอคที่มีความยาวคลื่น 900 นา	รอยย่นบนใบหน้าของเลเซอร์ไคโอคที่มีความ	นางขวัญฤทัย คำรงค์วัฒนโภคิน
	โนเมตรที่ส่งพลังงานควบคู่กับคลื่นวิทยุ	ยาวคลื่น 900 นาโนเมตรที่ส่งพลังงานควบคู่	
	ความถี่สูงกับเลเซอร์ลองพั้ลซ์เอ็นดีแย็กที่	กับคลื่นวิทยุความถี่สูงกับเลเซอร์ลองพั้ลซ์เอ็น	
	มีความยาวคลื่น 1,064 นาโนเมตร ใน	คีแย็กที่มีความความยาวคลื่น 1,064 นาโน	
	การลคริ้วรอยบนใบหน้า (Study the	เมตร (Comparative Study of skin wrinkle	
	efficiency anti-wrinkle of surface skin	reducing efficacy between diode laser (900	*
	comparison between diode laser (900	nm) with bipolar radio frequency and long	
	nm) with bipolar radio frequency and	pulsed Nd:YAG laser (1064 nm)	
	long pulsed Nd:YAG laser (1064 nm)		
6	การพัฒนาเจลให้ความชุ่มชื้น สำหรับผิว	การพัฒนาเจลให้ความชุ่ม ชื้นผิวจากสารสกัด	ผศ.คร.สุรพล นธการกิจกุล/
	จากสารสกัดเมล็ดมะขาม (The	เมล็คมะขาม (The Development of Skin	นส.บุญล้อม สิบหมื่นเปี่ยม
	Development of Skin Moisturizing Gel	Moisturizing Gel from Tamarind Seed	
	from Tamarind (Tamarindus Indica	Extract)	
	Linn.) Seed Extract)		
7	เวชสำอางสำหรับการรักษาสิว	การศึกษาประสิทธิภาพทางคลินิกของการใช้	ผศ.คร.สุรพล นธการกิจกุล/
	(Cosmeceutical for acne treatment)	โซเคียม แอล แอสคอร์บิล ทูฟอสเฟต	พญ.ชนม์ชนก ร่วมรักษ์ /
		เรตินอลและส่วนผสมในการรักษาสิว (The	
		clinical efficacy of sodium L-ascorbyl-2-	
		phosphate, retinol, and their combination	
		application in acne treatment)	

ที่	ชื่อการศึกษาโดยอิสระเดิม	ชื่อการศึกษาโดยอิสระที่เปลี่ยนแปลง	กรรมการสอบ/บัณฑิตศึกษา
8	การพัฒนาผลิตภัณฑ์สปา บาธ บอมบ์	การพัฒนาผลิตภัณฑ์สปาบาธบอมบ์	รศ.พิมพร ถีลาพรพิสิฐ/
	(Development of Spa Bath Bomb)	(Development of Spa Bath Bomb)	นายรวิสุต ใกรรวี
9	ศักยภาพของน้ำมันหอมระเหยจากพืช	ศักยภาพของน้ำมันหอมระเหยจากพืชหอม	ผศ.คร.สุนีย์ จันทร์สกาว
	หอมไทยเพื่อใช้ในผลิตภัณฑ์สุคนธบำบัค	ไทยเพื่อใช้ในผลิตภัณฑ์สุคนธบำบัด	/นางวิลาวัลย์ มณฑามณี
	(Potency of Essential Oils from Thai	(Potential of Essential Oils from Thai	G.57
	Aromatic Herbs Used in Aromatherapy	Aromatic Herbs Used in Aromatherapy	
	Products)	Products)	
10	การพัฒนาผลิตภัณฑ์ขัดผิวจากพืชไทย	การพัฒนาผลิตภัณฑ์ขัคผิวจากลูกเดือย	ผศ.คร.สุนีย์ จันทร์สกาว
	(Development of Scrub Product from	(Development of Scrub Product from Job's	/นส.ประดับฟ้า โหมคสุวรรณ
	Thai Plants)	Tear)	

จึงเรียนมาเพื่อโปรดทราบ

(รองศาสตราจารย์ คร.เทอค เทศประทีป)

ประธานคณะกรรมการจริยธรรมการวิจัยในมนุษย์



มหาวิทยาลัยแม่ฟ้าหลวง

คณะกรรมการจริยธรรมการวิจัยในมนุษย์

ขอรับรองว่า

โครงการ

: การศึกษาโด๊ยอิสระ (Independent Study) เรื่อง เวชสำอางสำหรับการรักษาสิว

(Cosmeceutical for acne treatment)

: REH-50021

ชื่อประธานคณะกรรมการสอบ : ผู้ช่วยศาสตราจารย์ คร.สุรพล นธการกิจกุล

ชื่อหัวหน้าโครงการ

: น้างสาวชนม์ชนก ร่วมรักษ์

สังกัด

สำนักวิชาวิทยาศาสตร์เครื่องสำอาง

เป็นโครงการที่ไม่ขัดต่อหลักจริยธรรมสากลตามคำประกาศเฮลซึงกิ และแนวทางจริยธรรม การวิจัยในคนแห่งชาติ พ.ศ. 2545

จึงเห็นสมควรให้ดำเนินการในขอบข่ายของโครงการที่เสนอต่อคณะกรรมการจริยธรรมการ วิจัยในมนุษย์ มหาวิทยาลัยแม่ฟ้าหลวงได้ ณ วันที่ 11 เดือน ตุลาคม พ.ศ. 2550

(รองศาสตราจารย์ คร.เทอค เทศประทีป) ประธานคณะกรรมการจริยธรรมการวิจัยในมนุษย์

มหาวิทยาลัยแม่ฟ้าหลวง

CURRICULUM VITAE

Name Ms. Chonchanok Ruamrak

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Education Background Doctor of Medicine Degree, Mahidol University, 2002

Diploma in Practical Dermatology, Cardiff University,

2007

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2005-Present Kanchanok Clinic