การเปรียบเทียบประสิทธิผลของโลชันทำให้ผิวขาวในอาสาสมัคร

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EFFICACY EVALUATION OF SKIN WHITENING LOTIONS IN VOLUNTEERS

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(EFFICACY EVALUATION OF SKIN WHITENING LOTIONS IN VOLUNTEERS)

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เปรียบเทียบประสิทธิผลและความระคายเคืองต่อผิวของผลิตภัณฑ์ทำให้ผิวขาวที่มีจำหน่ายในประเทศไทย จำนวน 6 ผลิตภัณฑ์ ซึ่งเป็นผลิตภัณฑ์สำหรับใช้กับใบหน้าและลำตัวอย่างละ 3 ผลิตภัณฑ์ การวิจัยในส่วนแรกเป็น การศึกษาประสิทธิผลของผลิตภัณฑ์สำหรับใบหน้า (ผลิตภัณฑ์ A B และ C) เปรียบเทียบกับการไม่ได้ทาในอาสา สมัครเพศหญิงสุขภาพดี 12 คน โดยอาสาสมัครแต่ละคนจะทาผลิตภัณฑ์ทั้ง 3 บริษัทบนบริเวณต่างๆของหน้าแขน ท่อนปลาย (forearm) ทั้งแขนซ้ายและขวา ตามลำดับการทาแบบละตินแสควร์ ซึ่งจะทาวันละสองครั้ง ติดต่อกันทุกวัน เป็นเวลา 12 สัปดาห์ จากนั้นทำการวัดปริมาณเมลานิน (melanin value) และ ปริมาณการเกิดผิวหนังแดง (erythema value) โดยใช้เครื่องมือ MEXAMETER MX 16[®] ทุกๆสัปดาห์ ผลิตภัณฑ์ A มีสารสำคัญ คือ สารสกัด จากชะเอมเทศ 5% ผลิตภัณฑ์ B มีสารสำคัญ คือ สารสกัดจากรากหม่อน 0.001% และสารสกัดจากสคูทีลาเรียไบคา เลนซิส (Scutellaria baicalensis) 0.01% และกรดคาพริโลอิลซาลิซัยลิก (capryloyl salicylic acid) 0.3% ขณะที่ ผลิตภัณฑ์ C มีสารสำคัญ คือ วิตามินบีสาม (vitamin B$_3$) 1% นอกจากนี้ทั้งสามผลิตภัณฑ์ต่างก็มีสารกรองรังสี อัลตราไวโอเลตผสมอยู่ด้วยจำนวนหนึ่งเพื่อช่วยป้องกันแสงแดด ผลการทดลองพบว่าผลิตภัณฑ์ทั้งสาม ต่างก็มีประ สิทธิผลในการลดปริมาณเมลานินได้เท่าๆกันเมื่อเทียบกับบริเวณที่ไม่ได้ทา (P < 0.05) โดยพบนัยสำคัญได้ตั้งแต่ สัปดาห์ที่สองของการทาเป็นต้นไป และยังพบว่าทั้งสามผลิตภัณฑ์ต่างก็มีคุณสมบัติในการช่วยลดปริมาณการเกิดผิว หนังแดงได้บ้าง ซึ่งอาจเป็นผลเนื่องมาจากคุณสมบัติป้องกันแสงแดดของสารกรองรังสีในตำรับ

จากนั้นจึงทำการศึกษาผลิตภัณฑ์ทำให้ผิวขาวสำหรับลำตัว 3 ผลิตภัณฑ์ โดยใช้ขั้นตอนการทดลองเหมือน เดิม แต่ใช้อาสาสมัครคนละชุด ผลิตภัณฑ์ E มีสารสำคัญคือ กรดแล็กติค (lactic acid) 8% ผลิตภัณฑ์ F มีสาร สำคัญ คือ สารสกัดจากชะเอมเทศ 0.5% ส่วนผลิตภัณฑ์ G มีสารสำคัญคือ วิตามินบีสาม (vitamin B$_3$) 1% และสาร สกัดจากผลไม้ 0.1% นอกจากนี้ ผลิตภัณฑ์ทั้งสามต่างก็มีสารกรองรังสีอัลตราไวโอเลตชนิดเดียวกันผสมอยู่ด้วย ผล การทดลองพบว่า ผลิตภัณฑ์ E F และ G สามารถลดปริมาณเมลานินได้อย่างมีนัยสำคัญ เมื่อเทียบกับบริเวณ ที่ไม่ได้ทา (P < 0.05) แต่ระยะเวลาที่ใช้ทาก่อนเกิดประสิทธิผลจะนานขึ้น (ประมาณ 3-5 สัปดาห์) นอกจากนี้ ผลิต ภัณฑ์สำหรับลำตัวทั้งสามชนิด ไม่พบว่ามีคุณสมบัติช่วยลดการเกิดผิวหนังแดงแต่อย่างใด โดยค่าปริมาณการเกิดผิว หนังแดงของตำแหน่งที่ทาผลิตภัณฑ์ E F และ G ไม่แตกต่างจากตำแหน่งที่ไม่ได้ทา (P > 0.05) ในทุกสัปดาห์ ทั้งนี้ อาจมีสาเหตุจากการควบคุมการทดลองที่เข้มงวดขึ้นเพื่อหลีกเลี่ยงไม่ให้อาสาสมัครสัมผัสกับแสงแดดที่อาจระคาย เคืองผิวระหว่างการทดลอง โดยสรุปแล้ว ผลิตภัณฑ์ที่ศึกษาทั้ง 6 ชนิด ต่างก็มีประสิทธิผลในการลดปริมาณเมลานิน ในผิวหนังอาสาสมัคร อย่างไรก็ตามผู้บริโภคควรได้รับทราบว่าประสิทธิผลดังกล่าวได้จากการวัดด้วยเครื่องมือพิเศษที่ มีความไวสูง ซึ่งถ้าใช้สายตาคนปกติ จะตรวจวัดประสิทธิผลได้ยาก และมีความไม่แน่นอน ขึ้นกับจิตใจหรือความรู้สึก ของผู้ประเมินอีกด้วย

ภาควิชา	เภสัชกรรม	ลายมือชื่อนิสิต	
สาขาวิชา	เภสัชกรรม	ลายมือชื่ออาจารย์ที่ปรึกษา	
ปีการศึกษา	2544	ลายมือชื่ออาจารย์ที่ปรึกษาร่วม	

The *in vivo* efficacy and skin irritation potential of six commercially available brands of skin whitening products, three for face and three for body application, was evaluated in healthy female Thai volunteers. The first study was to compared the skin whitening efficacy of the three face products A, B and C with the control (non-treatment). Each of the 12 volunteers received the three face products on the separate areas of her left and right forearms twice daily for 12 weeks according to the repeated Latin square sequence. The melanin and erythema values of the treated and untreated areas were then weekly monitored in each subject using Mexameter MX 16$^{®}$. Product A contained 5% licorice extract, product B contained 0.001% mulberry root extract, 0.01% *Scutellaria baicalensis* extract and 0.3% capryloyl salicylic acid whereas product C contained 1% vitamin B_3. The three products also contained some types of UV filters as sun screening agents. Products A, B and C were found to be equally effective in reducing the melanin content with a significant effect over the control ($P < 0.05$) observed at two weeks and afterwards. The three products also appeared to have some erythema-reducing property, which could be due to the UV-protective effect of the sun screening agents.

The three body-whitening products E, F and G were then evaluated using the same protocol but different set of volunteers. Product E contained 8% lactic acid whereas product F contained 0.5% licorice extract and product G contained 1% vitamin B_3 and 0.1% fruit extract. The same UV filters were also present in these products. The three body products were also found to be effective in reducing the melanin content over the control ($P < 0.05$) but the onset of significant whitening was somewhat longer (3 – 5 weeks). In addition, E, F and G did not show any significant erythema-reducing effect, yielding the erythema values similar to the control at all weeks ($P > 0.05$). This could be due to a more rigid control of subjects to avoid exposure to irritating sunlight during the study. In summary, all six brands of commercial whitening products evaluated here were effective in reducing the melanin content of the volunteers' skin. However, caution should be provided to consumers that the whitening effect was measured using a highly sensitive and specialized instrument. The effect was extremely difficult to detect by visual observation, which was also highly subjective.

Department.......………Pharmacy……................... Student's signature...…….

Field of study................Pharmacy...........……. Advisor's signature ....……………

Academic Year............2001...............…….. Co –advisor's signature......................………………

ACKNOWLEDGEMENTS

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สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

LIST OF ABBREVIATIONS

ANOVA	=	Analysis of variance
SPF	=	Sun Protection Factor
nm	=	Nanometer
UV	=	Ultraviolet
cm	=	Centimeter
cm^2	=	Squared centimeter
mL	=	Milliliter
S.E.M.	=	Standard Error of the Mean
IC_{50}	=	Concentration of 50% inhibiton
SC_{50}	=	Concentration of 50% scavening activity
UVA	=	Ultraviolet A
UVB	=	Ultraviolet B
UVC	=	Ultraviolet C
mM	=	Millimolar
et al.	=	and others
pH	=	The negative logarithm of the hydrogen ion concentration
w/w	=	weight by weight
am	=	Ante meridiem
pm	=	Post meridiem
g	=	gram
ε	=	Molar extinction coefficient (concentration in g-moles / l)
λ	=	Wavelength
L	=	Path length
T	=	Transmittance of a sample

LIST OF ABBREVIATIONS (Cont.)

I	=	Light intensity after passes through a sample
I_0	=	Initial light intensity.
μm	=	Micrometer
μl	=	Microliters
SS	=	Sum of squares
MS	=	Mean square
Fcal	=	F calculation
Ftab	=	F table
Prob	=	Probability distribution
df	=	Degrees of freedom
CV	=	Coefficient of variation
S.D.	=	Standard deviation
BHA	=	Beta hydroxy acid
AHA	=	Alpha hydroxy acid

CHAPTER I

INTRODUCTION

To have a white, smooth skin appears to be the most desirable feature among women, especially those from Asian countries like China, Japan, Korea and Southeast Asia. This is probably attributed to the traditional beliefs that white skin can convey the appearance of nobility, aristocracy and youthfulness. Since ancient times, poets had long described the beauty of ladies in relation to the fairness of their skin. Many surveys have also revealed that Asian men tend to prefer women with whiter skin to those with darker complexion.

Thailand is one of the Southeast Asian countries, most of which are situated around the equator, the truly tropical zone of the earth. This geographic location allows Thailand to enjoy an average sunshine of about 8 hours per day, much longer than those in Europe or North America. However, with the long sunlight Thai people are also exposed to the high intensity of the ultraviolet (UV) radiation. UVC, the most dangerous of the UV light, is fortunately filtered by the earth atmosphere and thus does not reach the earth surface. Only two major types of ultraviolet penetrate and reach our environment, i.e., UVA and UVB. UVA has a wavelength in the range of 320 – 400 nanometer (nm) whereas UVB ranges from 290 – 320 nm. Due to its lower energy, UVA generally induces less skin damages than UVB and is responsible for the skin aging and darkening of the skin (e.g. tanning). However, the more powerful UVB poses a greater threat of seriously damaging the skin, which may lead to melasma, freckles, sunburn and even skin cancer.

Several cosmetic and dermatological products are available in Thailand with numerous claims, ranging from simple sunscreens to the most sophisticated skin-whitening formulas. The early products for the treatment of freckles, melasma and other skin-darkening disorders contained hydroquinone, which used to be one of the most widely prescribed agents. However, due to its reported potential of mutagenicity and

onchronosis in African users, it has been prohibited for use in cosmetic products in many countries including Thailand. As a result, new research into finding novel active whitening /depigmenting agents has been extensively carried out. Many such agents have been introduced into the cosmetic market, which include several plant extracts like licorice, mulberry root, *Scutelleria baicalensis* extracts, and kojic acid, etc. The major mechanism of these natural agents is to inhibit tyrosinase, a principal enzyme involved in the formation of melanin pigments in the skin. Other effective skin whitening agents with different mechanisms include alpha hydroxy acid (lactic acid, glycolic acid) and beta hydroxy acid (e.g. capryloyl salicylic acid). These acids act mainly via stimulation of epidermal turnover or being a keratolytic agent. Other agents that have been used include vitamin C (antioxidant) and vitaminB$_3$ (Inhibition of melanosomes transfer from melanocyte to keratinocyte). Most of these agents have been formulated together with the conventional UVA and UVB absorbers to provide both the direct whitening action and indirect protective effect against irritating UV light.

It is interesting to note that competition in the cosmetic market among different skin whitening brands has always been on a rise. Cosmetic products manufacturers, with the help of computer graphics and ingenious advertising strategies, often launch attractive advertisements, which tend to dramatize their products' efficacy, particularly those appearing on the television. Some of these companies even claimed in their television commercials that their products can "visibly" whiten the skin within a relatively short period (e.g. 4 weeks). Chances are that, after seeing these advertisements, consumers who are too keen about being more beautiful may be tempted to rush out from their homes and buy these rather expensive products only to find out later that the efficacy may not be as dramatic as they have seen on television.

Thus, the primary purposes of this project were to evaluate the *in vivo* efficacy of various brands of skin whitening products available in the Thai market. Several brands were selected based on the variability of the active components in their formulas as well as their availability in the market. Apart from the efficacy evaluation, the skin irritation potential of these products was also evaluated in terms of erythema.

The specific objectives of this work were as follows:

1. To evaluate efficacy and safety of three whitening products intended for face application and compare the results with the untreated control using a Latin square design study with 12 healthy female volunteers.

2. To evaluate efficacy and safety of three whitening products intended for body application and compare the results with the untreated control using a Latin square design study with another set of 12 healthy female volunteers.

3. To compare the efficacy between different brands having different whitening agents in order to determine the relative activity of these products.

CHAPTER II

LITERATURES REVIEW

It is well known that ultraviolet (UV) radiation can cause damages to the skin. Even the relatively mild manifestations of UV-induced skin disorders such as hyperpigmentation and freckles are absolutely unacceptable by many women, particularly those from the Asian countries, since they impart "aging" and "rough" skin appearance.

Fitzpatrick and Aeling (1997) suggested that the adverse effects of excessive exposure to sunlight could be both acute and chronic. The acute effects include sunburn, transient immune suppression, drug-induced phototoxic reactions and exacerbation of an underlying photosensitivity disorder (such as lupus erythematosus). The chronic effects may impart skin disorders such as skin wrinkles, abnormal pigmentation, precancers (actinic keratoses), impaired immune surveillance after pre-skin cancer and skin cancer, cataracts, basal cell carcinoma, squamous cell carcinoma,, and melanoma.

Some of the important facts about skin cancer in American's people as compiled by Fitzpatrick and Aeling(1997) are listed below:

1. The sun causes at least 90% of all skin cancers.

2. One in six Americans will develop skin cancer during his or her lifetime.

3. In the United States, over 760,000 new cases of skin cancer are diagnosed annually, afflicting more people than any other cancer.

4. In 2002, more than 33,000 Americans will develop malignant melanoma and more than 6,000 will die.

5. Approximately 30% of melanomas occur in individuals less than 45 years of age.

6. Melanoma is the most common cancer in women aged 25-29 and the second most common (after breast cancer) for women aged 30-34.

7. The incidence of melanoma is increasing at a rate faster than that of any other cancer, having nearly doubled in the last decade.

8. Most people receive 50-80% of their cumulative lifetime of sun exposure before age 18.

The spectra of ultraviolet (UV) radiation and its effects on human skin

UV light is broken down into three major bands according to their physical characteristics and biological effects.

1). UVC (100-290 nm wavelength). UVC is a high-energy radiation that damages cells through direct DNA damage and through the generation of free radical species. Fortunately, UVC radiation is filtered by atmospheric ozone and does not reach the earth's surface.

2). UVB (290-320 nm). It is the mid-range radiation that is not completely filtered by atmospheric ozone. It is often called the "burning" ray because it causes sunburn. UVB injures skin cells primarily through formation of DNA thymine dimers and DNA 6-4 photoproducts, that, if not repaired properly, cause gene mutations and lead to alterations of cell functions and carcinogenesis.

3). UVA (320-400 nm). It is a long-wave radiation, which has the lowest energy spectrum of all the ultraviolet regions. UVA is not filtered by atmospheric ozone, and a 150-fold greater amount of UVA strikes the earth surface than UVB. UVA can damage the skin cells predominantly through the formation of free radicals. While UVB penetrates to the basal layer of the epidermis, UVA can penetrate deeper to the mid-dermis. Skin wrinkling following chronic sun exposure is due to the UVA-damaging effects on dermal fibroblasts, which result in altered collagen and elastin synthesis. UVA is also responsible for the tanning of the skin.

UV spectral characteristics

Frost and Horwitz (1982) suggested that light generally penetrates the skin to an extent proportional to its wavelength, that is, the longer the wavelength of irradiation, the greater will be the intensity in the deeper layers of the skin. The various regions of the UV light and length of skin penetration are depicted in Figures 1 and 2, respectively.
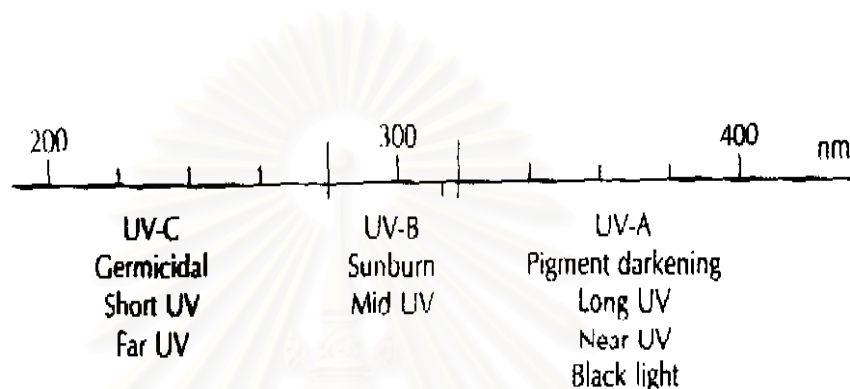
Figure 1. Biologically important regions of the UV spectrum (Frost and Horwitz, 1982)
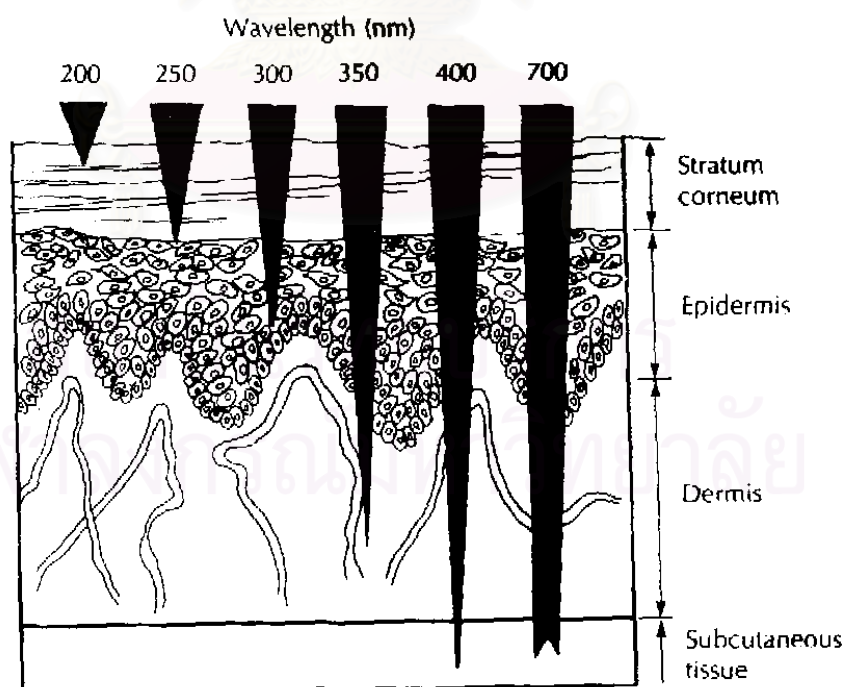
Figure 2. Scheme of human skin penetration by UV light (Frost and Horwitz, 1982)

Table 1. Human skin types (Deleo and Maso, 1985).

Type	Unexposed skin color	Classification	Reaction to sun	Example
I	white	Sensitive	Always burns easily, never tans	Red-haired, freckled
II	white	Sensitive	Always burns easily, tans minimally	Fair-skinned, blue-eyed
III	white	Normal	Burns moderately, tans gradually	Darker whites
IV	light brown	Normal	Burns minimally, tans always.	Mediterranean
V	Brown	Insensitive	Rarely burns, tans profusely	Middle Eastern, Latin American, light-skinned blacks
VI	Dark brown	Insensitive	Never burns, deeply pigmented	Dark-skinned blacks

Table 2. Skin color of various nationality (Deleo and Maso,1985).

Caucasian	Members of the white race as composed of persons of European, North African or Southwest Asian ancestry.
Mongoloid	Members of a major racial group native to Asia including people of Northern and Eastern Asia, Malaysians, Eskimos and often American Indians.
Negroid	Members of the black race as composed of the majority of the people of Africa, Melanesia and New Guinea.

Human skin can be classified into six types according to sensitivity to sunlight as shown in Table 1. The most sensitive skin type is type I, which has the least extent of melanin and the lightest skin complexion. The melanin content in the skin increases from type I to VI with a darker skin complexion and less sensitivity to sunlight. Skin color can also be classified according to race or nationality as shown in Table 2. Table 3 summarizes the various effects of UVA, UVB and composite sunlight (sunshine) on the skin erythema and pigmentation.

Table 3   Effect of UVA, UVB and sunshine on skin erythema and pigmentation
(Deleo and Maso, 1985).

Parameter	Erythema			Pigmentation		
	UVB	UVA	sunshine	UVB	UVA	sunshine
Relative dose Timing (hours)	1 6-24	1000 1-12	NA 6-24	1 72	500-1000 Immediate	NA Immediate and 72 hours
Maximal response	Severe	Mild	Severe	Marked	Moderate	Marked
Histology	Epidermal damage	Dermal alteration	Epidermal damage and dermal alteration	Melanocyte proliferation; increased melanin synthesis and transfer; all layers	Darkening of preformed melanin; basal layer	Both UVB and UVA histology

Tyrosine ————————————→ Dihydroxyphenylalanine (DOPA)
              tyrosinase + UV

                                                              | tyrosinase

5, 6 – Dihydroxyindole ←———— Leucodopachrome ←———— Dopaquinone

5, 6 – Indolequinone ————————————→ melanoprotein
              Polymerization and combine with protein
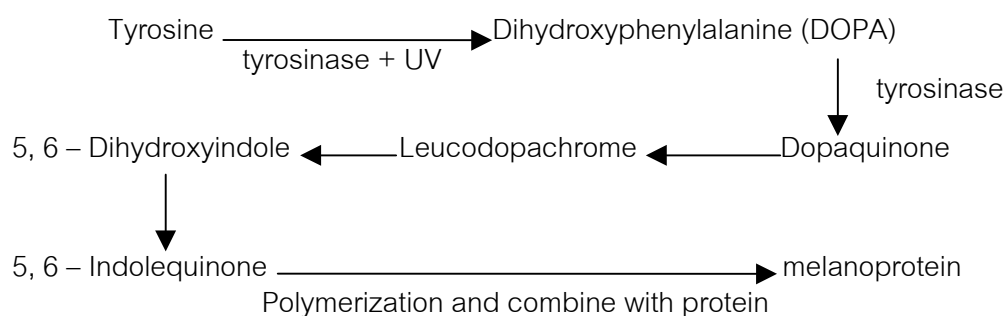
Figure 3. Melanin biosynthesis pathway (Ubonthip Nimmanit,1982)

Melanin Biosynthesis

Melanin is a common pigment of human skin and is the main factor determining the skin color (Lee and Kim, 1995). It is synthesized in specialized epidermal cells called melanocytes, which use enzyme tyrosinase to hydroxylate tyrosine into dihydroxyphenylalanine (DOPA). Tyrosinase further oxidizes DOPA into dopquinone, which is transformed into the melanin polymer through a complex chain of oxidative reactions (Figure 3).

There are two types of melanin, namely pheomelanin and eumelanin. Pheomelanin, a yellow or orange pigment, is synthesized via cysteinyl DOPA, glutathione DOPA and cysteinyl dopaquinone, in the presence of sulfhydryl (-SH) compounds like cysteine and glutathione. Eumelanin, the dark-brown pigment, is produced through the polymerization of dopaquinone via leucodopachrome, dopachrome, 5,6-dihydroxyindole (or 5,6 - dihydroxyindole-2-carboxylic acid DHICA), and melanochrome. Figure 4 is a diagram depicting the various stages of melanin synthesis in a melanocyte.

Melanin biosynthesis is influenced by genetic and environmental factors such as hormones, food and medicine. Skin color relates closely to the number and the distribution pattern of melanosomes, the brown cellular organelles containing the melanin pigment. The number of melanosomes manufactured and their transfer to the
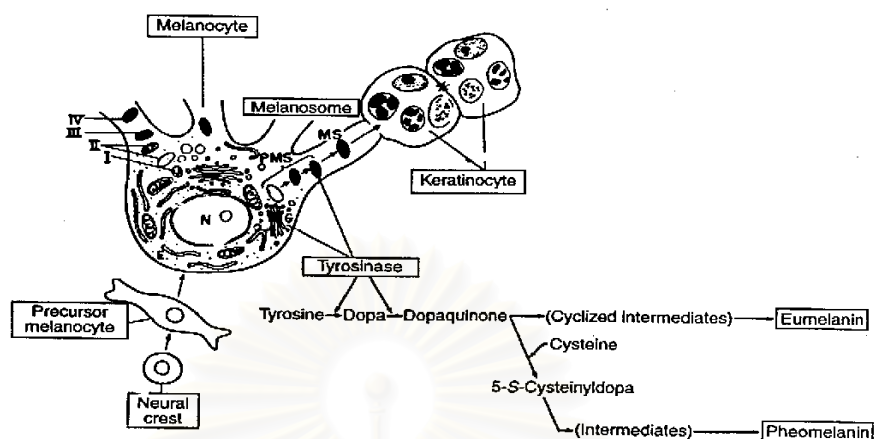
Figure 4. Diagram showing early stages of melanogenesis in a melanocyte.

(The epidermal melanin unit and melanogenesis) G, Golgi apparatus; E,endoplasmic –
reticulum; N, nucleus ; M, mitochondria; MS, melanosome; I, II, III and IV stages in
melanosomal development (Fitzpatrick et al.,1993)
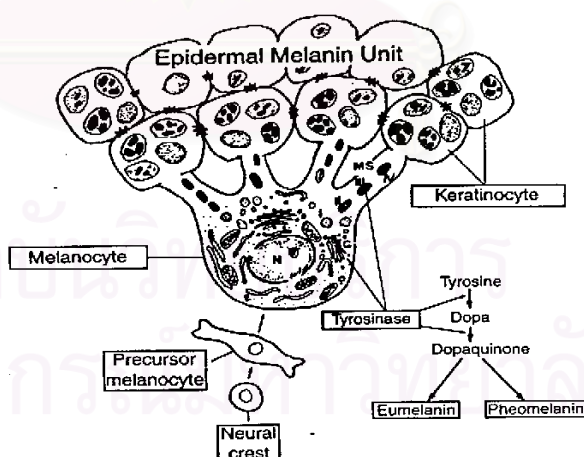
Figure 5. Diagram showing stages of melanogenesis in a melanocyte.

(The epidermal melanin unit : the partnership of an epidermal melanocyte and a
neighboring group of keratinocyte). Each epidermal melanocyte secrets
melanosomes into a definite number of neighboring keratinocytes MS,
melanosome in stages I to IV; G, Golgi apparatus (Fitzpatrick et al.,1993)

Malpighian cells are influenced mostly by genetic factors and partly by the presence of external factors like hormones and ultraviolet light.

Tyrosinase plays a key role in melanin biosynthesis. However, many other cellular factors regulate melanin biosynthesis, including the enzymes dopachrome tautomerase (also known as TRP-2, a tyrosinase-related protein), peroxidase, catalase and glutathione reductase, metallic ions like Cu^{2+}, Zn^{2+} and Fe^{2+} as well as hormone and histamine (Lee and Kim, 1995).

Whitening agents used for the treatment of skin hyperpigmentation

Since hyperpigmentation or the overproduction of melanin pigment is one of the most commonly found skin disorders. Several agents had been evaluated for their possible depigmenting or skin whitening effects. Some of these agents are listed in Table 4 together with their mechanisms of action.

Examples of whitening agents commonly used in the commercial preparations

1. **Mulberry root extract**

It is an extract from the root bark of paper mulberry (*Broussonetia kazinoki* xB. *papyrifera*, family Moraceae). Its major components are isoprenyl flavonoids and coumarin. Its skin whitening efficacy was studied in guinea pigs. The whiteness

(L-value) of the skin treated for 4 weeks increased much more than that of the vehicle-treated skin(Lee et al.,1997).

The safety of the mulberry root extract had also been evaluated. In studies for sensitizing potential using the Magnusson-Kligman protocol, no guinea pigs showed any erythema or edema. Likewise, acute eye irritation tests according to the CTFA guidelines showed Kazinol F (5 - [3 –(2,4 – dihydroxyphenyl) propyl] –3,4 – bis(3 – methyl – 2 – butenyl) –1,2 – benzenediol ,active compound isolated from paper mulberry) to be nonirritant (Lee and Kim, 1995). The mulberry root extract has been widely used in cosmetic products such as L' OREAL PLENITUDE.

Table 4. The action mechanisms of some depigmenting materials (Lee and Kim, 1985).

Mechanism	Depigmenting materials	Remark
Inhibit tyrosinase activity	Licorice extract, mulberry root extract, *Scutelleria baicalensis* extract, kojic acid, arbutin, glutathione, vitamin C derivatives, hydroquinone , others	-
Inhibition of melanosome transfer from melanocyte to keratinocyte	Niacinamide (Vitamin B_3)	-
Inhibit tyrosinase synthesis	Glucosamine, galactosamine, monosamine, tunicamycin, linoleic acid, others.	no specificity to tyrosinase, potent cytotoxic effect
Scavenges free radicals	Tocopherol	less whitening effect
Stimulate epidermal turnover	Capryloyl salicylic acid (BHA), lactic acid	-
Interrupts intermediates in melanin biosynthesis	Kojic acid	vague mechanism
Cytotoxic effect on melanocytes	Hydroquinone	high toxicity to the skin
Reduces melanin formed and inhibits auto-oxidation	Tocopherol, vitamin C derivatives	obscure effect
Stimulates melanin elimination through the keratinocytes	Placental protein, azelaic acid	obscure effect

2. Glabridin

Glabridin is the main ingredient in licorice extract. Its inhibitory effect on skin pigmentation had been investigated and the results showed that glabridin inhibited tyrosinase activity of melanocytes without any cytotoxicity. It was reported that UVB-induced pigmentation and erythema could be inhibited by topical application of 0.5% glabridin (Tabibian, 2001).

3. Niacinamide or niacin or nicotinic acid (Vitamin B$_3$)

Hakozaki et al. (2001) found from the *in vitro study* that 1 - 5% niacinamide inhibited melanosome transfer from melanocytes to keratinocytes. However, the exact skin whitening mechanism of niacinamide is still not clearly understood despite its popular use in both the cosmetic and dermatological preparations such as Ponds's whitening lotion.

4. Arbutin

Arbutin, the active component of the crude drug *Uvae ursi* folium described in the Japanese Pharmacopoeia, is a hydroquinone glycoside with strong tyrosinase inhibitory activity. Arbutin dose-dependently reduced tyrosinase activity per well at concentrations below 1.0 mM. The amount of melanin was reduced to 75% by arbutin. The effect of arbutin was about 1/100 that of hydroquinone. Arbutin can also act as a good substrate for tyrosinase similar to hydroquinone. The effectiveness of these substances as depigmenting agents may be related to their ability to act as substrates for enzyme tyrosinase. The depigmenting effect of a milky lotion containing 3% arbutin was tested in some forty individuals suffering UV irradiation on the inner side of the upper arms. The lotion was applied three times daily. After seven days, skin pigmentation was significantly inhibited compared with the placebo lotion (Maeda and Fukada ,1991).

5. Kojic acid

Kojic acid or 5-hydroxy–2-(hydroxymethyl)-4-pyrone is a substance extracted from the fermentation fluid of koji mold. It inhibits tyrosinase activity by chelating the copper in the tyrosinase molecule (Maeda and Fukada ,1991). The long-chain fatty acid, linoleic acid, also inhibits melanin production via similar mechanism.

In cultured human melanocytes, tyrosinase activity per well was slightly reduced by kojic acid at the concentration range between 0.1 mM and 0.5 mM but was rapidly and dose-dependently reduced at higher concentrations. At lower concentrations, a dose-dependent decrease was not observed. These findings suggested that the inhibitory effect of kojic acid on tyrosinase activity in the cell culture system is smaller than that of arbutin at concentrations that do not affect cell viability, even though marked inactivation was observed in isolated tyrosinase (Maeda and Fukada ,1991). Nair et al. (1989)using Yucatan minipigs as an assay *in vivo*, reported that kojic acid topically applied for 12 weeks resulted in no skin whitening activity. On the contrary, Mishima et al.(1988) reported that topically applied kojic acid prevented artificial pigmentation in humans by irradiation with UV. The discrepancy between these results may be ascribed to the difference in species or the methods of *in vivo* testing. Recently, Pengrungruangwong (2002) studied the skin whitening effect of 3% kojic acid in propylene glycol in 20 female volunteers. The study found that kojic acid significantly reduced the melanin content after 8 week-application.

6. Ascorbic acid (vitamin C) derivatives

In ascorbic acid-treated cells, tyrosinase activity per well was slightly reduced at final concentrations between 0.05 mM and 0.50 mM but rapidly and dose-dependently reduced at higher concentrations .Ascorbic acid was oxidized rapidly in the aqueous phase, with loss of activity in time and very limited transcellular potency owing to its being hydrophilic. Some ascorbic acid derivatives were considered stable and transcutaneous with regard to antipigmenting function.For example, magnesium ascorbic acid phosphate, which is a stable ascorbic acid derivative, prevented erythema and post-inflammatory hyperpigmentation following UV irradiation in humans.

Lipophilic ascorbic acid derivatives were also reported to prevent freckles and melanin spots on the skin. Ascorbic acid is a potent antioxidant in addition to its anti-enzymatic properties.   It may prevent melanin synthesis by suppressing inflammation and by inhibiting the auto-oxidation of DOPA and dopaquinone (Maeda and Fukada, 1991).

These results suggested that, to clarify those effects not ascribed to cytotoxicity, assays for both tyrosinase activity and cell viability in human melanocyte cultures are necessary to evaluate the depigmenting action. As whitening cosmetics are usually used daily, if the depigmenting effect is caused by cytotoxicity, irreversible hypopigmentation will occur somewhat in the skin or hair. In the *in vitro* assay systems, arbutin inhibits melanin production by reducing tyrosinase activity, not by non-specific cytotoxicity. However, the end exposure site for whitening cosmetics will usually be the intact skin. Thus, both the *in vitro* and *in vivo* effects need to be considered during the formulation and testing of whitening products. Comparison of the tyrosinase inhibitory activity (expressed as concentration of 50% inhibition, IC_{50}) of some tyrosinase inhibitors commonly used in cosmetic preparations is provided in Table 5. The scavenging property of ascorbic acid in comparison with alpha-tocopherol and paper mulberry compound (expressed as concentration of 50% scavenging activity, SC_{50}) is also shown in Table 6.

7. Skin rejuvenating agent

Alpha-hydroxy acids (AHA) such as L(+) lactic acid and glycolic acid are commonly used as skin rejuvenating agents. Recently, several beta-hydroxy acids (BHA) like salicylic acid and its derivative capryloyl salicylic acid have also received a great deal of attention. L(+) lactic acid is generally regarded as the human body's alpha hydroxy acid. It is one of the most well known and effective AHAs. Rijsbergen (2001). reported that at higher concentrations (12%) it was reported to inhibit tyrosinase formation and it stimulates epidermal turnover (and thus rejuvenating agent) A lower concentrations (5 %), only stimulate epidermal turnover. It is also the mildest AHA (see Table 7) possessing good water solubility and potent moisturizing property(Gijsen, 2001).

Table 5. Comparison of the tyrosinase inhibitory effect among different inhibitors (Tabibian, 2001).

Whitening substances	IC_{50} (mg / ml)
Ascorbic acid	70
Kojic acid	10
Hydroquinone	5.5
Paper – mulberry compound	0.396

Table 6. Scavenging effect against 1,1-diphenyl-2-picryl hydrazyl free radicals (Jang et al., 1997).

Whitening substances	SC_{50} (mg / ml)
L-ascorbic acid	3.3
α-tocopherol	9.5
Paper mulberry compound	6.7

Table 7. Differences in skin irritation potential of some alpha hydroxy acids (Gijsen, 2001).

Whitening substances	Irritation score at pH 3
L(+) lactic acid	2.2
D(-) lactic acid	2.8
synthetic lactic acid	2.7
glycolic acid	3.3

Table 7 demonstrates that the L(+) form is milder than D(-) or synthetic lactic acid. The same results were found in a comparative effectiveness study of different acids in which no irritation was present at neutral or slightly acidic pH. A difference in effectiveness between L(+) and D(-) lactic acid and their salts has been reported in other

studies.Combination of L(+) lactic acid and salicylic acid have been shown to be effective for the treatment of hyperkeratonic skin conditions. Although the difference in the behavior of L(+) and D(-) lactic acid when applied to the skin is not yet completely understood, it does indicate that the L(+) form is more compatible with the human skin. (Gijsen,2001)

There is now a renewed interest in L(+) lactic acid and lactates because they have been shown to possess skin lightening properties at higher concentrations, enabling formulators to improve the skin whitening efficiency of existing products and to develop a variety of interesting new formulations.

The skin whitening effect of conventional agents like hydroquinone is mainly due to the denaturation and death of pigment cell. This damaging action to the skin can cause irritation and inflammation. Other well-known skin whitening agents such as ascorbic acid inhibits the enzyme tyrosinase after is has been formed. The skin whitening action of lactates, however, is based on the suppression of the formation of tyrosinase. *In vivo* tests have shown that concentrations higher than 8% sodium lactate results in a significant skin whitening effect (Gijsen, 2001).

8. Sunscreen agents

Several classes of sunscreen agents are available for use in the sun-block and whitening products. They can be divided into physical and chemical sunscreens. Physical sunscreens act mainly by physically reflecting the UV light from the skin surface when covered with these substances. Titanium dioxide is an example of the most popular physical sunscreen. Chemical sunscreens are agents that absorb the UV light of some particular regions, which are harmful to our skin. Thus, they can be divided into UVA and UVB absorbers. Some of the sunscreen agents and their allowable concentrations in the United States are listed in Table 8 whereas those allowed in the European Union (EU), Japan and Thailand are shown in Table 9 and compared with the US values.Lee et al. (1997) reported that UV protection from herb have compounds with

unsaturated, carbonyl, aromatic and/or heterocyclic functional groups in plants usually absorb radiation near the UVA region of the spectrum. It was suggested that the UV-absorbing behavior of several plant extracts could be due to the presence of flavonoids. The alpine floras, which grow in areas of high altitude with high UV exposure, tend to contain higher amounts of flavonoids. The followings are some of the plants that have been shown to contain substances capable of absorbing UV radiation apart from chlorophyll. Extracts of these plants thus have the potential to be formulated in sun-protecting dermatological and cosmetic products.

Angelica keiskei: The leaves contain chalcone (chalkone) derivatives and coumarin.

Coptis: Coptis rhizome is grown mainly in China and Japan. It grows in the shade of mountains, producing white flowers in the early spring. In the rhizome, the major components are berberine and palmitine.

Lonicera: Lonicera contains caffeic acid, tannin and luteolin as major components.

Table 8   Category I (Safe and effective and not misbranded)– Sunscreen agents
 and concentrations allowed in the United States; FDA-OTC Panel, 1993
 (Porntip Nimmanitya, 2001).

Chemical Sunscreens	Approved Concentration
UVB absorbers	
2-Ethoxyethyl p-methoxycinnamate	1–3%
Diethanolamine p-methoxycinnamate	8-10%
Ethyl 4-bis (hydroxypropyl) aminobenzoate	1-5%
2-Ethylhexyl-2-cyano-3, 3-diphenyl-acrylate (Octocrylene)	7-10%
Ethylhexyl p-methoxycinnamate (Octyl methoxycinnamate)	2-7.5%
2-Ethylhexyl salicylate (Octyl salicylate)	3-5%
Glyceryl aminobenzoate	2-3%
Homomenthyl sallicylate	4-15%
Lawsone with dihydroxyacetone	0.25% with 3%
Octyl dimenthyl PABA (Padimate O)	1.4-8%
2-Phenylbenzimidazole-5-sulfonic acid	1-4%
Triethanolamine salicylate	5-12%
UVA absorbers	
Benzophenone-3 (Oxybenzone)	2-6%
Sulisobenzone	5-10%
Dioxybenzone	3%
Menthyl anthranilate	3.5-5%
Butyl methoxydibenzoylmethane*	2-3%
Physical sunblocks	
Red petrolatum	30-100%
Titanium dioxide	2-25%
Zinc oxide**	2-25%

* Federal Register, 1997   ** Federal Register, October 22, 1998

Table 9. Maximum concentration of sunscreen substances in various regions
(Porntip Nimmannitya,2001)

INCI Name	EU	USA	JAPAN	THAILAND
Ethylhexyl - Methoxycinnamate	+ (10%)	+ (7.5%)	+ (10%)	+ (7.5%)
Isoamyl - p-methoxycinnamate	+ (10%)	0 (aaf)	0	0
Phenylbenzimidazole - Sulfonic acid	+ (8%)	+ (4%)	0 (8%)	+ (8%)
Octyl dimethyl PABA	+ (8%)	+ (8%)	+ (10%)	+ (8%)
Octocrylene	+ (10%)	+ (10%)	0	+ (10%)
Ethylhexyl salicylate	+ (5%)	+ (5%)	+ (10%)	+ (5%)
Homomenthyl salicylate	+ (10%)	+ (15%)	+ (10%)	+ (10%)
4-Methylbenzylidene - Camphor	+ (4%)	0 (aaf)	0	0
Butyl methoxydibenzoyl - Methane	+ (5%)	+ (3%)	+ (10%)	+
Benzophenone-3	+ (10%)	+ (6%)	+ (5%)	+ (10%)
Benzophenone-4	+ (5%)	+ (10%)	+ (11%)	+ (10%)
Menthyl anthranilate	0	+ (5%)	0	+ (5%)

+   = approved ;   0 = not approved ;   aaf = approval applied for

( ) = maximum concentrations used in various regions.

Table 10 shows the wavelengths of maximum UV absorption of some of the commonly used chemical sunscreens. Most of these agents are UVB absorbers. Few are UVA absorbers or both UVA-UVB absorbers. It is recommended that a good sunscreen product should contain both the UVA and UVB filters in order to provide maximum and thorough protection against UV radiation (Porntip Nimmannitya, 2001).

Table 10. Wavelength of UV absorption by different sunscreens (Porntip Nimmannitya, 2001)

Sunscreen Substances	Type of UV-Absorber	Wavelength of maximum absorption (nm)
Ethylhexyl methoxycinnamate	UVB	308 (280-323)
Butylmethoxy –dibenzoylmethane	UVA	357 ± 2 (290-390)
Isoamyl p – methoxy - cinnamate	UVB	380 (275-320)
Octocrylene	UVB	302 (290-320)
Ethylhexyl salicylate	UVB	303 (290-320)
Homosalate	UVB	305 (280-320)
4-Methylbenzylidene camphor	UVB	299 ± 2 (277-317)
Benzophenone-3	UVB, UVA	286 (270-360)
Menthyl anthranilate	UVA	338 (300-370)
Zinc oxide	UVA, UVB	280-380
Octyl triazone	UVB	312
Octyl dimethyl PABA	UVB	310
Octyl methoxy cinnamate	UVB	308
Octyl salicylate	UVB	305

CHAPTER III

MATERIALS AND METHODS

Materials

Product A = Whitening face cream Lot No. 0008131A (Mfg. date 30/04/00)

Product B = Whitening face lotion Lot No.f (Mfg. date12/05/00)

Product C = Whitening face lotion Lot No. AI05 (Mfg. date 08/09/00)

Product E = Whitening body lotion Lot No.BE 14 (Mfg. date 26/05/01)

Product F = Whitening body lotion Lot No.1040041B (Mfg. date 09/02/01)

Product G = Whitening body lotion Lot No. BE04 (Mfg.date 04/05/01)

Equipment

1. Mexameter MX 16[®], Courage + Khazaka electronic GmbH, Germany.

2. SPF 290 S ANALYZER, Optometrics Inc., USA.

Methods

The primary purpose of this work was to investigate the whitening efficacy and irritation potential of some skin whitening lotions available in the Thai market. Evaluation was based on a Latin-square design study, in which each volunteer self-applied different brands of lotion on separate areas of her forearm twice a day for 12 weeks. Measurements of melanin and erythema values were then taken every week using a special instrument.

1. Survey of whitening lotions in the market

Whitening lotions were surveyed in the local supermarkets and department stores for their availability, price and popularity. Several brands were found which differed greatly in the type and concentration of the active whitening ingredients.

Selection of whitening lotions for testing

After survey of the available products, three lotions intended for the face and three for the body were selected and purchased from the supermarkets. The lot number was always the same for each brand to ensure the reliability of the results. Selection of the products was based on the differences in their active ingredients and formulas as shown in Tables 11 and 12.

Table 11. Formulas of face-whitening lotions

Product	Active ingredient	Quantity	Appearance
A (claimed SPF20) Price = 140 baht / 30 ml	licorice extract	5% w/w	Off white ,smooth-cream
	Octyl Triazone	1% w/w	
	Ethylhexyl p-methoxycinnamate	7.5% w/w	
	Titanium dioxide	4.5% w/w	
B (claimed SPF15) Price = 220 baht / 30 ml	Mulberry root extract	0.001% w/w	White , smooth-lotion
	Scutelleria baicalensis extract	0.01% w/w	
	Capryloyl salicylic acid	0.3% w/w	
	Terephthalylidene dicamphor-sulfonic acid	0.7% w/w	
	2-Ethylhexyl-2-cyano - 3,3-diphenylacrylate (Octocrylene)	1% w/w	
C (SPF unclaimed) Price = 110 baht / 70 ml	Vitamin B_3	1% w/w	White , smooth -lotion
	Ethylhexyl p-methoxycinnamate	1.2% w/w	
	Butylmethoxy dibenzoylmethane	4% w/w	

Table 12   Formulas of body-whitening lotions

Product	Active ingredient	Quantity	Appearance
E (SPF unclaimed) Price = 62 baht /120 ml	Lactic acid Ethylhexyl p-methoxycinnamate Butylmethoxy dibenzoylmethane Titanium dioxide	8 % w/w 1.25 % w/w 0.4 % w/w 0.5 % w/w	White,smooth - lotion
F (SPF unclaimed) Price = 76 bath / 150 ml	Licorice extract Ethylhexyl p-methoxycinnamate Butylmethoxy dibenzoylmethane	0.5 % w/w 1.3 % w/w 0.4 % w/w	White, oily smooth lotion
G (SPF unclaimed) Price = 62 bath / 150 ml	Vitamin B_3 Fruit extract Ethylhexyl p-methoxycinnamate Butylmethoxy dibenzoylmethane	1% w/w 0.1% w/w 1.2% w/w 0.4% w/w	White ,smooth - lotion

2. Selection of subjects

The subjects were female volunteers from the Faculty of Pharmaceutical Science and the Faculty of Dentistry of Chulalongkorn University. They ranged in age from eighteen to forty years and had initial melanin values in the range 500 - 600. All subjects had not taken any cosmetic products and/or topical medications on their two forearms for at least one week before and during the study. The study was a single-blinded, repeated randomized Latin square design. Before study, they received small samples of every product for allergy test. Only the subjects who did not show any allergic reactions were included in this study.

Four areas on the subject's left and right forearms (two on each forearm) were designated for application of the whitening products as shown in Figure 6. Each

application spot had a square shape with an area of 3×3 cm^2. The position of the two areas on each arm was close to each other and symmetrical to the other arm. This was to ensure the similarity of the initial melanin values among the four areas.

4. **Study protocol**

The protocol had been approved by the Ethics committee of the Faculty of Pharmaceutical Sciences of Chulalongkorn University. Each volunteer had given a written informed consent. They were allowed to quit the study at any time and were monitored by a physician for any undesirable effects that may have occurred during the study.

Each of the twelve volunteers received three face-whitening products (lotions A, B and C) and control (non-treatment or D) on her right and left forearms according to the randomized Latin Square sequence as shown in Table 13. Application of the products on each area of the individual subject was facilitated with the use of a plastic template, which was custom-made for each volunteer (Figure 7). The template was placed on each subject's left and right forearms such that the position of the square-shaped holes in the template was 4.5 cm below the antecubital fossa and about 2.5 cm above the wrist. The square-shaped holes or spots in each template were separated by a distance of 3 cm. The upper spot (below the antecubital fossa) on the right forearm was designated area 1 whereas the lower spot (above the wrist) was area 2. The upper and lower spots on the left forearm were respectively designated as area 3 and 4, as shown in Figure 6.

The two forearms were cleaned with water before applying the three face products and control (non-treatment). The same dose (0.2 ml) of each product was subsequently applied on each of the three application spots according to the predetermined sequence in Table 13. The products were applied twice a day in the morning (between 8.00 - 9.00 am) and in the evening (between 6.00 - 9.00 pm) by smearing each product onto each spot. Volunteers were encouraged to remain indoor during 7.00 am - 5.30 pm. If volunteers showed any signs of allergy, redness or pruritus

at the site of application, she would be excluded immediately from the study and received appropriate treatment from the physician.

Application of the three face products (A, B, C) were continued for 12 weeks, during which measurements of melanin and erythema values were made every week. Similar procedures were used for the study of whitening body products (E, F, G) with separate set of volunteers as shown in Table 14.

5. Measurements of melanin and erythema

During each visit five measurements of melanin and erythema values were made with Mexameter MX 16® on each application spot of the individual subjects. Precise positioning of the probe within the application spot was essential in obtaining accurate measurements of the melanin and erythema values. Thus, the position of the five measurements was fixed within each area according to the diagram shown in Figure 8. The values were then averaged to obtain the mean melanin and erythema values of each product for each subject. Measurements were taken at week 0 (immediately before product application) and once every week until the end of twelve-week study period.

The measuring principles of Mexameter MX 16®

Mexameter is a specific device, which measures the content of melanin and hemoglobin (erythema) in the skin. These two components are mainly responsible for the skin colors. The measurement is based on the absorption principles. The special probe of the Mexameter MX 16® emits light of three defined wavelengths (568 nm, 660 nm and 880 nm). A receiver insider the probe also measures the light reflected by the skin. The positions of the emitter and receiver were guaranteed that only the diffused and scattered lights are measured. As the quantity of the emitted light is defined, the quantity of the light absorbed by the skin can be calculated. The melanin is measured by two wavelengths (660 nm ,880 nm). These wavelengths have been chosen in order to achieve different absorption rates by the melanin pigments. For the erythema measurement, two different wavelengths (568 nm and 660 nm) are used to measure the

absorption capacity of the skin. One of these wavelengths (568 nm) corresponds to the spectral absorption peak of hemoglobin. The other wavelength (660 nm) has been chosen to avoid other color influences (e.g. bilirubin). The achieved results are shown on two clear digital displays ("E" for the erythema-values and "M" for the melanin-values).

$$\text{Melanin value} = \frac{500}{\log 5}\left(\log\frac{\text{Infrared}-\text{Reflection}}{\text{Red}-\text{Reflection}}+\log 5\right)$$

$$\text{Erythema value} = \frac{500}{\log 5}\left(\log\frac{\text{Red}-\text{Reflection}}{\text{Green}-\text{Reflection}}+\log 5\right)$$

Infrared-Reflection (reflected infrared light) = intensity of light at wavelength 880 nm

Red-Reflection (reflected red light)   = intensity of light at wavelength 660 nm

Green-Reflection (reflected green light)   = intensity of light at wavelength 568 nm

The maximum ratio between each color is 1:5. Thus, the range is 0-1000 with 500 being the value which corresponds to a ratio of 1:1. The higher the value the more melanin or erythema is detected.

The probe of Mexameter MX 16[®]

The probe is the core of the Mexameter MX 16[®] where the measuring electronics are located. The diameter of the measuring surface is 5 mm. The weight of the probe is about 55 g. As soon as the probe is placed on the skin's surface the measurement process automatically begins. A spring in the measuring head provides constant pressure on the skin. The values of melanin (M) and erythema (E) detected were immediately displayed after gently pressing the probe on the skin surface.

6. Statistical evaluation

Statistical evaluation was made at 5% significance level using randomized block analysis of variance (ANOVA), Latin square ANOVA, and Duncan's new multiple range test, where appropriate. The major parameters to be analyzed were the melanin and erythema values, which were expressed as difference from the initial time (week 0 or baseline).

7. Sun protection factor (SPF) determination

Sun Protection Factor (SPF) is defined as the ratio of the minimal erythema dose (minimal dose of sunlight which can cause redness on the skin) of the protected skin, which as been applied with a sunscreen, divided by the minimal erythema dose of the unprotected skin. A SPF value of 15 effectively reduced UV skin absorption by 94%. Measurements of the SPF values of the six whitening products (A, B, C, D, E, F) were made using a SPF 290 S ANALYSER (Optometrics Inc., USA.). The Theory of operation were as follows:

The SPF 290 S measures the transmittance of a sample. Transmittance is defined ass the ratio of the illumonation passed through a sample to the illumination on the sample. In mathematical terms we have:

$$T = I / I_0$$

where I is the light intensity after passes through a sample and I_0 is the initial light intensity. There are three factors affect the measured amount of light intensity transmitted by the sample absorption coefficient, the sample path length (thickness) and the sample concentration.

The absorption coefficient of a substance ; the relationship between the absorption coefficient, path length, concentration and transmittance is not linear, rather is exponential. According to Beer and Lambert relationship:

$$A = \varepsilon_\lambda .J. L$$

Because the well known relationship between transmittance and absorbance is:

$$A = \log 1 / T$$

In term of absorption coefficient, path length and concentration the transmittance is given by:

$$T = 1/10^{\varepsilon\lambda_{J}L}$$

Other factors that affect the transmittance measurement include:

1. The scattering of light due to particles in the sample,

2. Fluorescence or phosphorescence of the sample,

3. Reflectance of the sample at measurement wavelength,

4. Changes of the absorption coefficient at high solution concentrations,

5. The bandwidth of the monochromatic light

6. Light detected from any souce other than through the sample(stray light).

Some of these factors are inherent characteristics of the sample and cannot be influenced by the measurement system. However, instrument design choices can be made to minimize certain affects that could contribute to measurement uncertainly. or inaccuracy.

Fluorescence or phosphorescence causes the sample to emit light at wavelengths other than the excitation wavelength. This affect is common with many materials illuminated in the ultraviolet region of the spectrum. To minimize these affects,the SPF-290S s Monochromator is placed between the sample and the detector. Thus only if the fluorescence or phosphorescence of the sample occurs at the wavelength currently being measured by the system does it impact the measurement. Furthemore, the placement of the monochromator between the integrating sphere and the detector.

Absorption bands can be broad or narrow depending on the chemical composition of the sample. For accurate measurement the bandwidth of the wavelength isolator must be significantly narrower than the absorption bandwidth of the sample. The SPF-290S uses a monochromator with a bandwidth or resolution of about 1.7 nm, which is much narrower than the absorption bandwidths of the compounds used in sunscreen protection products.

As mentioned above, any light that is collected by the detector from a source other than the sample can affect the measurement of transmittance. Because of the placement of the monochromator, sources of stray light are limited to that generated by the monochromator or a light leak between the monochromator and the detector.

The SPF-290S monochromator is designed to minimize self-generated stray light, and the coupling between the monochromator and the PMT housing is also designed to minimize room light affects. In summary, the SPF-290S is designed to minimize factors other than the absorbance coefficient, path length or solution concentration from affecting the transmittance measurement of the sample.

Sample preparation

When the SPF-290S was first developed the standard for sample application rate was defined as 2 μl / cm^2 (micro-liters per square centimeter). The units translate directly to a sample thickness of 20 microns (0.000787inch). The US Food and Drug Administration (FDA) has recently issued a final standard that requires the sample to be applied at 2 mg / cm^2 (2 milligrams per square centimeter). The Australian standard also requires application at 2mg / cm^2 while CIE recommends either 2 mg/cm^2 or 2 μl / cm^2.

Sample measurements

It may appear that the sample used in a transmittance measurement is simply the solution, material, etc. that one places in the beam, but in fact the sample includes any change that affects control over factors that might cause an inaccurate transmittance measurement is highly recommended.

In most cases, the sample has some holder or container whose optical characteristics are taken into account during a reference scan measurement. Lotions and creames tested in the SPF-290S are generally applied to a substrate that has been placed in the light beam during the reference scan. Substrates of Transpore ®, Vitro-Skin® and in some limited cases, quartz have become staples for *in vitro* testing. Transpore and Vitro-Skin have been proven to adequately mimic the characteristics of skin and yield good correlation between *in vitro* and *vivo* testing. Quartz has come into

popularity because it is a requirement for certain testing by some certifying bodies and for the ease of high-viscosity sample application.

Because of reasons that will be discussed in detail later, the SPF-290S is designed to acquire several transmittance scans at different locations on the sample. Therefore, the substrate must have uniform transmittance characteristics and the characteristics must not change throughout the duration of the measurement. Transpore has proved to be satisfactory in this regard with the possible exception of the very beginning and ends of a roll.

One caution in using transpore, it has adhesive on one surface. Although Optometrics recommends the sample be applied to the opposite side because Transpore is also porous by design, sample material may contact the adhesive. If the sample solution can dissolve or change the adhesive characteristics, others choices for a substrate may be more appropriate. Using quartz as a substrate requires that it be cleaned uniformly and free of any residue left by the cleaning process.
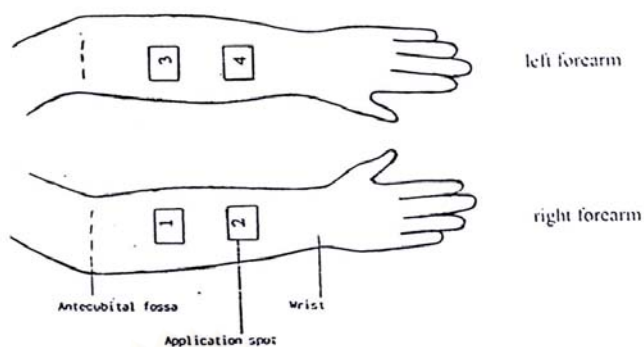
Figure 6. Diagram showing placement of templates on left and right forearms and area assignments.
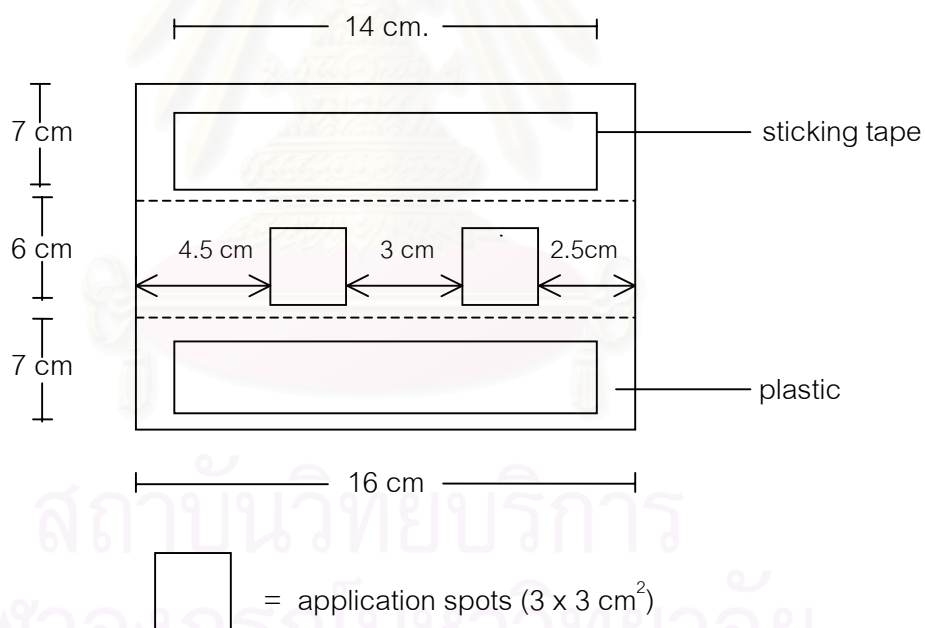
Figure 7. Design layout of a plastic template to be placed on either the left and right forearms of the individual subjects.(Dimension shown is only relative and not draw to scale).

Table 13 Randomized Latin square for application face-whitening products and control
in each volunteer

Area Volunteer no.	1	2	3	4
1	A	B	C	D
2	B	C	D	A
3	C	D	A	B
4	D	A	B	C
5	A	B	C	D
6	B	C	D	A
7	C	D	A	B
8	D	A	B	C
9	A	B	C	D
10	B	C	D	A
11	C	D	A	B
12	D	A	B	C

A   =   Product A

B   =   Product B

C   =   Product C

D   =   Control area (non-treatment)

Table 14. Randomized Latin square for application of body-whitening products and
control in each volunteer

Area / Volunteer no.	1	2	3	4
1	E	F	G	H
2	F	G	H	E
3	G	H	E	F
4	H	E	F	G
5	E	F	G	H
6	F	G	H	E
7	G	H	E	F
8	H	E	F	G
9	E	F	G	H
10	F	G	H	E
11	G	H	E	F
12	H	E	F	G

E   =   Product E

F   =   Product F

G   =   Product G

H   =   Control area (non-treatment)
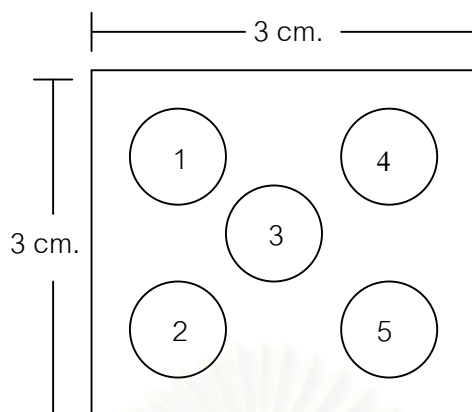
1 = first   measurement , 2 = second measurement , 3 = third measurement

4 = fourth measurement , 5 = fifth measurement

Figure 8. Diagram showing the five positions within each application spot, where the Mexameter MX[®] 16 probe was placed for measurements of melanin and erythema values

CHAPTER IV

RESULTS AND DISCUSSIONS

The purpose of this part was to evaluate the efficacy and irritation potential of three whitening products for the face and three whitening products for the body by comparison with control (non – treatment) in female volunteers.

1. Efficacy evaluation of the face whitening products.

1.1 Comparison of mean melanin values (difference from the initial value or baseline) among three face - whitening products and control.

Twelve female volunteers participated in this Latin square study. All subjects received the three face – whitening products (A ,B and C) at the same time but not the separate areas of their left and right forearms as previously described in Chapter III.

Prior to application of the whitening products, the initial melanin values (week 0) were measured to determine if there was any significant difference in the melanin values among the different areas on each subject. Table 15 shows the individual and average absolute melanin values of the twelve subjects at week 0 (before application of the products).

Table 15. Initial absolute melanin values of the twelve subjects at week 0 prior to
application of the face products.

Subject no.	Initial melanin values			
	Area 1	Area 2	Area 3	Area 4
1	544.60	554.20	544.60	542.40
2	573.20	579.80	568.40	572.00
3	568.40	564.60	563.20	560.60
4	554.80	563.00	550.00	553.80
5	554.40	552.20	560.80	560.80
6	574.40	575.00	582.40	577.00
7	550.00	545.80	552.00	539.60
8	541.80	538.20	536.00	534.40
9	552.00	551.00	544.20	549.00
10	544.20	544.20	544.60	546.40
11	544.40	542.20	543.00	537.80
12	548.60	548.00	546.20	552.60
Mean $\pm$ S.E.M.	554.23 $\pm$ 3.34	554.85 $\pm$ 3.79	552.95 $\pm$ 3.83	552.20 $\pm$ 3.88

From this table it can be seen that the twelve subjects had initial mean melanin values of all the four areas in the range of 552.20 – 554.85. The values were quite similar to one another. Randomized block ANOVA was then applied to these data and the results are shown in table 17 , which reveals that there was no significant difference in the initial melanin values among the four areas within each subject (P >0.05). Significant intersubject variability was detected (P << 0.05) with regards to the melanin values among different volunteers. However, this was not surprising since the differences in the initial melanin content among individual subjects naturally existed. Randomized block ANOVA has separated the variability due to subjects from the total error term and thus the intersubject variation in melanin content would not interfere with

the evaluation of the area effect. Therefore , it can be concluded that there was no significant difference in the melanin values among the four application areas within each subject. This would facilitated evaluation of the product 's whitening efficacy since the starting melanin values (before product application) were similar in each subject regardless of the areas.

Table 16   Comparison of the initial absolute melanin values among the four areas prior to application of the face products.

ANOVA for Randomized block design at initial period.

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Prob.	ANOVA result
subject	11	6903.00	627.55	44.34	2.10	0.0001	Sig
area	3	32.00	10.67	0.75	2.90	0.5308	NS
error	33	467.00	14.15				
total	47	7402					

NS = non - significant among three face products and control.

Sig = significant among three face products and control.

At week 0, after the initial melanin values had been measured, the individual subject self – applied the three products A, B and C on the pre–specified areas on her left and right forearms using the tailor – made template. The formulation, appearance and their SPF values are shown in Tables 17 and 18 ,respectively. The non treatment area was assigned the letter as D and served as the self – control within each subject. The products were applied twice daily for twelve consecutive weeks as described in Chapter III. The subject's melanin (M) and erythema (E) values were then measured every week until twelve weeks using Mexameter MX 16[®].

Table 17 Formulation of whitening face products

Product	Active ingredient	Quantity	Mechanism of action
A claimed SPF 20	Licorice extract	5% w/w	Inhibit enzyme tyrosinase
	Octyl triazone	1% w/w	Chemical sunscreen
	Ethylhexyl p-methoxycinnamate	7.5% w/w	UVB absorber
	Butyl methoxy dibenzoylmethane	0.3% w/w	UVA absorber
	Titanium dioxide	4.5% w/w	Physical sunblock
B claimed SPF 15	Mulberry root extract	0.001% w/w	Inhibit enzyme tyrosinase
	Scutelleria baicalensis extract	0.01% w/w	Inhibit enzyme tyrosinase
	Capryloyl salicylic acid	0.3% w/w	increases keratin - formation and turnover epidermis
	Terephthalylidene dicamphor-sulfonic acid	0.7% w/w	UVA absorber
	2-Ethylhexyl-2-cyano - 3,3-diphenylacrylate (Octocrylene)	1% w/w	UVB absorber
C SPF unclaimed	Vitamin B_3	1% w/w	Inhibition of melanosomes transfer from melanocyte to keratinocyte.
	Ethylhexyl p – methoxycinnamate	1.2% w/w	UVB absorber
	Butyl methoxy dibenzoylmethane	0.4% w/w	UVA absorber

Table 18 Sun Protection Factor (SPF) values of three whitening face products

Product	SPF			Mean ±S.D.	% CV
	Measurement 1	Measurement 2	Measurement 3		
A	18.50 ± 0.80	18.30± 0.80	18.50± 0.50	18.43 ± 0.12	0.65
B	5.40 ± 0.70	5.70 ± 1.00	5.40 ± 0.60	5.50 ± 0.17	3.09
C	5.10 ± 0.30	5.20 ± 0.40	5.00 ± 0.50	5.10 ± 0.10	1.96

Following the application of three face products (A , B and C), the absolute melanin values decreased from the initial values in all subjects. The absolute melanin data of the individual subjects are provided in Appendix I. As seen from this appendix , the absolute values gradually decreased in every subject from week 0 through week 12 after application of the three face products. The differences in the melanin values between the initial and 12th week period were apparently greater after treatment with either A,B or C than that of the non – treatment (control D). Thus, to facilitate the comparison, the extent of melanin decrease at any time was used instead of the absolute melanin value. This was achieved by subtracting the initial absolute melanin value of the individual subject with the absolute value measured from the same subject after applying the product (or control) for a particular period of time. The individual data for the extent of melanin decrease are also provided in Appendix II whereas the average values are given below in Table 19.

Table 19 The average extent of melanin decrease (difference in the absolute melanin

values between initial and time t) of twelve subjects after application of three

face products (A,B,C) for different periods. ANOVA results are also provided.

Data = Mean $\pm$ S.E.M.(N = 12)

Week of application	Average melanin decrease				ANOVA result
	Product A	Product B	Product C	D(control)	
1	4.05 $\pm$ 1.06	3.92 $\pm$ 1.40	3.82 $\pm$ 1.83	2.60 $\pm$ 1.46	NS
2	4.20 $\pm$ 0.95	2.43 $\pm$ 1.37	3.80 $\pm$ 1.51	-0.48 $\pm$ 1.20	P < 0.05
3	6.23 $\pm$ 0.88	3.90 $\pm$ 1.68	5.12 $\pm$ 1.51	0.78 $\pm$ 1.27	P < 0.05
4	7.72 $\pm$ 1.44	4.97 $\pm$ 1.76	6.23 $\pm$ 1.69	0.65 $\pm$ 1.41	P < 0.05
5	7.25 $\pm$ 1.43	7.03 $\pm$ 1.53	8.12 $\pm$ 1.81	2.55 $\pm$ 1.04	P < 0.05
6	8.75 $\pm$ 1.13	8.22 $\pm$ 1.40	8.38 $\pm$ 1.74	1.92 $\pm$ 1.22	P < 0.05
7	7.88 $\pm$ 1.61	9.15 $\pm$ 2.16	9.82 $\pm$ 1.93	1.60 $\pm$ 1.07	P < 0.05
8	8.07 $\pm$ 1.58	8.73 $\pm$ 2.21	9.56 $\pm$ 1.46	2.35 $\pm$ 1.15	P < 0.05
9	8.10 $\pm$ 1.53	8.52 $\pm$ 1.64	9.75 $\pm$ 2.22	0.65 $\pm$ 0.93	P < 0.05
10	10.60 $\pm$ 1.75	10.48 $\pm$ 1.96	12.42 $\pm$ 1.94	-0.02 $\pm$ 1.22	P < 0.05
11	11.87 $\pm$ 1.86	11.55 $\pm$ 1.73	14.82 $\pm$ 1.72	1.08 $\pm$ 1.03	P < 0.05
12	10.22 $\pm$ 1.42	10.68 $\pm$ 1.45	12.72 $\pm$ 1.91	0.03 $\pm$ 1.08	P < 0.05

NS = non - significant among three face products and control.

P < 0.05 = significant among three face products and control.

Data in Table 19 indicate that all three products demonstrated noticeable changes in the extent of melanin decrease. The extent slowly increased with time, starting from 4.05, 3.92, and 3.82 at week 1 and reaching the mean values of 10.22, 10.68 and 12.72 at week 12 for products A, B and C, respectively. On the other hand, the control area (D) hardly showed any sign of changes in the melanin values. The extent of melanin decrease was negligible with the maximum mean value of only 2.60 observed at week 1 whereas the value was only 0.03 at week 12. The value even fluctuated into the negative region, which was observed at week 2 (-0.48) and week 10 (-0.02) implying that the melanin of some subjects even increased from the initial values.

On the contrary, the extent of melanin decrease was in the positive range for all products, indicating their ability to reduce the melanin content after daily application. The effect seemed to be maximum at week 11 since all products gave the highest positive values of 11.87, 11.55 and 14.82 for A, B and C, respectively.

Latin square ANOVA was applied to test for significant difference in the extent of melanin content among the three products and control at 5% significance level. Latin square ANOVA separated the total variability of the data (total sum of squares) into variations due to subject, area, product and residual error. Thus, the test should have sufficient sensitivity in detecting any significant difference in the data due to the product difference because other interfering factors, particularly the influences from the subject and area effects, had been subtracted from the error sum of squares. The ANOVA results are summarized in Table 19 whereas the individual ANOVA for each week are provided in Appendix III.

From the ANOVA results in Table 19, there was no significant difference in the extent of melanin decrease among the three face products and control after one-week application (P>0.05). This implied that the three products were not significantly different from control (non-treatment). Nevertheless, their slightly greater extent of melanin decrease than the control at this period suggested the tendency of the three products to produce significant whitening effect upon a more prolonged application.

After 2 weeks, significant difference was detected in the extent of melanin decrease among the three products and control, indicating that some of these products had become effective by this time. ANOVA also showed significant differences in the melanin data of all subsequent weeks until the end of the study (P < 0.05). Duncan's new multiple range test was further applied to rank for the melanin-reducing ability of the three products in comparison with the control. The results are summarized in Table 20.

Table 20   Duncan's new multiple range test results of melanin values at various periods
          of face products application.

Week	Results
2 - 4 , 6	Control < product B< product C < product A
5,10,11	Control < product B< product A < product C
7-9,12	Control < product A< product B < product C

As seen from this table, all the three products (A, B, C) became effective over
the control at all weeks starting from week 2. There was no line joining between the
control (D) and that of A, B or C, indicating that application of any one of these products
resulted in significant reduction of the melanin content over the non-treatment area.
Nevertheless, the three products were also found to have similar whitening activity since
they were joined together by the same underline ($P > 0.05$). This type of behavior was
observed in all measurements from week 2 to week 12 although there appeared to be a
small change in the ranking order within the three products from week to week. The
extent of melanin decrease was also graphically represented in Figures 9 and 10 for
the face products.

Despite the similarity in the extent of melanin decrease, closer examination of the
data in Tables 19 and 20 revealed that product A tended to give slightly higher extent of
melanin decrease than B and C in the early periods of application up to the first six
weeks. However, at week 7 and afterwards product C appeared to give the highest
extent of melanin decrease (although not significant), with a maximum drop observed at
week 11 (14.82 unit).

A subtle difference in their whitening activity could be due to the difference in the
major active components of the three products. Product A contained 5% licorice extract
as tyrosinase inhibitor plus three UV absorbers (1% octyl triazone , 0.3 % butylmethoxy
dibenzoylmethane and 7.5% ethylhexyl p-methoxycinnamate) and a physical sun-

blocking agent (4.5% titanium dioxide). Product B contained 0.001% mulberry root extract and 0.01% *Scutellaria baicalensis* extract as tyrosinase inhibitors plus an epidermal turnover-stimulating agent (0.3% capryloyl salicylic acid) and two UV-filters (0.7% terephthalylidene dicamphorsulfonic acid and 1% 2-ethylhexyl-2-cyano-3,3-diphenylacrylate).Product C contained three listed active ingredients, i.e.,1% Vitamin B_3 (nicotinamide) and two UV absorbers (1.2% ethylhexyl-p-methoxycinnamate and 0.4% butylmethoxy dibenzoylmethane).

It is interesting to note that product B, which contained the highest number of active ingredients with differing mechanisms of action, seemed to have the smallest whitening activity during the early periods from week 2 to week 6. Its performance was better in the latter periods (weeks 7 -12) but never took over product C, which contained fewer components. Thus, multi-component formulation of a whitening product may not necessarily perform better than a formula with single or smaller number of active ingredients. Other factors must also be taken into account such as the concentration and potency of the individual active ingredient, the SPF of the formulation as well as the type and formula of cream base. The SPF value of product B measured in this study (5.50 ± 0.17) was also much lower than the claimed value of 15 whereas the measured value for product A was consistent with its label claim $(18.43 \pm 0.12$ versus 20). The concentrations of the tyrosinase inhibitors (0.001% mulberry root and 0.01% *Scutelleria baicalensis* extracts) in product B were also relatively low compared to product A, which also contained tyrosinase inhibitor but of different plant extract and concentration (5% licorice extract). It is possible that differences in the potency of these plant extracts may have contributed to the subtle difference in the skin whitening activity of products A and product B.

Vitamin B_3 was the major component of product C recently it has been reported that it may inhibit melanogenesis by interfering with the transfer of melanosomes from melanocytes to keratinocytes (Hakozaki et al., 2001). It has gained a quick reputation as an effective skin whitening agent, with a commonly used concentration in the range of 1 to 5 **%**. Since product C was the least expensive of the three face products, it was

considered to have the best price-performance in this study. It contained vitamin B_3 in a simple combination with UV-absorbers, which are common ingredients used in many whitening products. However, there has been no report of a combined use of vitamin B_3 with other tyrosinase inhibitors nor any such products are available in the Thai market. Thus, it would be interesting to see if combination of vitamin B_3 and other tyrosinase inhibitors (or other whitening agents apart from the UV filters / absorbers) would produce any synergism in the skin whitening activity.

Data on the melanin values have indicated that products A, B and C were equally effective over the non-treatment (D) in decreasing the melanin content in the forearms of female volunteers. However, subtle differences in the ranking order were noticed among the three products during various periods of application. This could be due to the differences in the type, concentration and mechanisms of action of the whitening agents present in each product as well as the formulas of their cream base.

Figure 9   Comparison of mean melanin values (difference from initial value) among

three face whitening products and control after application at various

periods (value = Mean ± S.E.M., N =12)
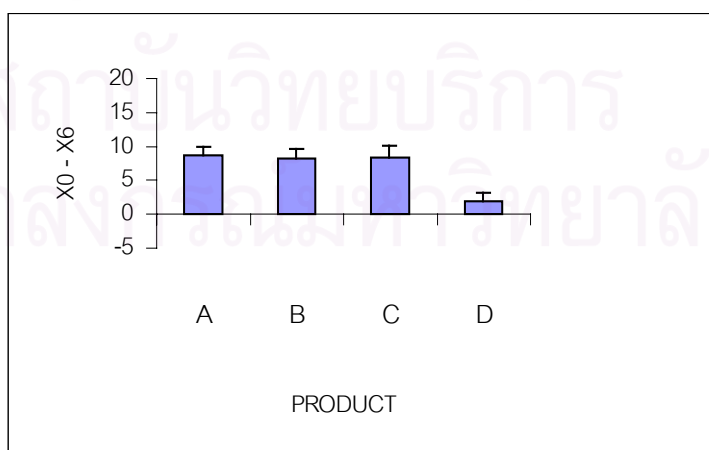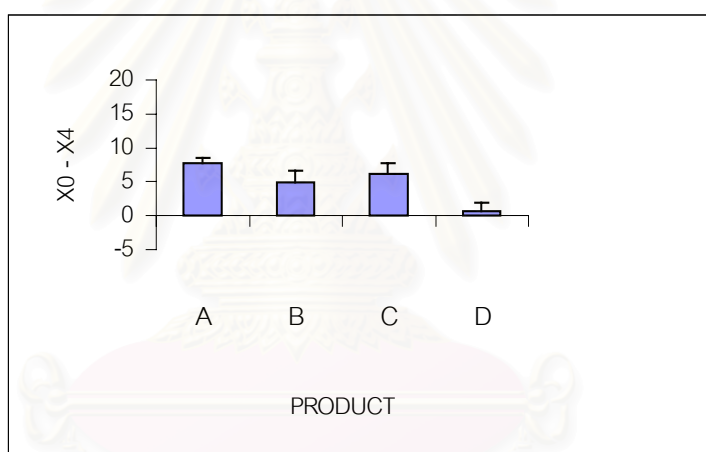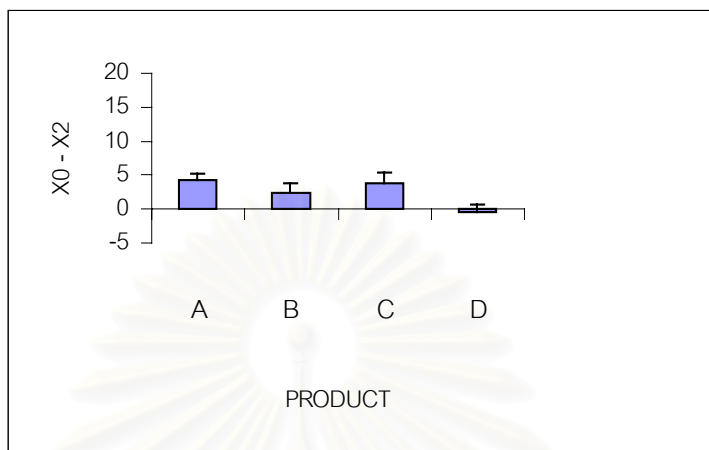
A = Product A , B = Product B , C = Product C , D = Control

$X0 - Xi$ = initial melanin value at week i,i=2,4,6,8,10,12

Figure 9 Comparison of mean melanin values (difference from initial value) among

three face whitening products and control after application at various

periods(cont.).(value = Mean ± S.E.M., N =12)
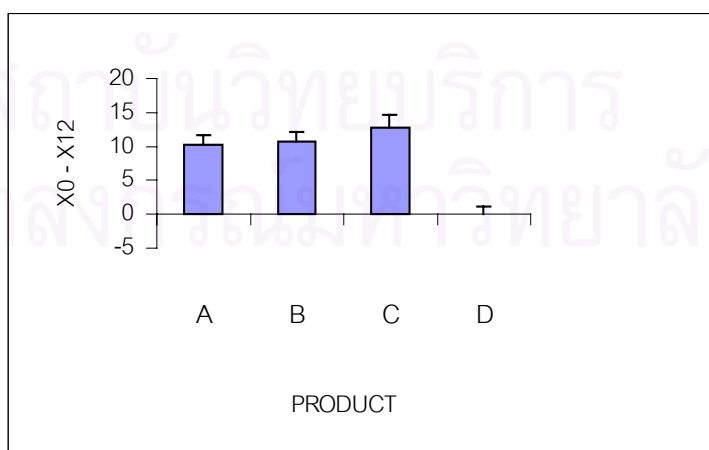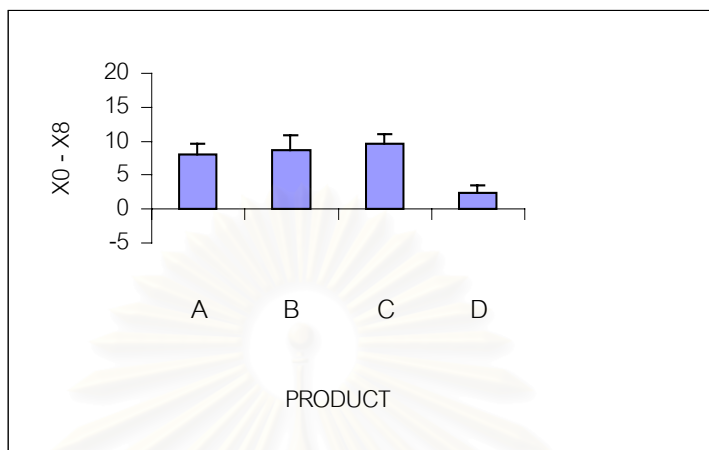
A = Product A , B = Product B , C = Product C , D = Control

$X_0 - X_i$ = initial melanin value at week $i, i = 2, 4, 6, 8, 10, 12$

Figure10. Comparison of mean melanin values (difference from initial value) among three whitening face products and control after application at various periods.(value = Mean ± S.E.M., N = 12)

Product A = ◆ , Product B = ■ , Product C = Δ , Control = X

* = Significant difference among product A, B, C and Control
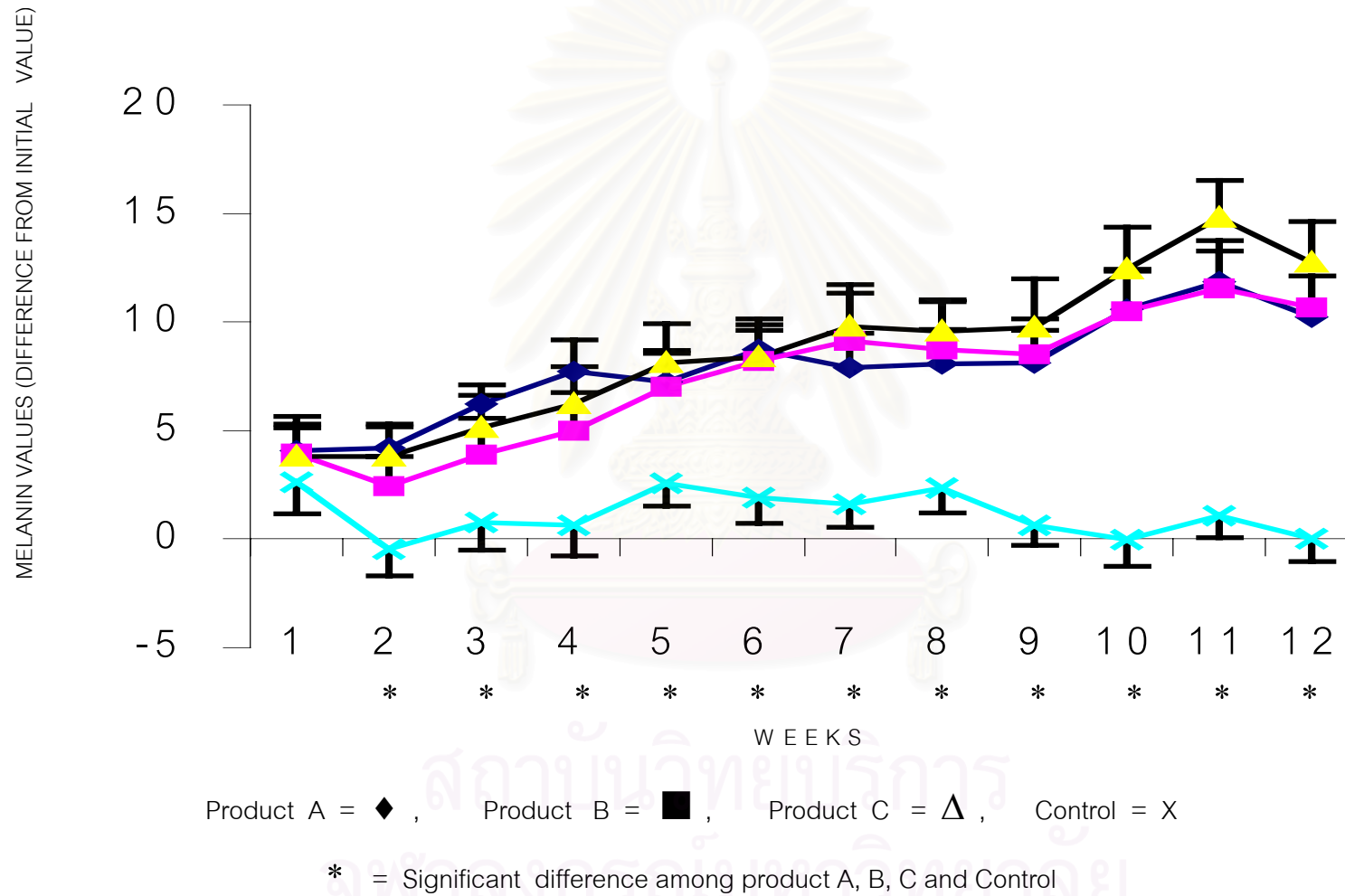
1.2 Comparison of the mean erythema values (difference from the initial value or baseline) among three face-whitening products and control.

Table 21.   Initial absolute erythema values of the twelve subjects at week 0 prior to application of the face products.

Subject no.	Initial erythema values			
	Area 1	Area 2	Area 3	Area 4
1	597.00	596.60	600.20	592.00
2	619.40	618.20	618.40	616.80
3	619.20	621.00	619.80	620.20
4	618.40	625.40	611.00	616.80
5	618.20	618.40	621.00	615.40
6	622.20	627.80	631.40	623.80
7	611.40	611.80	612.40	608.80
8	606.40	610.20	599.80	604.40
9	613.00	612.40	608.40	608.80
10	602.40	603.00	601.20	606.20
11	607.20	606.20	602.00	601.40
12	603.80	604.00	610.60	612.20
Mean $\pm$ S.E.M.	611.55 $\pm$ 2.35	612.92 $\pm$ 2.75	611.35 $\pm$ 2.86	610.57 $\pm$ 2.56

Table 21 shows the inividual and average absolute erythema values of the twelve subjects at week 0 (before application of the products). The initial erythema values were similar among the four areas, with the mean values between 610.57 and 612.92. Application of randomized block ANOVA revealed that there was no significant difference in the initial absolute erythema values among the four application areas of each subject ($P > 0.05$, Table 22).

Table 22   Comparison of the initial absolute erythema values among the four areas prior to application of the face products.

ANOVA for Randomized block design at initial period.

Source of variation	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Prob.	ANOVA result
subject	11	3308.00	300.72	28.19	2.10	0.0001	Sig
area	3	32.00	10.67	1.00	2.90	0.4065	NS
error	33	352.00	10.67				
total	47	3692					

NS = non - significant among three face products and control.

Sig = significant among three face products and control.

This would facilitate evaluation of the products' irritation potential since the starting erythema values (before product application) were similar in each subject.

After the four products had been applied to each subject, the absolute erythema values were subsequently measured at a weekly interval in concomitance with the melanin measurements. For statistical comparison, the value of change in erythema values (difference in the absolute erythema values between the initial and time t) was used instead of the raw data. The average values of change in erythema are shown in Table 23 whereas the individual data of each subject are provided in appendix I (part 2) and in appendix II (part 2) . The data are also graphically represented in Figures 11–12.

Table 23 The average chage in erythema (difference in the absolute erythema values
between initial and time t) of twelve subjects after application of three face
products (A,B,C) for different periods. ANOVA results are also provided.
Data = Mean $\pm$ S.E.M. (N = 12)

Week of application	Average change in erythema values				ANOVA result
	Product A	Product B	Product C	D(control)	
1	2.43 $\pm$ 1.82	1.85 $\pm$ 2.57	-1.93 $\pm$ 2.51	-3.72 $\pm$ 1.71	NS
2	-1.75 $\pm$ 1.92	-2.58 $\pm$ 1.79	-7.23 $\pm$ 1.23	-6.68 $\pm$ 1.77	P < 0.05
3	2.65 $\pm$ 2.14	-0.65 $\pm$ 1.86	-3.38 $\pm$ 2.19	-1.90 $\pm$ 2.22	P < 0.05
4	1.28 $\pm$ 1.32	0.93 $\pm$ 2.10	-1.27 $\pm$ 1.74	-0.32 $\pm$ 1.39	NS
5	2.12 $\pm$ 2.30	1.08 $\pm$ 1.89	-2.3 $\pm$ 2.49	-3.68 $\pm$ 1.62	NS
6	3.17 $\pm$ 2.04	1.07 $\pm$ 1.46	-2.20 $\pm$ 1.52	-5.00 $\pm$ 1.78	P < 0.05
7	5.13 $\pm$ 2.60	4.43 $\pm$ 1.58	2.05 $\pm$ 1.79	-0.23 $\pm$ 1.73	NS
8	6.12 $\pm$ 2.71	4.38 $\pm$ 2.60	3.80 $\pm$ 2.26	0.97 $\pm$ 1.84	NS
9	3.37 $\pm$ 1.87	2.40 $\pm$ 2.10	3.57 $\pm$ 1.97	0.25 $\pm$ 2.42	NS
10	1.33 $\pm$ 1.77	1.05 $\pm$ 2.49	2.32 $\pm$ 2.45	-3.13 $\pm$ 1.80	NS
11	2.95 $\pm$ 1.66	3.45 $\pm$ 2.19	5.65 $\pm$ 2.15	2.08 $\pm$ 2.19	NS
12	5.50 $\pm$ 2.25	4.28 $\pm$ 2.48	5.97 $\pm$ 2.28	2.42 $\pm$ 2.61	NS

NS = non - significant among three face products and control.

P < 0.05 = significant among three face products and control.

Latin square ANOVA was applied to the data in Table 23 and results are given in the same table. In general, there was no significant difference in the values of change in erythema among the three face products and control (P > 0.05), with the exception at week 2, 3 and 6. The observed change was quite small compared to the change in melanin, particularly during week 1- 11. Some negative values were observed which implied that there had been an increase in skin redness at the time of measurements. However, this behavior was also observed in the non-treated area (control). Moreover, the three products yielded the erythema change in the positive region, indicating that the erythema values were even reduced after application of these products. This was clearly seen at week 12, at which maximum positive values were detected for product A and C (A = 5.50, C = 5.97). The mean values at week 12 were also greater than control (2.42) although significant difference was not detected.

Subsequent Duncan's new multiple range test was also applied to the data at week 2, 3 and 6, where significant differences were detected by ANOVA. The ranking results are shown in Table 24.

Table 24 Duncan's new multiple range test results of erythema values at various periods of face products application.

Week	Results
2	product C < control < product B < product A
3	product C < control< product B < product A
6	control < product C < product B < product A

From this table and data in Table 23, product A gave the most positive (or least negative) values followed by B whereas product C and control D always gave the negative values, indicating that treatment with these products (especially A) resulted in a decrease in erythema values with time. Thus, Duncan's test results at week 2, 3 and 6, together with the greatest value of C observed at week 12, tended to suggest that the three products may be able to provide protection against increase in erythema. This is possible because all of them contained UV-filters, which may help protect the individual subjects from the UV. Since the application spots were located in the lower forearm areas and the subjects were not requested to wear long-sleeve dress, exposure to sunlight was unavoidable during certain times of day, such as the commuting time between the workplace and home. Prolonged application of these sunscreen-containing products may have helped alleviate the skin from the irritating sun and thus resulted in decrease in erythema (more positive value) when compared to the untreated area. Nevertheless, this protection effect against skin erythema needs further proof (such as in a larger, more prolonged study) since significant ANOVA was observed only at some weeks.

Figure 11   Comparison of mean erythema values (difference from baseline) among
            three whitening face products and control after application at various
            periods.(value = Mean $\pm$ S.E.M., N = 12)

A = Product A , B = Product B, C = Product C, D = Control

X0 – Xi = initial melanin value – melanin value at week i,i= 2,4,6,8,10,12

Figure 11   Comparison of mean erythema values (difference from baseline) among three

whitening face products and control after application at various periods(cont.).

(value = Mean $\pm$ S.E.M., N = 12)

A = Product A , B = Product B, C = Product C, D = Control

X0 – Xi = initial melanin value – melanin value at week i,i= 2,4,6,8,10,12

Figure 12. Comparison of mean erythema values (difference from initial value) among three whitening face products and control after application at various periods. (value = Mean $\pm$ S.E.M., N = 12)

Product A = ◆ , Product B = ■ , Product C = Δ , Control = X

* = Significant difference among product A, B, C and Control

2.   Efficacy evaluation of the body-whitening products.

2.1 Comparison of the mean melanin values (difference from the initial value or baseline) among three body-whitening products and control.

Another set of twelve female volunteers participated in this Latin square study. They were all in the same age range as in the first study. Each subject received the three body-whitening products (E, F and G) at the same time on the separate areas of her forearms in a manner similar to the previous study.

Prior to product application of the body-whitening products, the initial melanin value (week 0) was measured in each subject. As seen in Table 25.

Table 25. Initial absolute melanin values of the twelve subjects at week 0 prior to application of the body products.

Subject no.	Initial melanin value			
	Area 1	Area 2	Area 3	Area 4
1	554.00	553.00	547.20	545.20
2	586.60	582.40	587.20	582.40
3	575.00	565.60	574.60	564.00
4	552.80	554.60	556.20	550.60
5	567.20	536.60	564.00	559.20
6	535.40	536.20	544.60	547.40
7	553.40	551.80	552.60	551.20
8	543.80	541.60	548.40	548.00
9	558.60	556.20	552.00	550.60
10	550.40	546.00	542.80	539.80
11	575.60	572.80	573.60	568.00
12	579.40	587.00	584.40	587.60
Mean ±S.E.M.	561.02 ± 4.51	556.98 ± 4.87	560.63 ± 4.53	557.83 ± 4.33

There was closeness in the initial melanin values among the four areas within each subject, the mean initial values ranging from 556.98 to 561.02. Randomized block ANOVA was further applied and results in Table 26 show that there was no significant difference among the different areas of each subject's forearms (P > 0.05).

Table 26   Comparison of the initial absolute melanin values among the fours areas prior to application of the body products.

ANOVA for Randomized block design at baseline (before treatment)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Prob.	ANOVA result
subject	11	10047.00	913.36	32.10	2.10	0.0001	Sig
area	3	147.00	49.00	1.72	2.90	0.1805	NS
error	33	939.00	28.45				
total	47	11133.00					

NS = non - significant among three body products and control.

Sig = significant among three body products and control.

Thus, the starting melanin values of the application spots were the same in each subject, thereby facilitating the data evaluation after treatment with the body products.

At week 0, after the initial melanin values had been measured, the individual subject self-applied the three body products E, F, G on the pre-specified areas on her left and right forearms using the tailor-made template. The formulation and their SPF values are shown in Tables 27 and 28, respectively.

Table 27 Formulation of whitening body products.

Product	Active ingredient	Quantity	Mechanism of action
E	Lactic acid	8 % w/w	Increase keratin formation and turnover epidermis
	Titanium dioxide	0.5 % w/w	Physical sunblock
	Ethylhexyl p – methoxy -cinnamate	1.25% w/w	UVB absorber
	Butyl methoxydibenzoylmethane	0.4% w/w	UVA absorber
F	Licorice extract	0.5 % w/w	Inhibit enzyme tyrosinase
	Ethylhexyl p – methoxy -cinnamate	1.3 % w/w	UVB absorber
	Butyl methoxydibenzoylmethane	0.4% w/w	UVA absorber
G	Vitamin B$_3$	1% w/w	Inhibit enzyme tyrosinase and increase blood flow
	Fruit extract	0.1% w/w	inhibit enzyme tyrosinase
	Ethylhexyl p – methoxy -cinnamate	1.2% w/w	UVB absorber
	Butyl methoxydibenzoylmethane	0.4% w/w	UVA absorber

Table 28 Sun Protection Factor (SPF) values of three whitening body products.

Product	SPF			Mean ± S.D.	% CV
	Measurement 1	Measurement 2	Measurement 3		
E	4.20 ± 0.20	4.30 ± 0.20	4.50 ± 0.20	4.33 ± 0.15	3.46
F	6.70 ± 0.30	6.70 ± 0.20	6.60 ± 0.40	6.67 ± 0.06	0.90
G	5.30 ± 0.10	5.70 ± 0.30	5.60 ± 0.20	5.53 ± 0.21	3.80

The non-treatment area was assigned as H and served as the self-control within each subject. The products were applied twice daily for 12 consecutive weeks similar to the face products.

As with the previous study on face products, the absolute melanin values also decreased in all subjects following treatment with the body products. The absolute melanin data of the individual subjects are provided in Appendix I.The extent of melanin

decrease at any time was calculated for each subject from the difference in the absolute values at initial time and time t. The individual data are provided in Appendix II, whereas the average values are given below in Table 29.

Table 29   The average change in melanin (difference in the absolute melanin values between initial time and time t) of twelve subjects after application of three body products (E,F,G) for different periods. ANOVA results are also provided. Data = Mean ± S.E.M. (N = 12)

Week of application	Average change in melanin values				ANOVA result
	product E	product F	product G	H(control)	
1	10.97 ± 1.89	10.87 ± 1.41	8.85 ± 1.27	7.95 ± 1.49	NS
2	8.73 ± 0.90	10.73 ± 1.55	8.05 ± 1.79	8.05 ± 1.23	NS
3	12.90 ± 1.58	12.05 ± 1.92	9.82 ± 1.48	9.20 ± 2.06	P < 0.05
4	9.18 ± 4.1.43	8.28 ± 1.36	7.03 ± 2.01	8.30 ± 1.51	NS
5	12.75 ± 1.86	12.10 ± 1.88	11.12 ± 1.52	9.63 ± 1.56	NS
6	16.20 ± 2.38	14.80 ± 1.94	13.62 ± 2.23	11.33 ± 2.15	P < 0.05
7	16.13 ± 1.89	15.65 ± 2.01	14.38 ± 1.79	10.90 ± 1.68	P < 0.05
8	15.38 ± 1.72	15.73 ± 1.78	15.98 ± 1.72	11.83 ± 2.01	P < 0.05
9	19.18 ± 2.28	15.82 ± 1.75	15.62 ± 1.97	12.28 ± 1.73	P < 0.05
10	17.02 ± 1.90	15.93 ± 1.97	16.55 ± 2.25	11.75 ± 2.15	P < 0.05
11	17.27 ± 1.95	15.28 ± 1.66	16.72 ± 2.23	12.78 ± 1.76	P < 0.05
12	17.63 ± 2.43	15.90 ± 1.77	16.10 ± 2.15	11.20 ± 1.29	P < 0.05

NS = non - significant among three face products and control.

P < 0.05 = significant among three face products and control.

Data in Table 29 indicate that all three products demonstrated a marked drops in the melanin values. The extent of melanin drop increased with time as with the face products.   However, the values seemed to fluctuate more than the face products, especially with product E, which showed average extent of melanin decrease of 8.73 at

week 2, reaching maximum drop of 19.18 at week 9 before slightly decreasing in value to 17.63 at week 12. Product F showed a steady increase in the extent of melanin drop, from 10.87 at week 1 to 15.65 at week 7, after which time the value stayed relatively constant in the narrow range of 15.28 – 15.93. Product G also showed a similar pattern, with the average melanin drop increasing from 8.85 at week 1 to 15.98 at week 8 and then remained stable afterwards with the value in the range of 15.62 – 16.72.

It is interesting to note that the control area (non-treatment, H) also showed a marked drop in melanin content, with the mean value of 7.95 at week 1 and slowly increased to reach maximum of 12.78 at week 11 before slightly decreased to 11.20 at week 12. This was in contrast to the control values observed in the first study, in which all subjects showed negligible changes in melanin values. The exact reasons as to this discrepancy in results are not clearly known. However, the subjects in this set of study were instructed to strictly avoid exposure to sunlight as much as possible throughout the entire period of study, particularly when they were outdoors commuting between workplace and home. This may partly explain the sharp drop in the melanin values observed after only one week with both the product-treated and the untreated (control) areas. The extra precautionary measures taken by the subjects to avoid exposure to sunlight included wearing long-sleeve dress as much as possible, always staying or walking under the shades or using an umbrella. Thus, even the untreated areas also showed some degree of whitening as seen from Table 29. Application of the three whitening products, however, was found to induce a further drop in melanin over the control particularly during week 6-12.

Latin square ANOVA was then applied to test for significant differences among the three products and the control at different weeks. The results are also summarized in Table 29. ANOVA data for the individual weeks are provided in Appendix I.

No significant differences were detected in the extent of melanin decrease during the first two weeks. Small but significant difference was observed at week 3 ($P < 0.05$), indicating that some of these products (E and F) might have started to produce a greater whitening effect than the control. However, subsequent Duncan's

test failed to show significant ranking as the three products were joined together by the same underline as the control (Table 30).

Table 30   Duncan's new multiple range test results of melanin values at various periods
of body products application.

Week	Results
3	Control < product G< product F< product E
6	Control < product G< product F< product E
7	Control < product G< product F < product E
8	Control < product E < product F < product G
9	Control < product G< product F < product E
10 ,12	Control < product F< product G < product E
11	Control < product F < product G < product E

This was due to the fact that the calculated F-value obtained from the ANOVA table at week 3 and week 8 (3.29 and 3.07) and was only slightly greater than the tabulated F-value (2.92), indicating a marginal significant difference.   Furthermore, ANOVA at week 4 and 5 resulted in non-significance among the products E, F, G and control H ($P > 0.05$).   This implied that the three products still could not produce an adequate whitening effect to be significantly greater than the control.   Only at week 6 that ANOVA showed a distinctly significant difference ($P << 0.05$, calculated F = 3.90 versus tabulated F = 2.92).   Significant differences were also detected in all subsequent

weeks (week 7 – 12) although the extent of significance appeared to vary from week to week as seen from this appendix.

Duncan's new multiple range test was also applied to the data at weeks 6 to 12 to rank the three products and control. The results are shown in Table 23. The ranking pattern of the three body products was somewhat more complicated than that previously observed with the face products. Nevertheless, based on evaluation of the data from weeks 9 through 12, product E appeared to have the highest whitening effect although significance was observed only at week 9. Products F and G were equally effective over the control as judged from the Duncan's test results of weeks 7, 9, 10 and 12. The two products also induced slightly less whitening effect than product E but significance was observed only at week 9. The whitening data (extent of melanin decrease) are also graphically represented in Figures 13 to 14.

Formulas in Table 27 revealed that product E contained an alpha hydroxy acid (8% lactic acid), a physical sunblock (0.5% titanium dioxide) and two UV absorbers (1.25% ethylhexyl-p-methoxy cinnamate and 0.4% butylmethoxy dibenzoylmethane). Product F contained a tyrosinase inhibitor (0.5% licorice extract) and two UV absorbers (1.3% ethylhexyl-p-methoxy cinnamate and 0.4% butylmethoxy dibenzoyl methane). Product G contained two tyrosinase inhibitors (1% vitamin B_3 and 0.1% of unidentified fruit extract and two UV absorbers (1.2% ethylhexyl-p-methoxy cinnamate and 0.4% butylmethoxy dibenzoylmethane).

Since the three products contained the same type and amount of UV-A absorber (ethylhexyl-p-methoxy cinnamate) and UV-B absorber(butylmethoxy dibenzoylmethane), evaluation of the whitening activity was facilitated by allowing direct comparison on the true whitening agents present in each product.

Lactic acid is an alpha hydroxy acid commonly used in stimulating epidermal turnover. At high concentrations it is also a keratolytic agent (Gijsen, 2001). The commonly used concentration of lactic acid in whitening products is in the range of 5 to 10%. It is possible that 8% lactic acid present in product E may be responsible for its

apparently greater whitening activity than products F and G in this study, which appeared to have similar efficacy. Closer examination of the data, nevertheless, revealed that product G tended to give slightly greater melanin drop than product F, especially at week 8, 10, 11 and 12 although significance was not observed. This could be due to the effect of 1% vitamin B_3 in the formulation. The results were in agreement with the previous study, in which the face product C (also containing 1% vitamin B_3) gave a slightly greater whitening effect than the products containing tyrosinase inhibitors (see discussion in section 1.1).

Cross comparison of the whitening activity between the face products (A, B, C) and the body products (E, F, G) was more difficult to make because the two studies were separately conducted at different times using separate panels of subjects. However, assuming that the sun-screening agents (UV-absorbers and physical sunblock) did not have direct effects on the melanogenesis, the present data generally suggested that the product containing lactic acid tended to produce greater whitening effect than vitamin B_3, which in turn, seemed to give higher efficacy than tyrosinase inhibitor. Nevertheless, this trend was only general. The observed differences among products are very subtle (not significant) and depended pretty much on the appropriate concentration of each active ingredient, the type and formulation of the cream base, as well as the presence of other whitening agents in the product.

Data on the melanin values have thus indicated that the three body-whitening products E, F and G were similarly effective over the non-treatment (H) in decreasing the melanin content in the forearms of female volunteers. However, subtle differences in the ranking order were noticed from week to week, with product E having the highest whitening activity, followed by products G and F

Figure 13   Comparison of mean melanin values (difference from initial value) among

three body-whitening products and control after application at various

periods. (value = Mean ± S.E.M., N =12)
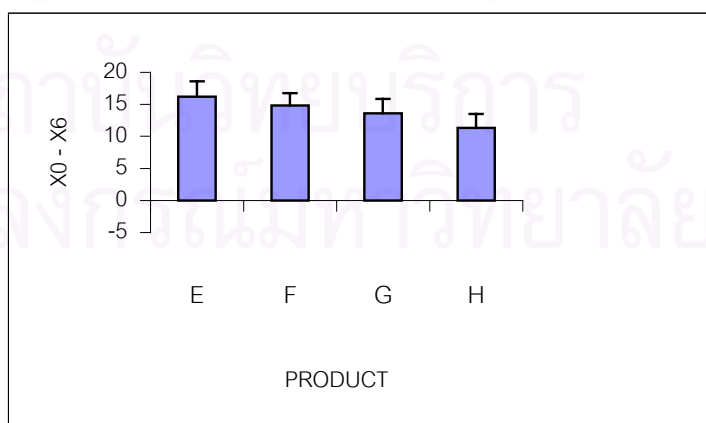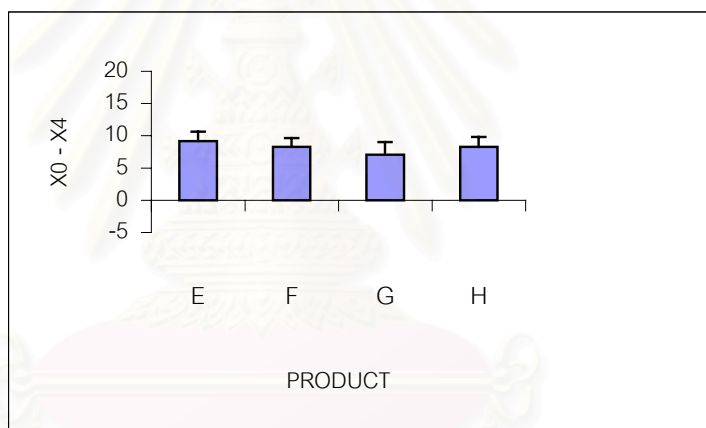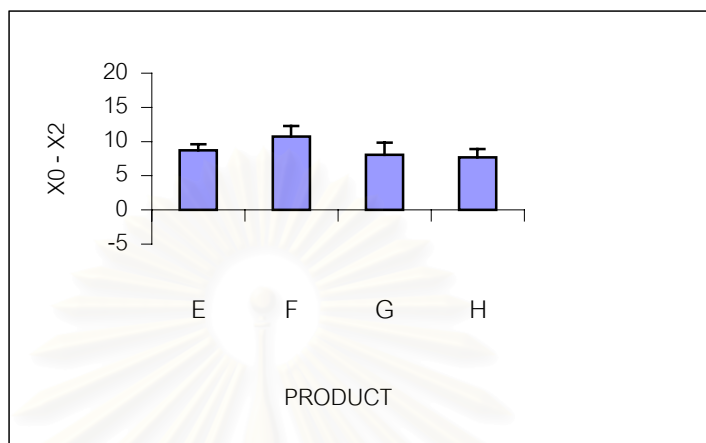
E = Product E , F = Product F , G = Product G , H = Control

$X_0 – X_i$ = initial melanin value – melanin value at week i,i=2,4,6,8,10,12

Figure 13   Comparison of mean melanin values (difference from initial value) among

three body-whitening products and control after application at various

periods (cont.). (value = Mean ± S.E.M., N =12)
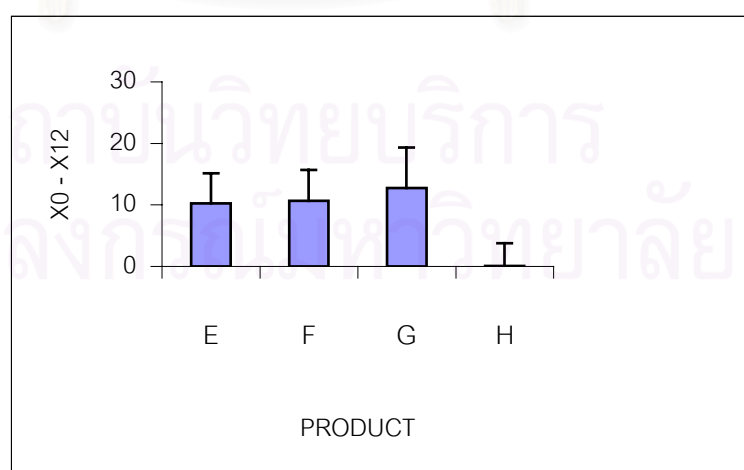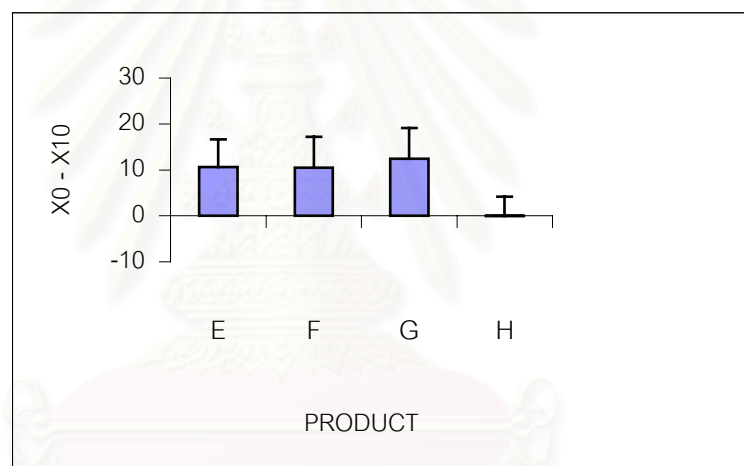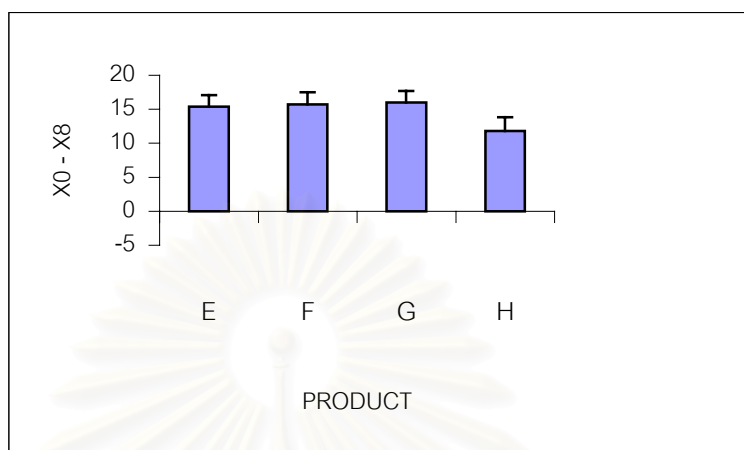
E = Product E , F = Product F , G = Product G , H = Control

$X_0 - X_i$ = initial melanin value - melanin value at week i,i=2,4,6,8,10,12
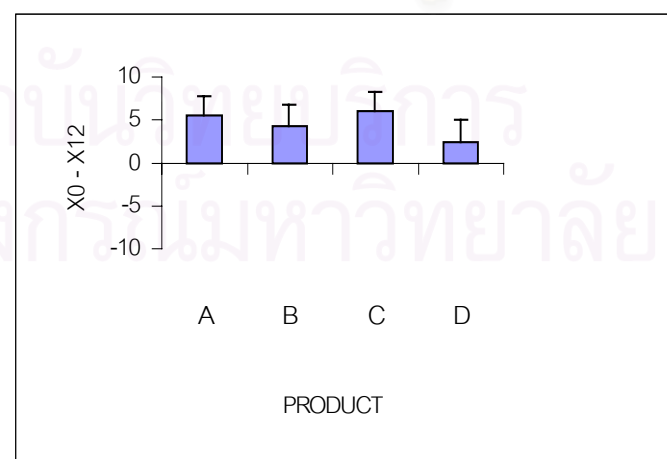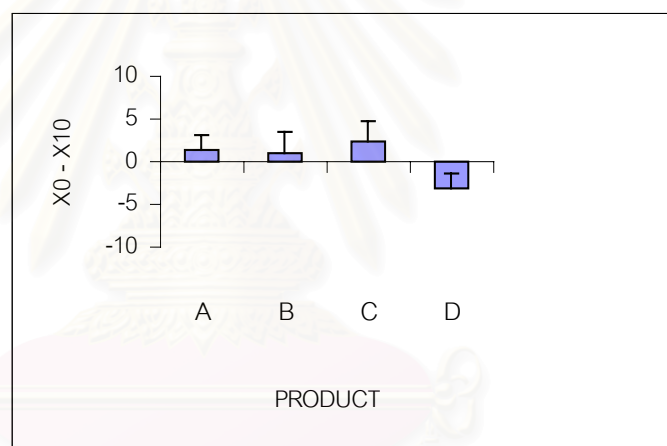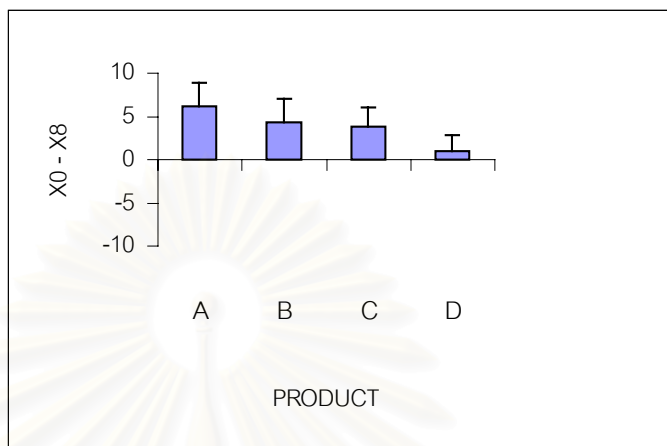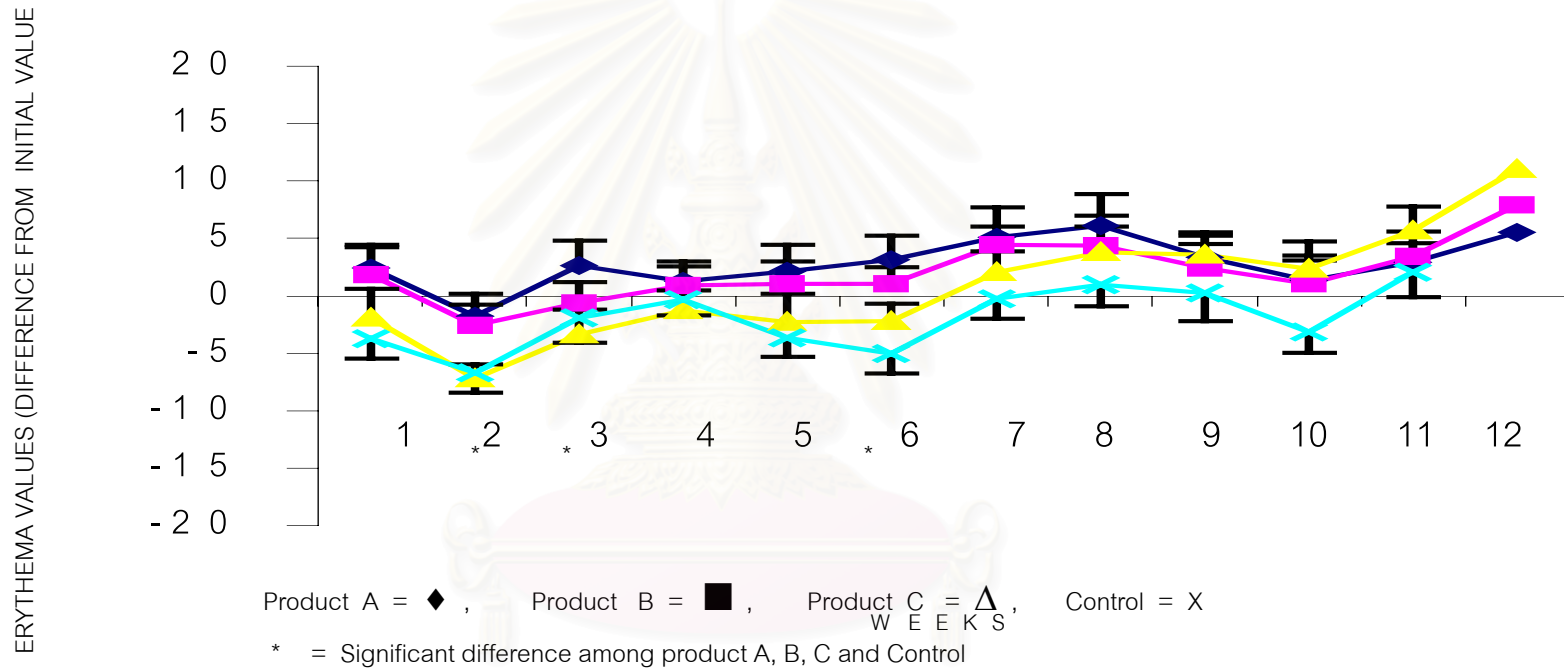
Figure 14.   Comparison of mean melanin values (difference from initial value) among three whitening body products and control after application at   various periods. (value = Mean $\pm$ S.E.M., N = 12)

Product E = ◆ ,   Product F = ■ ,   Product G = Δ ,   Control = X

*   = Significant difference among product E,F ,G and Control
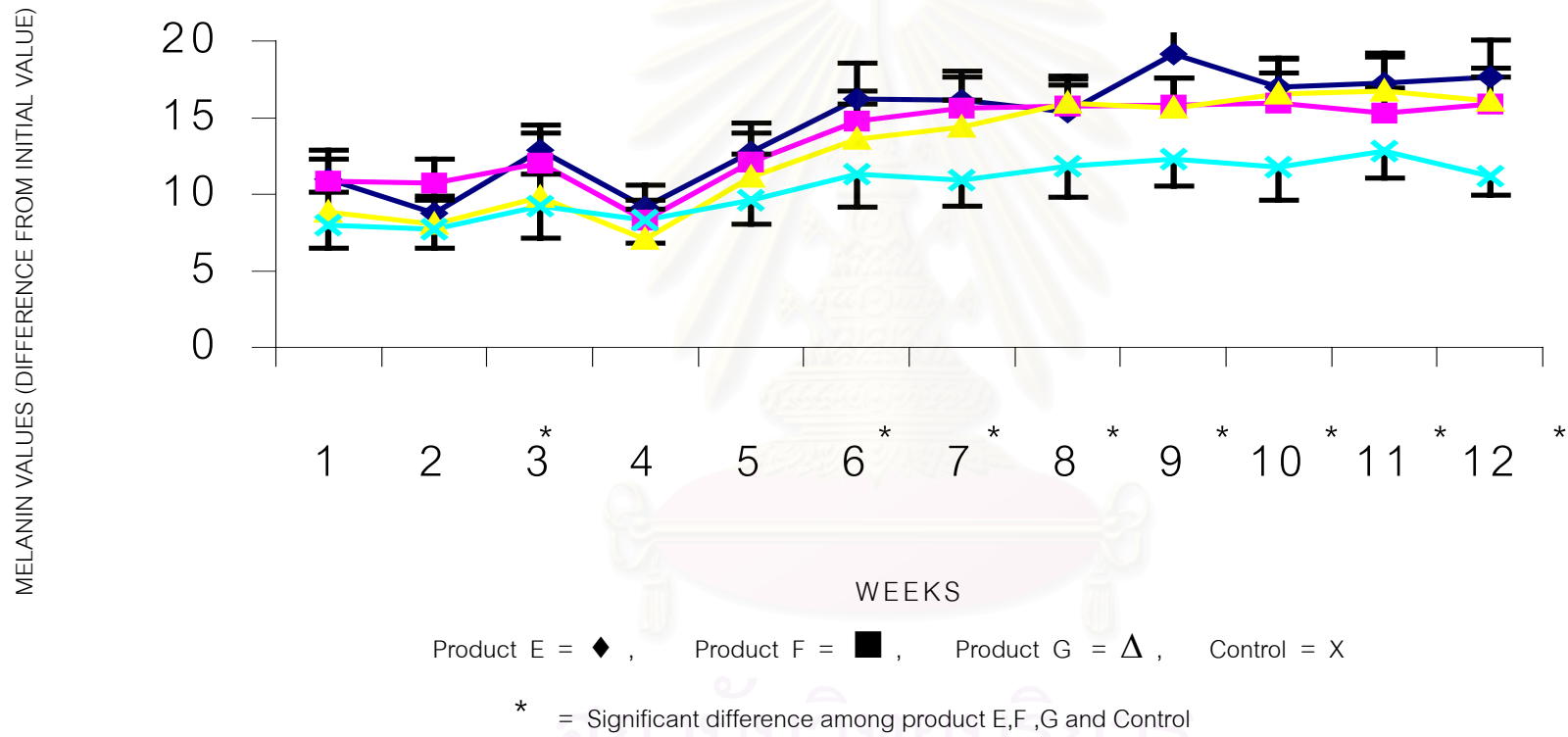
2.2 Comparison of the mean erythema values (difference from the initial value or baseline) among three body-whitening products and control.

Table 31. Initial absolute body erythema values of the twelve subjects at week 0 prior to the start of the study.

Subject no.	Initial erythema values			
	Area 1	Area 2	Area 3	Area 4
1	620.20	619.60	618.20	608.80
2	640.00	632.00	628.80	634.80
3	632.40	632.00	631.80	627.80
4	622.40	623.20	613.40	612.20
5	612.60	606.20	603.60	607.60
6	602.80	608.20	613.60	616.80
7	624.80	626.80	624.40	618.20
8	606.00	600.80	606.40	606.60
9	624.80	626.80	624.40	618.20
10	616.60	612.60	607.80	608.60
11	619.40	620.40	615.80	613.60
12	615.20	625.20	616.40	619.40
Mean $\pm$ S.E.M.	619.77 $\pm$ 3.00	619.48 $\pm$ 2.98	617.05 $\pm$ 2.57	616.05 $\pm$ 2.47

Table 31 shows the individual and average absolute erythema values of the twelve subjects at week 0 (before application of the products). The initial erythema values were similar among the four areas, with the mean values between 616.05 and 619.77. Application of randomized block ANOVA revealed that there was no significant difference in the initial absolute erythema values among the four application areas of each subject ($P > 0.05$, Table 32).

Table 32.   Comparison of the initial absolute erythema values among the four areas
prior to application of the body products.

ANOVA for Randomized block design at initial period.

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Prob.	ANOVA result
subject	11	3474.00	315.82	18.95	2.10	0.0001	Sig
area	3	118.00	39.33	2.36	2.90	0.8830	NS
error	33	550.00	16.67				
total	47	4142.00					

NS = non - significant among three face products and control.

Sig = significant among three face products and control.

Table 33 The average change in erythema decrease (difference in the absolute erythema values between initial and time t) of twelve subjects after application of three body products (E, F, G) for different periods. ANOVA results are also provided. Data = Mean ± S.E.M.(N = 12)

Week of application	Average change in melanin values				ANOVA result
	Product E	Product F	Product G	H(control)	
1	-4.82 ± 1.63	-8.57 ± 1.73	-7.90 ± 1.73	-6.83 ± 2.59	NS
2	-4.95 ± 3.12	-8.63 ± 2.15	-8.27 ± 2.10	-5.87 ± 3.19	NS
3	-4.87 ± 2.48	-4.32 ± 2.07	-6.23 ± 1.57	-5.82 ± 2.60	NS
4	1.38 ± 2.63	-1.05 ± 2.32	0.18 ± 2.29	2.62 ± 2.01	NS
5	-0.55 ± 2.06	-0.53 ± 2.95	-2.27 ± 1.90	-0.98 ± 2.44	NS
6	1.17 ± 2.20	0.45 ± 2.06	-0.63 ± 2.29	-2.03 ± 2.26	NS
7	2.22 ± 2.34	-1.48 ± 2.55	1.12 ± 2.31	-0.30 ± 3.10	NS
8	3.78 ± 2.51	3.42 ± 2.58	-0.08 ± 2.00	0.33 ± 2.30	NS
9	4.30 ± 1.56	-0.23 ± 2.20	-0.25 ± 2.29	-1.25 ± 2.67	NS
10	2.18± 3.01	3.70 ± 2.47	1.97 ± 2.16	-0.48 ± 2.43	NS
11	-0.23 ± 2.07	-2.21 ± 1.85	-1.18 ± 2.10	-2.03 ± 2.90	NS
12	4.62 ± 2.19	-0.85 ± 2.36	0.95 ± 1.98	-1.35 ± 3.02	NS

NS = non - significant among three face products and control.

$P < 0.05$ = significant among three face products and control.

The average values of change in erythema are shown in Table 33 whereas the individual data of each subject are provided in Appendix I and II. Latin square ANOVA was applied to the data in Table 33 and results are given in the same table.

No significant difference was detected in the values of change in erythema among the three body products and control in all weeks ($P > 0.05$). The observed change was as small as opposed to the change in melanin. Small negative values were also observed in both the product-treated and untreated areas, which implied that there had been a slight increase in skin redness at the time of measurements.

However, the erythema data from this study was somewhat different from the previous study with the face products in that the three body products failed to provide protective effect against erythema when compared to the control (non-treatment). The values among the three products were not different from the control at all weeks (P > 0.05). Nevertheless, there was a general trend that the change in erythema tended to increase from the more negative values during the early periods to the less negative or more positive values in the later periods (Table 33). This indicated that all the four areas of each subject showed a gradual decrease in the absolute erythema values with time regardless of the treatment or control. This had resulted in an increase in the change in erythema values for E, F, G and H. For example, the values of erythema change increased from –4.82 at week 1 to 4.62 at week 12 for product E. Similarly, the values increased from –8.57 to –0.85, –7.90 to 0.95, and from –6.83 to –1.35 for products F, G and control, respectively.

Similarity in the effect on skin erythema among the three body products and the control could be due to the strict adherence of each subject to the testing protocol, i.e., avoiding exposure to direct sunlight as much as possible. As a result, the UV-absorbers present in the formulations of E, F and G might not be able to exert its protective effect against erythema-inducing UV radiation. This had also led to a natural decrease in the absolute erythema values, which was also observed in the untreated control area as the subjects tried to stay indoors as much as possible. Therefore, the results from this study indicated that the three body-whitening products were well tolerated by the subjects. No subjects complained of any skin disorders such as rash or contact dermatitis, at least during the 12-week study. Changes in skin erythema were minimal and similar to control.

Hence, it can be concluded from the two studies that all the six products were effective in significantly reduce the melanin content of the subjects. The onset of effective whitening was also slightly faster with the face products (2 weeks) than the body products (3-6 weeks). Nevertheless, it should be emphasized that the melanin content was measured with a highly sensitive instrument (Mexameter MX16[®]), which

could differentiate a small difference in the melanin values whereas the highly subjective human eyes could not. During week 10-12 when highly significant differences in the melanin content were detected in subjects by Mexameter, visual observation failed to make a clearly visible distinction between the treated and untreated areas. Therefore, cautions should be given to consumers regarding the advertisements of these whitening products, which often try to impress the viewers by showing the face of a model being gradually but visibly whiter after application of their products within a few weeks.

Figure 15   Comparison of mean erythema values (difference from baseline) among

three whitening body products and control after application at various

periods. (value = Mean $\pm$ S.E.M., N = 12)

E = Product E , F = Product F, G = Product G, H = Control

X0 – Xi = initial melanin value – melanin value at week i,i= 2,4,6,8,10,12

Figure 11   Comparison of mean erythema values (difference from baseline) among

three whitening body products and control after application at various

periods.(cont.) (value = Mean $\pm$ S.E.M., N = 12)

E = Product E , F = Product F, G = Product G, H = Control

X0 – Xi = initial melanin value – melanin value at week i,i= 2,4,6,8,10,12

Figure 16.　　　Comparison of mean erythema values (difference from initial value) among three whitening body products and control after

application at various periods (value = Mean $\pm$ S.E.M, N = 12)

Product E = ◆ ,　　　Product F = ■ ,　　　Product G = Δ ,　　Control = X
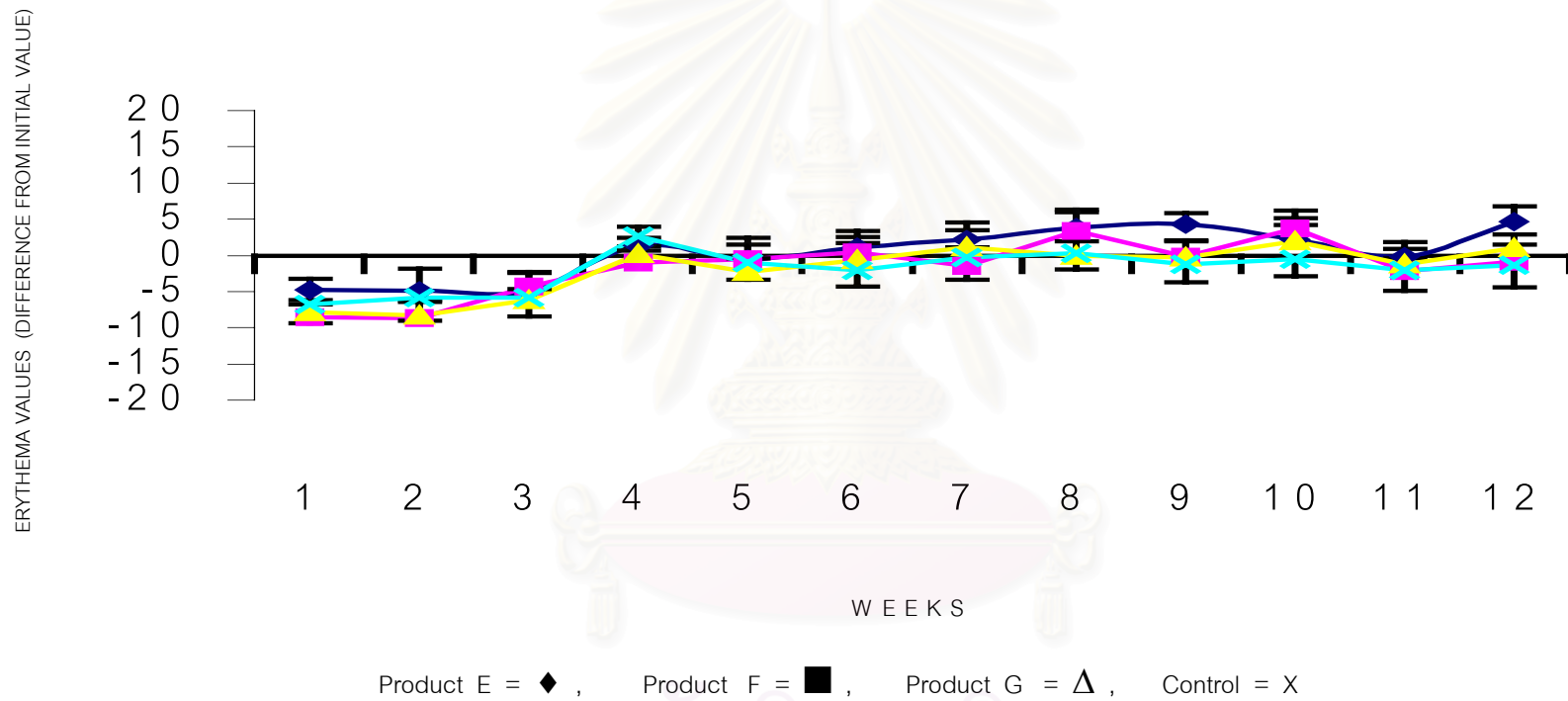
CHAPTER V

CONCLUSIONS

Six commercial whitening products, three for the face (A, B, C) and three for the body (E, F, G) have been evaluated in this study for their *in vivo* whitening activity and erythema inducing potential. The six products contained different types and concentrations of whitening agents such as tyrosinase inhibitors, vitamin B_3 and lactic acid. All of them also contained UV-A and UV-B absorbers used as sun-screening agents.

Two sets of 12 female volunteers (age 18-40) participated in two separate single-blinded studies with a Latin square design, one for the evaluation of the face products and the other for the body products. The protocol was similar between the two studies, which involved application of the three face products (or the three body products) on the pre-designated square-shaped areas of each subject's left and right forearms. One area was also allocated as a control area on which no product was applied. Thus, each subject would have four areas, three of which would be applied with the three whitening products and one would serve as an untreated control. Each subject applied the three products at the same time twice daily for 12 executive weeks according to the Latin square sequence. The melanin and erythema values of each subject were recorded at the start of the study (week 0) and every week after product application until 12 weeks using Mexameter MX$^{®}$ 16.

Results from the first study involving evaluation of the three face products can be summarized as follows:
1. All the three products (A, B and C) were equally effective in reducing the melanin content of the subjects, with a significant effect over the control ($P < 0.05$) first observed at 2 weeks after application. Significant difference from control was also detected in all subsequent weeks until 12 weeks.

2. Subtle differences among the three face products were noticed as a result of differences in the type and amount of active ingredients.

Product C, which contained 1% vitamin B_3, was found to give slightly greater whitening effect than product A (5% licorice extract) and product B (0.001% mulberry root extract, 0.01% Scutellaria baicalensis extract and 0.3% capryloyl salicylic acid. The results suggested that, depending on the concentration of each ingredient in the formulation, vitamin B_3 might be a more potent whitening agent than the tyrosinase inhibitors. Nevertheless, the three products were not statistically different in terms of their whitening efficacy during the 12-week period based on the Duncan's test.

3.   Results from erythema data revealed that the three face products were capable of reducing erythema from the initial values, implying that they might have a protective effect against erythema. This could be due to the presence of sun-screening agents (UV-A and UV-B absorbers) in the three products, which may have helped prevent the treated area from the irritating sunlight during the subject's routine outdoor activities (e.g. commuting between home and workplace).

Results from the second study on the three body products can be summarized as follows:

1. All the three products (E, F and G) were equally effective in reducing the melanin content of the subjects, with a significant effect over the control ($P < 0.05$) first observed at 3 weeks after application. However, significance was not observed at week 4 and 5. Only at week 6 and afterwards that significance from control was observed again, indicating a slower onset of action than the face products.

2. Subtle differences also existed among the three body products. Product E, which contained 8% lactic acid, was found to give slightly greater whitening effect than product G (1% vitamin B_3 and 0.1% fruit extract) and product F (0.5% licorice extract). The data from the body products suggested a general trend that a product, which contained a moderate to high concentration of lactic acid, might give

higher whitening effect than vitamin B_3, which in turn was more effective than tyrosinase inhibitors. However, more studies are needed to confirm this observation since several other factors must be taken into consideration such as the optimal concentration of each active ingredient, the type and formulation of the cream base as well as the presence of other whitening agents in the product.

3.   The effect of the three body products on skin erythema was similar to the control (non-treatment) at all weeks ($P > 0.05$). Also, the absolute erythema values tended to slowly decrease with time regardless of the treatment or control. This could be a result of the strict compliance of each subject to avoid exposure to sunlight, thereby causing a natural decrease in the absolute erythema values in both the treated and control areas.

The results from the two studies indicated that the six whitening products were well tolerated by the subjects. No subjects complained of any skin disorders such as rash or contact dermatitis, at least during the 12-week study. All six products were effective in significantly reduce the melanin content of the subjects. However, the effect was detected using a highly sensitive instrument (Mexameter MX 16[®]) whereas the normal human eyes could not. Therefore, cautions should be given to consumers regarding the advertisements of these whitening products, which tend to persuade them into believing that their products are "visibly" effective after only a few weeks of application.

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APPENDICES

APPENDIX I

Part 1   Absolute melanin values of the individual subjects after application of the three face products for different periods.(Data = mean $\pm$ S.E.M., N = 5 measurements)

Part 2   Absolute erythema values of the individual subjects after application of the three face products for different periods.(Data = mean $\pm$ S.E.M., N = 5 measurements)

Part 3   Absolute melanin values of the individual subjects after application of the three body products for different periods.(Data = mean $\pm$ S.E.M., N = 5 measurements)

Part 4   Absolute erythema values of the individual subjects after application of the three body products for different periods.(Data = mean $\pm$ S.E.M., N = 5 measurements)

PART 1   Absolute melanin values of the individual subjects after application of the three

face products for different periods. (Data = mean $\pm$ S.E.M., N = 5 measurements).

Subject 1 / Week	area1 (product A)	area2 (product B)	area3 (product C)	area4 (D=control)
0	544.60 $\pm$ 0.69	544.20 $\pm$ 0.83	544.60 $\pm$ 0.70	542.40 $\pm$ 0.60
1	538.20 $\pm$ 1.81	541.60 $\pm$ 1.27	549.60 $\pm$ 1.45	549.80 $\pm$ 1.25
2	542.60 $\pm$ 1.22	546.20 $\pm$ 0.51	546.20 $\pm$ 1.38	552.20 $\pm$ 1.81
3	536.40 $\pm$ 1.25	547.20 $\pm$ 0.85	542.40 $\pm$ 1.40	545.80 $\pm$ 0.55
4	534.20 $\pm$ 0.85	538.80 $\pm$ 0.63	544.00 $\pm$ 1.02	550.40 $\pm$ 0.53
5	535.20 $\pm$ 1.38	530.20 $\pm$ 0.63	537.40 $\pm$ 0.93	544.20 $\pm$ 0.92
6	533.40 $\pm$ 1.42	534.00 $\pm$ 1.14	529.40 $\pm$ 0.86	542.40 $\pm$ 0.44
7	527.80 $\pm$ 1.39	535.00 $\pm$ 0.77	532.20 $\pm$ 0.55	545.20 $\pm$ 0.63
8	535.40 $\pm$ 0.44	533.40 $\pm$ 0.93	535.20 $\pm$ 1.05	541.00 $\pm$ 0.41
9	532.60 $\pm$ 0.44	533.00 $\pm$ 0.41	532.60 $\pm$ 0.90	546.20 $\pm$ 0.66
10	527.40 $\pm$ 0.39	527.80 $\pm$ 0.95	527.80 $\pm$ 0.69	544.80 $\pm$ 0.55
11	531.40 $\pm$ 0.95	530.40 $\pm$ 0.73	527.00 $\pm$ 0.98	542.00 $\pm$ 0.98
12	533.60 $\pm$ 1.24	527.60 $\pm$ 0.86	528.00 $\pm$ 1.24	546.40 $\pm$ 0.26

Subject 2 / Week	area1 (product B)	area2 (product C)	area3 (D=control)	area4 (product A)
0	573.20 $\pm$ 1.45	579.80 $\pm$ 1.42	568.40 $\pm$ 1.05	572.00 $\pm$ 0.84
1	566.40 $\pm$ 0.78	574.00 $\pm$ 1.32	562.80 $\pm$ 0.92	573.40 $\pm$ 0.56
2	573.00 $\pm$ 0.45	573.60 $\pm$ 1.13	563.20 $\pm$ 0.69	573.00 $\pm$ 1.80
3	564.00 $\pm$ 0.64	575.20 $\pm$ 0.66	568.80 $\pm$ 0.75	567.40 $\pm$ 1.22
4	558.20 $\pm$ 0.32	573.00 $\pm$ 0.35	560.80 $\pm$ 0.43	564.20 $\pm$ 0.97
5	564.80 $\pm$ 0.88	574.80 $\pm$ 1.18	565.80 $\pm$ 0.43	568.20 $\pm$ 1.38
6	558.60 $\pm$ 1.34	565.60 $\pm$ 0.60	562.80 $\pm$ 0.85	561.20 $\pm$ 0.90
7	552.00 $\pm$ 0.29	563.80 $\pm$ 0.52	561.00 $\pm$ 1.40	560.00 $\pm$ 1.32
8	553.80 $\pm$ 0.43	570.40 $\pm$ 0.63	567.60 $\pm$ 1.20	565.20 $\pm$ 1.39
9	568.00 $\pm$ 0.35	579.00 $\pm$ 0.50	569.00 $\pm$ 0.74	567.60 $\pm$ 0.33
10	561.22 $\pm$ 0.75	571.40 $\pm$ 0.53	568.20 $\pm$ 1.44	568.00 $\pm$ 0.54
11	554.80 $\pm$ 0.47	566.00 $\pm$ 0.79	566.00 $\pm$ 1.06	565.40 $\pm$ 0.56
12	561.80 $\pm$ 0.24	573.00 $\pm$ 0.74	568.40 $\pm$ 0.83	564.80 $\pm$ 0.38

Subject 3 / Week	area1 (product C)	area2 (D=control)	area3 (product A)	area4 (product B)
0	568.40 ± 0.86	564.60 ± 1.01	563.20 ± 0.97	560.60 ± 0.78
1	552.20 ± 1.11	553.40 ± 1.32	549.80 ± 1.44	552.60 ± 1.44
2	558.40 ± 1.89	561.40 ± 1.34	556.00 ± 1.86	551.00 ± 0.87
3	553.20 ± 1.01	556.00 ± 1.02	552.20 ± 1.28	547.60 ± 0.86
4	552.00 ± 1.08	558.40 ± 1.71	543.40 ± 1.55	547.20 ± 2.10
5	553.20 ± 0.90	553.80 ± 1.25	546.20 ± 1.49	544.00 ± 0.21
6	557.40 ± 1.17	554.00 ± 1.34	549.60 ± 1.62	546.60 ± 1.36
7	551.20 ± 0.83	557.00 ± 1.26	551.40 ± 1.09	536.00 ± 0.46
8	552.00 ± 0.35	558.40 ± 1.09	547.60 ± 1.77	541.40 ± 1.24
9	550.60 ± 1.09	561.60 ± 1.32	554.60 ± 1.30	546.80 ± 0.66
10	552.00 ± 1.31	557.60 ± 1.03	548.00 ± 1.08	537.20 ± 1.07
11	544.20 ± 1.25	557.00 ± 1.17	546.80 ± 0.85	543.00 ± 0.68
12	550.80 ± 0.47	556.60 ± 0.53	549.80 ± 1.05	543.00 ± 1.53

Subject 4 / Week	area1 (D=control)	area2 (product A)	area3 (product B)	area4 (product C)
0	554.80 ± 0.63	563.00 ± 1.24	550.00 ± 0.89	553.80 ± 0.32
1	550.00 ± 1.12	557.40 ± 1.50	545.00 ± 0.41	550.40 ± 1.42
2	557.00 ± 0.89	558.40 ± 1.17	548.60 ± 0.63	558.60 ± 0.86
3	559.80 ± 1.07	560.40 ± 1.25	547.60 ± 1.11	553.80 ± 1.25
4	560.00 ± 1.26	561.40 ± 1.66	545.60 ± 0.56	552.80 ± 0.38
5	551.80 ± 0.88	556.80 ± 1.58	542.20 ± 1.09	552.80 ± 0.72
6	555.20 ± 1.03	561.60 ± 0.56	544.20 ± 0.32	554.20 ± 0.80
7	555.00 ± 0.58	562.20 ± 0.66	541.80 ± 0.97	549.80 ± 0.32
8	553.80 ± 0.90	554.40 ± 0.78	539.40 ± 0.48	542.60 ± 1.11
9	555.20 ± 0.80	555.00 ± 0.21	534.80 ± 0.92	541.40 ± 0.60
10	555.60 ± 0.97	553.00 ± 0.54	530.80 ± 1.32	545.00 ± 0.74
11	558.40 ± 0.93	554.20 ± 0.32	539.80 ± 0.52	542.40 ± 0.39
12	552.40 ± 0.56	552.40 ± 0.83	538.80 ± 0.85	544.80 ± 0.66

Subject 5 / Week	area1 (product A)	area2 (product B)	area3 (product C)	area4 (D=Control)
0	554.40 ± 0.97	552.20 ± 1.25	560.80 ± 1.28	560.80 ± 0.97
1	550.20 ± 0.47	544.60 ± 0.86	553.00 ± 0.68	562.00 ± 0.46
2	550.60 ± 0.48	551.00 ± 1.04	553.40 ± 1.13	562.80 ± 0.52
3	550.00 ± 0.79	545.00 ± 0.68	555.40 ± 0.44	562.00 ± 0.21
4	546.80 ± 0.92	546.40 ± 0.88	547.80 ± 0.75	557.00 ± 1.62
5	549.40 ± 0.95	545.60 ± 1.18	549.00 ± 0.96	561.00 ± 0.91
6	545.80 ± 0.75	546.80 ± 0.55	555.60 ± 0.56	561.80 ± 0.38
7	548.20 ± 0.38	544.40 ± 0.97	550.60 ± 0.33	563.00 ± 0.74
8	553.80 ± 0.75	557.80 ± 0.24	553.80 ± 0.92	564.00 ± 1.08
9	552.00 ± 0.46	547.80 ± 0.66	549.60 ± 0.48	563.40 ± 0.75
10	547.00 ± 0.58	540.80 ± 0.24	547.20 ± 1.09	563.00 ± 0.21
11	545.20 ± 0.47	540.80 ± 0.77	549.40 ± 0.78	562.60 ± 0.93
12	544.60 ± 0.80	540.60 ± 0.56	550.60 ± 0.33	562.00 ± 0.46

Subject 6 / Week	area1 (product B)	area2 (product C)	area3 (D =control)	area4 (product A)
0	574.40 ± 0.97	575.00 ± 1.31	582.40 ± 0.60	577.00 ± 0.54
1	573.80 ± 1.35	576.40 ± 0.75	574.20 ± 0.75	574.20 ± 0.61
2	572.20 ± 1.52	570.60 ± 0.75	586.20 ± 1.93	571.60 ± 0.91
3	570.00 ± 1.24	570.00 ± 1.24	579.40 ± 1.03	570.40 ± 1.40
4	576.00 ± 1.06	571.60 ± 0.70	583.40 ± 1.03	567.60 ± 0.86
5	567.60 ± 1.50	573.00 ± 1.29	578.20 ± 0.47	569.60 ± 0.56
6	566.80 ± 0.32	569.40 ± 0.44	573.40 ± 1.18	566.80 ± 1.60
7	568.00 ± 0.84	572.80 ± 1.25	577.20 ± 0.97	573.00 ± 0.91
8	567.60 ± 0.56	568.00 ± 0.41	570.80 ± 0.75	569.80 ± 1.38
9	563.40 ± 0.60	566.20 ± 0.43	577.20 ± 0.14	566.00 ± 0.84
10	566.40 ± 0.75	563.00 ± 0.96	574.60 ± 0.81	565.20 ± 0.32
11	563.60 ± 0.53	561.40 ± 0.39	576.60 ± 0.83	566.60 ± 0.44
12	567.20 ± 0.77	561.00 ± 0.00	578.60 ± 1.11	569.40 ± 0.33

Subject 7 / Week	area1 (product C)	area2 (D=control)	area3 (product A)	area4 (product B)
0	550.00 ± 0.46	545.80 ± 0.80	552.00 ± 0.68	539.60 ± 0.33
1	537.40 ± 1.11	543.20 ± 0.55	549.60 ± 1.45	527.20 ± 1.09
2	540.20 ± 0.80	544.40 ± 0.75	540.40 ± 0.86	529.40 ± 0.73
3	540.00 ± 0.71	542.20 ± 1.66	539..80 ± 0.90	532.80 ± 1.07
4	540.20 ± 0.75	546.00 ± 0.35	541.60 ± 1.05	533.80 ± 1.03
5	532.20 ± 0.55	544.80 ± 1.18	537.00 ± 1.28	535.80 ± 1.05
6	533.20 ± 0.75	545.60 ± 0.88	537.60 ± 0.44	525.60 ± 0.56
7	531.60 ± 0.69	544.20 ± 1.28	539.80 ± 0.72	528.80 ± 0.24
8	535.80 ± 0.99	544.60 ± 0.88	531.60 ± 0.63	521.80 ± 0.69
9	532.20 ± 0.59	540.60 ± 0.73	534.20 ± 1.13	523.60 ± 0.44
10	529.20 ± 0.59	545.40 ± 0.69	528.60 ± 0.75	522.60 ± 0.53
11	523.80 ± 0.63	545.80 ± 0.63	523.00 ± 0.05	525.80 ± 0.24
12	524.60 ± 0.44	545.20 ± 0.55	528.40 ± 0.53	525.20 ± 0.32

Subject 8 / Week	area1 (D=control)	area2 (product A)	area3 (product B)	area4 (product C)
0	541.80 ± 0.55	538.20 ± 0.65	536.00 ± 0.54	534.40 ± 1.20
1	538.60 ± 0.56	536.80 ± 1.25	535.00 ± 0.54	533.60 ± 1.11
2	540.00 ± 0.41	532.60 ± 0.44	534.40 ± 0.26	529.00 ± 1.00
3	540.80 ± 1.11	532.80 ± 1.14	536.00 ± 1.06	531.80 ± 0.75
4	543.20 ± 0.38	535.20 ± 0.83	537.60 ± 1.05	535.80 ± 1.33
5	540.40 ± 0.73	535.60 ± 0.60	536.40 ± 0.73	530.80 ± 1.28
6	542.20 ± 0.69	532.60 ± 0.84	532.60 ± 0.44	529.20 ± 1.07
7	540.60 ± 0.88	532.00 ± 0.84	533.60 ± 0.53	530.80 ± 0.24
8	540.00 ± 0.71	531.40 ± 0.56	530.20 ± 0.66	530.20 ± 0.65
9	542.20 ± 0.88	533.80 ± 0.75	531.20 ± 0.55	532.60 ± 0.53
10	541.20 ± 0.59	532.40 ± 0.39	531.40 ± 0.81	526.40 ± 0.44
11	539.40 ± 0.70	525.60 ± 0.33	525.60 ± 0.16	525.80 ± 0.88
12	540.00 ± 0.46	531.40 ± 0.44	527.60 ± 0.39	528.40 ± 0.48

Subject 9 / Week	area1 (product A)	area2 (product B)	area3 (product C)	area4 (D = control)
0	552.00 ± 0.74	551.00 ± 0.79	544.20 ± 0.75	549.00 ± 0.71
1	547.40 ± 1.30	545.60 ± 1.07	544.00 ± 0.50	544.40 ± 0.75
2	550.00 ± 1.14	543.00 ± 0.58	543.60 ± 0.88	548.00 ± 1.23
3	544.60 ± 0.53	540.00 ± 1.17	540.00 ± 0.41	544.20 ± 0.52
4	546.40 ± 1.01	541.40 ± 0.90	538.60 ± 1.01	544.80 ± 0.85
5	545.00 ± 0.68	539.40 ± 0.60	535.00 ± 0.84	541.00 ± 1.34
6	543.20 ± 0.52	540.20 ± 1.20	534.80 ± 0.72	547.20 ± 1.21
7	545.80 ± 0.69	545.20 ± 0.80	538.20 ± 0.55	545.20 ± 1.09
8	548.00 ± 0.91	543.80 ± 0.38	537.20 ± 0.69	544.60 ± 0.83
9	546.40 ± 0.93	540.80 ± 1.03	532.20 ± 0.47	545.80 ± 0.77
10	546.80 ± 0.43	540.60 ± 1.07	534.60 ± 0.48	547.60 ± 1.13
11	542.20 ± 1.07	535.20 ± 0.55	529.40 ± 0.44	546.00 ± 0.54
12	542.00 ± 0.41	538.80 ± 0.32	532.40 ± 0.70	551.00 ± 1.24

Subject 10 / Week	area1 (product B)	area2 (product C)	area3 (D=control)	area4 (product A)
0	544.20 ± 1.03	544.20 ± 1.60	544.60 ± 0.97	546.40 ± 1.30
1	547.80 ± 0.72	546.60 ± 1.35	548.20 ± 0.43	541.00 ± 0.91
2	549.20 ± 1.05	547.20 ± 0.95	548.80 ± 1.14	545.80 ± 1.23
3	547.20 ± 1.25	546.80 ± 1.55	551.00 ± 0.82	542.00 ± 0.35
4	543.20 ± 0.63	545.00 ± 0.82	548.60 ± 0.48	543.80 ± 0.88
5	542.20 ± 1.14	535.80 ± 1.20	543.80 ± 0.80	540.20 ± 0.66
6	537.20 ± 0.32	542.80 ± 1.66	547.80 ± 0.77	541.00 ± 0.82
7	543.60 ± 0.86	542.60 ± 0.81	547.80 ± 0.63	547.80 ± 0.80
8	542.40 ± 0.26	543.00 ± 0.68	547.00 ± 1.66	544.60 ± 0.70
9	539.40 ± 0.66	535.80 ± 0.72	543.60 ± 0.56	541.20 ± 0.38
10	538.00 ± 0.74	536.20 ± 0.63	552.00 ± 0.98	540.00 ± 1.24
11	537.00 ± 0.35	533.60 ± 0.66	549.40 ± 0.66	540.40 ± 0.56
12	537.00 ± 0.82	536.40 ± 0.66	550.20 ± 0.63	539.40 ± 0.33

Subject 11 / Week	area1 (product C)	area2 (D =control)	area3 (product A)	area4 (product B)
0	544.40 ± 0.95	542.20 ± 0.75	543.00 ± 0.84	537.80 ± 1.35
1	544.00 ± 0.54	539.00 ± 0.74	542.00 ± 1.65	542.00 ± 0.87
2	543.20 ± 0.95	538.80 ± 1.36	539.40 ± 1.09	535.60 ± 1.55
3	542.60 ± 1.35	537.80 ± 0.83	540.40 ± 0.39	535.80 ± 0.97
4	536.00 ± 0.98	537.00 ± 0.46	538.80 ± 0.77	533.20 ± 1.09
5	545.00 ± 0.35	542.20 ± 0.47	544.00 ± 0.68	536.00 ± 0.84
6	542.40 ± 0.26	542.40 ± 0.56	538.80 ± 1.20	535.20 ± 0.80
7	537.80 ± 0.52	541.80 ± 0.24	537.80 ± 0.43	527.40 ± 0.73
8	535.80 ± 0.47	537.40 ± 0.44	536.40 ± 0.26	528.60 ± 0.97
9	540.60 ± 0.16	546.40 ± 0.39	541.60 ± 0.56	534.60 ± 0.44
10	543.60 ± 0.48	546.20 ± 0.80	537.60 ± 0.78	534.80 ± 0.63
11	536.60 ± 0.53	541.80 ± 0.52	537.60 ± 1.05	530.40 ± 0.48
12	539.40 ± 0.66	545.80 ± 0.52	538.80 ± 0.47	534.40 ± 0.56

Subject 12 / Week	area1 (D=control)	area2 (product A)	area3 (product B)	area4 (product C)
0	548.60 ± 0.88	548.00 ± 0.74	546.20 ± 0.38	552.60 ± 0.16
1	548.60 ± 0.33	545.20 ± 1.13	540.60 ± 0.93	545.20 ± 0.55
2	548.40 ± 0.60	543.00 ± 0.71	543.00 ± 1.36	542.60 ± 0.60
3	548.20 ± 0.83	542.60 ± 1.05	542.00 ± 0.82	539.60 ± 0.53
4	548.00 ± 1.08	537.80 ± 1.27	538.80 ± 0.75	540.60 ± 1.20
5	547.80 ± 1.07	539.60 ± 0.53	536.00 ± 1.02	535.80 ± 1.41
6	547.60 ± 1.20	537.20 ± 0.99	536.80 ± 1.28	537.60 ± 1.01
7	548.20 ± 0.69	533.40 ± 0.53	535.40 ± 1.17	533.00 ± 0.71
8	548.00 ± 0.74	538.80 ± 0.85	534.80 ± 0.47	533.80 ± 0.83
9	546.40 ± 0.66	531.60 ± 0.26	528.20 ± 0.59	525.40 ± 1.09
10	549.40 ± 1.30	532.60 ± 1.05	532.00 ± 0.98	526.80 ± 0.83
11	547.40 ± 0.44	533.00 ± 0.74	530.60 ± 1.33	527.00 ± 0.94
12	548.40 ± 0.83	536.60 ± 1.09	530.40 ± 0.53	530.20 ± 1.01

PART 2   Absolute erythema values of the individual subjects after application of the three

face products for different periods. (Data = mean $\pm$ S.E.M., N = 5)

Subject 1 / Week	area1 (product A)	area2 (product B)	area3 (product C)	area4 (D=control)
0	597.00 $\pm$ 1.21	596.60 $\pm$ 1.29	600.20 $\pm$ 1.13	592.00 $\pm$ 1.19
1	595.60 $\pm$ 1.11	615.20 $\pm$ 1.20	607.60 $\pm$ 1.17	609.80 $\pm$ 0.66
2	603.80 $\pm$ 1.32	605.60 $\pm$ 1.27	612.20 $\pm$ 0.66	608.20 $\pm$ 0.43
3	592.80 $\pm$ 1.18	604.80 $\pm$ 0.55	603.80 $\pm$ 1.01	604.00 $\pm$ 1.37
4	594.00 $\pm$ 1.24	594.00 $\pm$ 0.86	594.00 $\pm$ 0.73	594.00 $\pm$ 0.90
5	592.80 $\pm$ 0.38	595.60 $\pm$ 1.17	596.20 $\pm$ 1.03	601.40 $\pm$ 0.90
6	592.00 $\pm$ 1.50	594.20 $\pm$ 1.38	613.40 $\pm$ 1.63	611.20 $\pm$ 1.13
7	594.60 $\pm$ 0.75	593.00 $\pm$ 1.28	595.20 $\pm$ 1.03	604.60 $\pm$ 0.99
8	589.60 $\pm$ 0.78	584.80 $\pm$ 0.92	584.20 $\pm$ 0.80	591.20 $\pm$ 0.52
9	596.60 $\pm$ 1.17	595.80 $\pm$ 1.47	592.60 $\pm$ 1.35	604.60 $\pm$ 1.24
10	598.20 $\pm$ 1.33	596.80 $\pm$ 0.75	595.20 $\pm$ 1.38	606.60 $\pm$ 0.26
11	596.80 $\pm$ 1.11	593.20 $\pm$ 0.38	591.20 $\pm$ 1.51	605.00 $\pm$ 1.04
12	601.80 $\pm$ 0.95	592.60 $\pm$ 0.70	588.60 $\pm$ 1.56	610.00 $\pm$ 1.58

Subject 2 / Week	area1 (product B)	area2 (product C)	area3 (D =control)	area4 (product A)
0	619.40 $\pm$ 0.90	618.20 $\pm$ 1.55	618.40 $\pm$ 1.24	616.80 $\pm$ 1.13
1	616.00 $\pm$ 1.02	618.20 $\pm$ 1.09	616.40 $\pm$ 1.50	629.00 $\pm$ 1.23
2	628.80 $\pm$ 1.05	628.80 $\pm$ 1.03	634.20 $\pm$ 0.88	627.80 $\pm$ 0.66
3	624.40 $\pm$ 1.56	638.40 $\pm$ 1.41	633.00 $\pm$ 1.04	629.40 $\pm$ 1.38
4	615.20 $\pm$ 1.47	615.60 $\pm$ 0.60	611.60 $\pm$ 1.17	619.00 $\pm$ 1.34
5	622.80 $\pm$ 0.80	619.20 $\pm$ 1.36	623.00 $\pm$ 1.21	623.80 $\pm$ 1.11
6	622.60 $\pm$ 0.78	621.20 $\pm$ 1.33	622.00 $\pm$ 1.02	627.60 $\pm$ 0.97
7	611.60 $\pm$ 1.01	618.00 $\pm$ 1.02	622.40 $\pm$ 0.78	625.80 $\pm$ 0.99
8	611.40 $\pm$ 5.52	615.00 $\pm$ 1.29	616.80 $\pm$ 1.22	617.80 $\pm$ 0.79
9	618.00 $\pm$ 1.58	620.00 $\pm$ 1.34	618.60 $\pm$ 1.41	626.60 $\pm$ 0.33
10	614.60 $\pm$ 0.86	618.80 $\pm$ 0.72	613.20 $\pm$ 0.83	622.80 $\pm$ 0.52
11	613.20 $\pm$ 0.95	615.80 $\pm$ 1.55	611.20 $\pm$ 0.88	613.20 $\pm$ 0.75
12	616.60 $\pm$ 1.47	620.20 $\pm$ 0.55	617.60 $\pm$ 0.59	619.80 $\pm$ 1.03

Subject 3 / Week	area1 (product C)	area2 (D=control)	area3 (product A)	area4 (product B)
0	619.20 ± 1.01	621.00 ± 0.96	619.80 ± 0.95	620.20 ± 0.85
1	613.60 ± 1.45	623.40 ± 1.77	613.20 ± 0.90	614.00 ± 1.40
2	624.20 ± 1.25	624.60 ± 1.66	625.20 ± 1.13	619.20 ± 1.39
3	620.20 ± 0.38	624.80 ± 1.14	606.20 ± 1.43	620.40 ± 0.53
4	620.80 ± 0.75	622.20 ± 0.85	613.20 ± 1.03	610.20 ± 1.33
5	619.80 ± 1.18	619.20 ± 1.53	605.80 ± 1.60	614.40 ± 1.42
6	622.60 ± 0.78	620.00 ± 1.51	618.00 ± 0.54	613.80 ± 0.88
7	605.80 ± 1.11	610.00 ± 1.17	607.60 ± 1.72	610.40 ± 1.25
8	609.20 ± 1.14	609.40 ± 1.32	603.20 ± 1.15	607.60 ± 1.40
9	609.20 ± 1.51	612.00 ± 1.31	607.80 ± 1.70	609.00 ± 0.54
10	611.60 ± 0.66	615.60 ± 0.56	621.40 ± 0.97	613.80 ± 0.75
11	603.00 ± 1.60	619.80 ± 1.55	609.60 ± 1.36	609.60 ± 1.27
12	602.20 ± 1.35	605.40 ± 1.30	618.20 ± 0.24	616.40 ± 1.25

Subject 4 / Week	area1 (D =control)	area2 (product A)	area3 (product B)	area4 (product C)
0	618.40 ± 0.75	625.40 ± 0.97	611.00 ± 1.61	616.80 ± 0.90
1	614.60 ± 1.51	615.00 ± 0.46	607.40 ± 1.20	621.40 ± 1.32
2	620.80 ± 0.55	612.60 ± 0.66	612.60 ± 1.38	625.80 ± 1.03
3	615.20 ± 0.95	618.80 ± 0.97	612.60 ± 1.18	625.20 ± 1.07
4	623.40 ± 1.07	618.40 ± 1.36	618.80 ± 1.39	627.40 ± 1.36
5	618.60 ± 1.01	609.00 ± 0.91	615.80 ± 1.20	620.60 ± 0.93
6	620.20 ± 0.99	614.00 ± 1.51	616.00 ± 1.31	627.40 ± 1.51
7	621.20 ± 0.90	602.40 ± 1.15	607.80 ± 0.88	620.40 ± 1.40
8	622.20 ± 1.25	604.60 ± 0.73	607.60 ± 1.25	613.80 ± 0.69
9	623.20 ± 0.85	623.00 ± 0.54	617.40 ± 1.17	625.80 ± 1.58
10	621.20 ± 1.44	613.40 ± 1.59	613.00 ± 1.34	619.20 ± 1.49
11	617.00 ± 1.00	611.20 ± 0.80	616.20 ± 0.75	618.40 ± 1.63
12	609.60 ± 1.38	614.40 ± 1.27	616.80 ± 1.44	621.00 ± 0.58

Subject 5 / Week	area1 (product A)	area2 (product B)	area3 (product C)	area4 (D = control)
0	618.20 ± 0.66	618.40 ± 1.54	621.00 ± 1.65	615.40 ± 1.62
1	619.00 ± 1.75	618.60 ± 1.13	628.00 ± 0.84	620.20 ± 1.35
2	616.80 ± 0.38	621.20 ± 1.35	623.20 ± 1.33	620.20 ± 1.09
3	620.60 ± 0.56	622.80 ± 1.14	623.20 ± 1.35	617.80 ± 0.90
4	620.60 ± 1.86	620.40 ± 1.62	625.20 ± 1.55	621.80 ± 0.69
5	617.80 ± 1.28	614.80 ± 0.80	628.60 ± 1.24	627.60 ± 1.27
6	609.00 ± 1.17	617.00 ± 1.67	619.40 ± 1.27	613.80 ± 1.60
7	614.00 ± 1.36	613.40 ± 0.86	617.40 ± 1.05	617.60 ± 1.17
8	606.40 ± 1.25	602.60 ± 1.20	621.60 ± 1.24	614.80 ± 1.25
9	611.80 ± 1.38	611.60 ± 0.88	616.80 ± 0.55	619.80 ± 1.70
10	605.20 ± 0.83	605.20 ± 1.03	613.60 ± 0.88	615.40 ± 1.24
11	609.60 ± 1.71	616.20 ± 0.92	616.20 ± 1.65	604.40 ± 1.27
12	604.00 ± 0.84	604.00 ± 1.29	609.60 ± 1.11	620.80 ± 1.60

Subject 6 / Week	area1 (product B)	area2 (product C)	area3 (D =Control)	area4 (product A)
0	622.20 ± 1.30	627.80 ± 1.28	631.40 ± 1.47	623.80 ± 1.07
1	621.60 ± 1.30	626.80 ± 1.35	632.40 ± 1.66	627.20 ± 1.51
2	636.60 ± 0.44	635.00 ± 1.56	633.60 ± 0.93	632.60 ± 1.45
3	626.60 ± 1.42	634.40 ± 0.78	635.80 ± 0.55	630.00 ± 0.94
4	626.00 ± 1.45	625.00 ± 0.71	629.80 ± 1.25	624.80 ± 1.28
5	624.40 ± 1.51	628.00 ± 1.36	632.20 ± 1.03	625.00 ± 1.06
6	629.20 ± 1.32	625.80 ± 1.58	630.20 ± 1.62	629.60 ± 0.60
7	620.40 ± 1.05	620.60 ± 1.01	626.80 ± 0.63	633.60 ± 0.60
8	626.60 ± 1.03	617.60 ± 1.30	628.40 ± 1.32	627.80 ± 0.69
9	620.00 ± 1.42	622.00 ± 1.06	621.20 ± 1.33	624.00 ± 1.39
10	623.40 ± 1.18	616.40 ± 1.40	636.60 ± 1.58	626.20 ± 1.52
11	620.60 ± 0.39	632.60 ± 0.56	623.00 ± 1.10	626.00 ± 1.34
12	629.40 ± 0.73	620.20 ± 1.33	623.60 ± 1.09	625.40 ± 0.86

Subject 7 / Week	area1 (product C)	area2 (D = control)	area3 (product A)	area4 (product B)
0	611.40 ± 1.45	611.80 ± 1.41	612.40 ± 1.56	608.80 ± 1.47
1	612.60 ± 1.52	618.40 ± 1.03	612.00 ± 1.45	607.80 ± 1.25
2	627.60 ± 0.75	618.20 ± 1.55	618.00 ± 1.67	603.00 ± 0.71
3	617.80 ± 0.80	613.20 ± 1.70	612.40 ± 1.68	611.20 ± 1.05
4	621.40 ± 1.44	612.40 ± 1.34	614.40 ± 1.44	610.80 ± 1.28
5	609.40 ± 1.86	613.40 ± 1.36	617.00 ± 0.61	611.60 ± 0.73
6	614.60 ± 0.97	622.00 ± 1.70	602.60 ± 1.01	611.20 ± 1.25
7	619.40 ± 0.55	614.60 ± 0.97	608.00 ± 1.16	608.60 ± 1.17
8	617.40 ± 1.13	604.00 ± 1.02	613.60 ± 1.32	610.80 ± 1.01
9	602.80 ± 1.38	599.80 ± 1.03	608.60 ± 1.40	608.80 ± 1.47
10	619.60 ± 1.11	615.60 ± 1.09	611.00 ± 0.71	617.80 ± 0.90
11	612.20 ± 0.80	600.40 ± 1.32	617.40 ± 1.09	607.20 ± 1.28
12	606.60 ± 1.25	600.20 ± 1.47	605.60 ± 1.05	601.20 ± 1.29

Subject 8 / Week	area1 (D = control)	area2 (product A)	area3 (product B)	area4 (product C)
0	606.40 ± 1.38	610.20 ± 0.95	599.80 ± 1.28	604.40 ± 1.20
1	606.20 ± 0.85	604.00 ± 1.08	593.60 ± 1.15	612.00 ± 1.19
2	609.00 ± 0.98	605.20 ± 1.33	607.20 ± 1.22	608.60 ± 0.48
3	606.20 ± 1.20	600.80 ± 0.59	605.00 ± 1.51	605.40 ± 1.17
4	613.80 ± 1.45	605.60 ± 0.75	608.60 ± 0.93	609.60 ± 1.03
5	615.40 ± 1.30	606.80 ± 1.68	605.60 ± 0.78	607.00 ± 1.21
6	613.60 ± 1.48	599.20 ± 0.69	601.20 ± 0.83	606.40 ± 1.77
7	601.80 ± 1.25	598.60 ± 1.59	607.80 ± 1.13	609.80 ± 1.25
8	605.20 ± 1.52	595.60 ± 1.51	601.80 ± 1.20	607.60 ± 1.34
9	612.40 ± 1.09	602.80 ± 0.90	611.40 ± 1.13	612.00 ± 1.23
10	619.40 ± 0.83	610.80 ± 1.01	618.00 ± 1.02	616.60 ± 1.13
11	603.20 ± 0.80	606.60 ± 1.07	611.00 ± 1.12	607.80 ± 1.42
12	605.40 ± 1.48	603.00 ± 1.10	600.40 ± 1.54	604.40 ± 1.62

Subject 9 / Week	area1 (product A)	area2 (product B)	area3 (product C)	area4 (D= control)
0	613.00 ± 1.17	612.40 ± 1.58	608.40 ± 1.52	608.80 ± 1.42
1	607.00 ± 0.01	603.20 ± 0.01	613.80 ± 0.97	613.20 ± 1.13
2	612.00 ± 0.71	609.40 ± 1.52	617.20 ± 1.33	620.20 ± 1.60
3	604.20 ± 0.80	607.60 ± 1.03	612.20 ± 1.28	598.00 ± 1.02
4	606.00 ± 1.10	605.80 ± 1.07	605.20 ± 1.27	605.00 ± 1.36
5	603.20 ± 1.28	600.60 ± 0.81	608.00 ± 0.68	605.00 ± 1.24
6	608.00 ± 0.98	608.40 ± 1.01	609.00 ± 1.49	613.40 ± 1.11
7	602.40 ± 1.15	602.00 ± 1.60	606.80 ± 1.18	610.20 ± 1.41
8	598.80 ± 1.42	602.20 ± 0.72	605.80 ± 0.55	613.60 ± 1.39
9	601.40 ± 1.44	605.60 ± 1.30	604.60 ± 1.52	607.20 ± 0.83
10	612.40 ± 0.75	608.20 ± 0.75	609.00 ± 1.14	613.80 ± 0.92
11	607.60 ± 1.36	608.60 ± 0.73	598.60 ± 1.48	613.20 ± 1.51
12	592.40 ± 1.73	596.80 ± 0.90	601.40 ± 0.95	608.80 ± 1.63

Subject 10 / Week	area1 (product B)	area2 (product C)	area3 (D = control)	area4 (product A)
0	602.40 ± 1.37	603.00 ± 1.32	601.20 ± 0.88	606.20 ± 0.75
1	606.40 ± 1.29	620.60 ± 0.88	609.80 ± 1.01	604.20 ± 1.14
2	603.40 ± 1.41	607.60 ± 1.64	611.40 ± 1.41	610.20 ± 1.05
3	604.80 ± 0.55	607.20 ± 1.36	610.80 ± 0.55	607.60 ± 1.40
4	605.00 ± 1.68	610.40 ± 0.75	606.80 ± 1.68	605.20 ± 1.20
5	609.00 ± 1.28	628.40 ± 0.81	613.40 ± 1.63	611.20 ± 1.13
6	601.20 ± 1.03	603.40 ± 0.99	612.60 ± 1.50	601.20 ± 0.66
7	600.80 ± 1.03	603.40 ± 1.09	603.00 ± 0.82	600.00 ± 0.77
8	603.60 ± 1.05	609.60 ± 1.36	610.20 ± 1.07	608.60 ± 1.13
9	597.80 ± 0.97	597.60 ± 1.30	612.40 ± 1.20	602.80 ± 1.38
10	596.40 ± 0.97	604.60 ± 1.30	606.80 ± 1.41	607.00 ± 1.43
11	600.20 ± 0.55	594.80 ± 1.14	608.80 ± 1.60	607.80 ± 1.16
12	604.60 ± 1.35	609.60 ± 0.88	605.60 ± 1.40	603.40 ± 1.01

Subject 11 / Week	area1 (product C)	area2 (D = control)	area3 (product A)	area4 (product B)
0	607.20 ± 1.30	606.20 ± 1.33	602.00 ± 1.40	601.40 ± 1.32
1	605.40 ± 1.20	595.80 ± 0.72	605.80 ± 0.80	598.00 ± 1.02
2	609.20 ± 1.60	602.80 ± 0.77	603.80 ± 0.63	597.40 ± 1.11
3	601.20 ± 1.41	598.20 ± 1.07	595.20 ± 0.83	595.40 ± 0.44
4	603.60 ± 1.24	601.00 ± 0.98	609.60 ± 0.99	602.60 ± 1.01
5	611.00 ± 1.14	605.80 ± 1.55	609.60 ± 1.40	597.60 ± 0.88
6	601.40 ± 1.05	607.80 ± 1.13	605.20 ± 1.44	592.60 ± 1.22
7	605.80 ± 1.07	604.00 ± 0.79	601.20 ± 1.47	595.80 ± 1.16
8	606.60 ± 0.48	609.00 ± 1.14	609.60 ± 1.64	614.60 ± 1.56
9	605.20 ± 0.95	605.40 ± 1.13	620.40 ± 0.95	606.40 ± 1.27
10	604.00 ± 0.96	605.40 ± 1.45	607.20 ± 0.99	603.40 ± 1.47
11	597.00 ± 1.28	599.00 ± 1.26	602.80 ± 1.22	595.00 ± 0.77
12	599.80 ± 0.95	603.40 ± 0.86	602.60 ± 1.60	602.20 ± 1.13

Subject 12 / Week	area1 (D = control)	area2 (product A)	area3 (product B)	area4 (product C)
0	603.80 ± 0.63	604.00 ± 0.74	610.60 ± 1.09	612.20 ± 1.38
1	610.60 ± 0.99	601.80 ± 1.35	592.00 ± 0.61	594.60 ± 1.20
2	610.20 ± 1.42	601.80 ± 0.92	609.80 ± 0.88	617.20 ± 1.60
3	600.60 ± 1.45	599.00 ± 1.36	595.40 ± 1.01	601.40 ± 1.52
4	600.80 ± 1.14	602.60 ± 0.73	594.60 ± 1.54	606.80 ± 1.20
5	604.00 ± 1.02	601.40 ± 1.35	598.00 ± 0.61	601.20 ± 0.75
6	607.00 ± 1.47	604.40 ± 0.97	603.00 ± 1.34	611.60 ± 0.48
7	598.00 ± 0.84	599.00 ± 0.65	598.40 ± 0.66	602.60 ± 1.40
8	593.20 ± 0.75	599.80 ± 1.69	597.00 ± 1.31	595.80 ± 1.01
9	595.20 ± 0.72	595.80 ± 1.60	595.60 ± 1.20	598.40 ± 1.09
10	602.80 ± 1.30	597.20 ± 1.22	600.00 ± 0.91	593.40 ± 0.70
11	604.80 ± 1.09	604.80 ± 0.32	590.80 ± 1.14	594.40 ± 0.83
12	595.40 ± 1.36	592.20 ± 1.33	590.80 ± 1.22	594.60 ± 1.20

PART 3   Absolute melanin values of the individual subjects after application of the three

body products for different periods (Data = mean $\pm$ S.E.M., N = 5)

Subject 1 / Week	area1 (product E)	area2 (product F)	area3 (product G)	area4 (H =control)
0	554.00 $\pm$ 0.68	553.00 $\pm$ 0.84	547.20 $\pm$ 0.63	545.20 $\pm$ 0.52
1	539.00 $\pm$ 0.89	539.20 $\pm$ 0.52	536.80 $\pm$ 1.30	531.60 $\pm$ 0.26
2	548.80 $\pm$ 0.32	541.80 $\pm$ 0.38	545.20 $\pm$ 1.38	539.60 $\pm$ 0.83
3	543.80 $\pm$ 0.43	542.40 $\pm$ 0.26	538.00 $\pm$ 0.54	531.60 $\pm$ 0.39
4	544.40 $\pm$ 0.44	546.40 $\pm$ 0.56	540.60 $\pm$ 0.16	534.40 $\pm$ 0.66
5	539.60 $\pm$ 0.53	540.00 $\pm$ 0.41	536.00 $\pm$ 0.54	531.40 $\pm$ 0.33
6	535.80 $\pm$ 0.38	537.40 $\pm$ 1.01	532.40 $\pm$ 0.86	533.80 $\pm$ 0.24
7	531.20 $\pm$ 0.38	535.20 $\pm$ 0.24	531.80 $\pm$ 0.63	530.20 $\pm$ 0.55
8	530.80 $\pm$ 0.38	531.60 $\pm$ 0.16	530.40 $\pm$ 0.60	531.00 $\pm$ 0.35
9	526.80 $\pm$ 0.77	531.00 $\pm$ 0.54	525.80 $\pm$ 0.47	526.40 $\pm$ 0.48
10	531.80 $\pm$ 0.66	536.00 $\pm$ 0.29	532.80 $\pm$ 0.38	531.20 $\pm$ 0.13
11	536.40 $\pm$ 0.93	544.20 $\pm$ 0.24	536.20 $\pm$ 0.32	530.00 $\pm$ 0.68
12	537.80 $\pm$ 0.72	542.00 $\pm$ 0.35	536.40 $\pm$ 1.56	535.60 $\pm$ 0.63

Subject 2 / Week	area1 (product F)	area2 (product G)	area3 (H =control)	Area4 (product E)
0	586.60 $\pm$ 1.09	582.40 $\pm$ 0.83	587.20 $\pm$ 0.88	582.40 $\pm$ 0.75
1	582.80 $\pm$ 0.55	568.40 $\pm$ 0.95	571.60 $\pm$ 1.03	569.80 $\pm$ 0.83
2	581.60 $\pm$ 0.88	572.40 $\pm$ 0.63	583.80 $\pm$ 0.13	573.20 $\pm$ 0.43
3	572.80 $\pm$ 0.69	565.20 $\pm$ 0.43	580.20 $\pm$ 1.22	568.80 $\pm$ 1.58
4	575.60 $\pm$ 0.44	566.60 $\pm$ 0.73	569.60 $\pm$ 0.63	571.80 $\pm$ 0.97
5	576.00 $\pm$ 0.46	570.20 $\pm$ 0.24	573.60 $\pm$ 0.26	569.40 $\pm$ 0.39
6	570.80 $\pm$ 0.38	564.00 $\pm$ 0.29	573.20 $\pm$ 0.55	567.60 $\pm$ 0.60
7	567.80 $\pm$ 0.43	563.80 $\pm$ 0.13	571.60 $\pm$ 0.33	562.60 $\pm$ 0.16
8	564.80 $\pm$ 0.38	560.60 $\pm$ 0.26	568.20 $\pm$ 0.77	567.40 $\pm$ 0.16
9	567.20 $\pm$ 0.80	565.00 $\pm$ 0.87	573.00 $\pm$ 0.41	562.00 $\pm$ 0.58
10	583.40 $\pm$ 0.44	566.80 $\pm$ 0.99	580.80 $\pm$ 0.77	572.40 $\pm$ 0.44
11	568.00 $\pm$ 0.21	565.20 $\pm$ 0.38	575.80 $\pm$ 0.75	567.60 $\pm$ 0.60
12	572.60 $\pm$ 0.60	566.80 $\pm$ 0.72	575.60 $\pm$ 1.05	568.00 $\pm$ 0.46

Ssubject 3 / Week	area1 (product G)	area2 (H=Control)	area3 (product E)	area4 (product F)
0	575.00 ± 0.46	565.60 ± 0.60	574.60 ± 0.33	564.00 ± 0.46
1	572.20 ± 1.05	561.80 ± 0.43	573.00 ± 0.84	555.20 ± 0.75
2	576.00 ± 1.50	560.60 ± 0.95	568.40 ± 0.53	556.00 ± 0.74
3	569.20 ± 0.80	561.40 ± 0.70	564.40 ± 0.60	551.40 ± 0.78
4	572.40 ± 1.03	562.00 ± 0.54	565.80 ± 0.47	557.00 ± 0.61
5	570.00 ± 0.96	559.00 ± 0.35	565.20 ± 0.47	557.20 ± 0.32
6	567.60 ± 0.26	558.80 ± 0.66	562.80 ± 0.75	552.60 ± 0.73
7	562.60 ± 0.16	551.60 ± 0.33	557.80 ± 0.32	544.20 ± 0.24
8	560.00 ± 0.46	553.00 ± 0.21	559.60 ± 0.33	550.60 ± 0.53
9	555.20 ± 0.90	554.20 ± 0.85	558.00 ± 0.98	550.20 ± 0.55
10	551.20 ± 0.59	548.60 ± 1.13	554.00 ± 0.54	546.20 ± 0.63
11	548.80 ± 1.03	553.60 ± 0.66	554.80 ± 0.83	547.40 ± 0.66
12	548.60 ± 1.54	554.80 ± 1.44	553.60 ± 0.33	545.00 ± 0.61

Subject 4 / Week	area1 (H =control)	area2 (product E)	area3 (product F)	area4 (product G)
0	552.80 ± 1.25	554.60 ± 0.86	556.20 ± 0.63	550.60 ± 0.33
1	552.40 ± 0.97	551.00 ± 0.58	546.60 ± 0.66	538.20 ± 0.24
2	545.40 ± 1.09	546.40 ± 0.90	548.60 ± 0.73	543.80 ± 0.88
3	547.20 ± 0.83	549.80 ± 0.52	548.60 ± 0.48	544.40 ± 0.78
4	541.40 ± 0.33	547.00 ± 0.21	544.60 ± 0.33	540.20 ± 0.24
5	546.20 ± 0.38	551.20 ± 0.13	545.80 ± 0.52	540.80 ± 0.24
6	551.40 ± 0.33	550.60 ± 0.39	549.20 ± 0.38	547.60 ± 1.18
7	551.60 ± 0.26	547.20 ± 0.24	543.00 ± 0.46	540.80 ± 0.69
8	545.80 ± 0.55	551.20 ± 0.43	543.80 ± 0.43	543.20 ± 0.52
9	542.00 ± 0.54	546.60 ± 0.39	547.80 ± 0.47	542.60 ± 1.09
10	549.00 ± 0.41	543.60 ± 0.66	542.00 ± 0.21	540.40 ± 0.33
11	543.00 ± 0.35	545.60 ± 0.39	545.20 ± 0.95	544.00 ± 0.74
12	544.80 ± 0.90	543.00 ± 0.84	543.20 ± 1.14	542.20 ± 0.38

Subject 5 / Week	area1 (product E)	area2 (product F)	area3 (product G)	area4 (H =control)
0	567.20 ± 1.47	563.60 ± 0.56	564.00 ± 1.06	559.20 ± 0.63
1	555.40 ± 0.53	554.00 ± 0.96	559.20 ± 0.55	556.20 ± 0.52
2	551.20 ± 0.47	546.80 ± 0.63	554.20 ± 1.20	552.20 ± 0.43
3	552.00 ± 0.41	550.80 ± 0.69	555.40 ± 0.33	556.60 ± 0.33
4	556.20 ± 0.80	550.00 ± 0.21	551.00 ± 0.79	553.00 ± 0.21
5	552.40 ± 0.39	550.80 ± 0.38	550.60 ± 0.48	555.00 ± 0.21
6	546.20 ± 0.13	548.20 ± 0.63	552.60 ± 0.16	556.00 ± 0.68
7	546.60 ± 0.44	546.20 ± 0.59	545.80 ± 0.43	554.20 ± 0.63
8	549.20 ± 0.55	546.80 ± 0.55	550.00 ± 0.74	556.00 ± 0.65
9	544.00 ± 0.79	547.20 ± 0.55	550.80 ± 0.38	556.40 ± 0.39
10	544.00 ± 0.61	543.60 ± 0.63	546.40 ±0.26	554.60 ± 0.44
11	542.40 ± 0.56	543.40 ± 0.26	545.60 ± 0.16	556.60 ± 0.72
12	543.60 ± 0.93	545.20 ± 0.55	544.00 ± 0.21	551.80 ± 0.32

Subject 6 / Week	area1 (product F)	area2 (product G)	area3 (H =control)	area4 (product E)
0	535.40 ± 0.33	536.20 ± 0.52	544.60 ± 0.40	547.40 ± 0.33
1	529.40 ± 1.17	531.80 ± 1.66	534.60 ± 1.44	535.40 ± 0.93
2	535.80 ± 0.55	536.60 ± 0.44	540.60 ± 0.75	540.60 ± 0.66
3	535.00 ± 1.73	533.60 ± 0.99	543.20 ± 0.80	538.00 ± 0.46
4	539.00 ± 0.74	547.00 ± 0.82	546.60 ± 1.09	545.40 ± 0.83
5	536.00 ± 0.46	535.60 ± 0.97	540.40 ± 0.78	543.40 ± 0.16
6	535.20 ± 0.47	538.80 ± 0.72	536.40 ± 0.70	539.60 ± 0.88
7	535.60 ± 0.53	535.40 ± 0.33	539.80 ± 0.38	538.20 ± 0.63
8	526.80 ± 0.13	531.60 ± 0.16	543.00 ± 0.29	534.40 ± 0.33
9	530.20 ± 0.55	536.60 ± 1.20	540.60 ± 1.82	535.00 ± 0.68
10	531.20 ± 0.47	534.60 ± 1.59	542.20 ± 0.38	535.80 ± 0.32
11	531.20 ± 0.59	535.60 ± 0.60	533.40 ± 1.09	536.00 ± 0.68
12	529.20 ± 0.63	532.80 ± 0.88	535..80 ± 0.24	531.80 ± 0.88

Subject 7 / Week	area1 (product G)	area2 (H =control)	area3 (product E)	area4 (product F)
0	553.40 ± 0.56	551.80 ± 0.47	552.60 ± 0.86	551.20 ± 0.47
1	550.40 ± 0.40	550.40 ± 0.33	553.20 ± 0.90	547.00 ± 0.46
2	545.20 ± 0.72	543.80 ± 1.44	541.20 ± 1.11	538.60 ± 0.33
3	551.60 ± 0.33	554.40 ± 0.66	547.20 ± 0.13	546.00 ± 0.35
4	550.60 ± 0.66	543.60 ± 1.18	547.00 ± 0.41	545.20 ± 0.66
5	543.40 ± 0.66	544.80 ± 0.24	537.60 ± 0.26	538.20 ± 0.13
6	537.60 ± 0.48	549.40 ± 0.33	538.80 ± 0.52	540.80 ± 0.47
7	540.20 ± 0.77	543.60 ± 0.44	542.00 ± 0.41	540.80 ± 0.24
8	540.20 ± 0.63	550.20 ± 0.90	541.80 ± 0.72	543.20 ± 0.43
9	542.40 ± 0.60	546.40 ± 0.81	542.00 ± 0.41	543.00 ± 0.35
10	539.40 ± 0.56	544.20 ± 0.24	541.20 ± 0.47	540.60 ± 0.72
11	538.80 ± 0.47	548.00 ± 0.46	544.40 ± 0.75	542.00 ± 0.46
12	538.20 ± 0.24	544.80 ± 0.43	540.80 ± 0.69	543.20 ± 0.24

Subject 8 / Week	area1 (H =Control)	area2 (product E)	area3 (product F)	area4 (product G)
0	543.80 ± 0.88	541.60 ± 0.66	548.40 ± 0.99	548.00 ± 0.35
1	533.20 ± 0.75	524.80 ± 0.97	534.60 ± 1.27	532.60 ± 0.83
2	535.80 ± 0.38	533.60 ± 0.60	537.80 ± 0.24	539.20 ± 0.69
3	530.80 ± 0.66	527.00 ± 0.82	543.20 ± 0.38	537.80 ± 0.88
4	532.80 ± 0.47	526.60 ± 0.83	540.20 ± 1.20	536.40 ± 0.39
5	533.80 ± 0.38	525.20 ± 0.47	541.20 ± 0.32	535.00 ± 0.46
6	526.60 ± 0.44	517.60 ± 0.44	527.20 ± 0.38	525.80 ± 0.13
7	531.60 ± 0.16	523.60 ± 0.60	532.80 ± 0.47	531.40 ± 0.56
8	522.00 ± 0.54	528.60 ± 0.73	527.00 ± 0.68	526.80 ± 0.13
9	528.40 ± 0.81	518.40 ± 0.16	528.20 ± 0.99	524.40 ± 0.26
10	515.40 ± 0.66	522.40 ± 0.26	524.40 ± 0.53	525.60 ± 0.53
11	520.80 ± 0.32	518.20 ± 0.24	527.00 ± 0.29	525.40 ± 0.44
12	527.40 ± 0.48	516.60 ± 0.44	526.20 ± 0.59	524.80 ± 0.63

Subject 9 / Week	area1 (product E)	area2 (product F)	area3 (product G)	area4 (H = Control)
0	558.60 ± 0.83	556.20 ± 0.92	552.00 ± 0.79	550.60 ± 0.53
1	548.40 ± 0.83	546.20 ± 0.47	544.00 ± 0.46	539.20 ± 0.95
2	552.20 ± 1.47	549.40 ± 0.33	545.40 ± 0.93	546.60 ± 0.48
3	543.00 ± 0.65	540.00 ± 0.77	539.80 ± 0.99	536.20 ± 0.92
4	552.20 ± 0.52	548.00 ± 0.21	545.60 ± 0.33	546.80 ± 0.24
5	538.80 ± 0.47	538.00 ± 0.96	535.00 ± 0.91	535.60 ± 0.44
6	536.40 ± 0.26	536.80 ± 0.32	535.20 ± 0.43	535.60 ± 0.56
7	539.60 ± 0.26	538.80 ± 0.63	536.00 ± 0.35	540.00 ± 0.46
8	537.40 ± 0.63	533.80 ± 0.55	530.40 ± 0.88	532.60 ± 0.53
9	527.60 ± 1.07	531.60 ± 0.33	531.60 ± 0.48	530.60 ± 0.56
10	536.60 ± 0.44	535.80 ± 0.24	534.60 ± 0.33	533.60 ± 0.78
11	536.80 ± 0.47	542.00 ± 1.10	531.40 ± 0.26	536.00 ± 0.54
12	542.40 ± 0.39	539.40 ± 0.56	540.40 ± 0.53	543.20 ± 0.43

Subject 10 / Week	area1 (product F)	area2 (product G)	area3 (H =control)	area4 (product E)
0	550.40 ± 0.60	546.00 ± 0.68	542.80 ± 0.55	539.80 ± 0.63
1	535.80 ± 1.18	533.00 ± 0.58	529.40 ± 0.63	527.60 ± 0.73
2	535.00 ± 0.68	536.80 ± 0.24	532.40 ± 0.48	533.00 ± 1.08
3	531.20 ± 1.42	529.80 ± 0.59	526.80 ± 0.47	527.80 ± 0.59
4	543.60 ± 0.26	541.00 ± 0.35	537.20 ± 0.38	537.80 ± 0.38
5	537.20 ± 0.55	536.80 ± 0.55	541.40 ± 0.33	537.00 ± 0.68
6	534.20 ± 0.13	532.80 ± 0.52	532.00 ± 0.21	536.20 ± 0.24
7	537.80 ± 0.38	536.60 ± 0.26	534.20 ± 0.13	534.80 ± 0.24
8	534.60 ± 0.26	527.00 ± 0.00	527.20 ± 0.52	530.40 ± 0.26
9	532.00 ± 0.29	531.80 ± 0.95	528.80 ± 0.63	528.20 ± 1.18
10	533.80 ± 0.32	538.40 ± 1.20	531.40 ± 0.48	533.40 ± 0.44
11	533.00 ± 0.79	531.00 ± 0.74	531.80 ± 0.52	531.60 ± 0.95
12	537.40 ± 0.53	535.80 ± 0.52	532.60 ± 0.86	539.60 ± 1.34

Subject 11 / Week	area1 (product G)	area2 (H=control)	area3 (product E)	area4 (product F)
0	575.60 ± 0.39	572.80 ± 0.55	573.60 ± 0.88	568.00 ± 1.06
1	568.00 ± 1.57	565.60 ± 0.63	551.20 ± 0.38	550.20 ± 0.97
2	555.20 ± 0.90	553.80 ± 0.59	561.20 ± 0.63	561.00 ± 0.50
3	563.60 ± 0.46	558.80 ± 0.66	552.80 ± 0.97	550.60 ± 1.24
4	566.60 ± 1.05	559.40 ± 0.70	555.00 ± 1.15	553.00 ± 0.84
5	565.00 ± 1.72	559.00 ± 0.96	552.20 ± 0.52	553.80 ± 0.80
6	554.80 ± 0.66	553.00 ± 0.35	547.60 ± 0.83	546.20 ± 0.38
7	554.20 ± 0.55	552.40 ± 0.53	547.60 ± 0.48	549.60 ± 0.33
8	562.40 ± 0.26	557.40 ± 0.39	553.80 ± 0.63	555.20 ± 0.13
9	556.00 ± 0.54	552.60 ± 0.63	543.20 ± 0.95	548.40 ± 0.16
10	547.80 ± 0.13	556.80 ± 1.52	546.40 ± 0.93	548.20 ± 0.32
11	549.80 ± 1.68	551.80 ± 0.75	547.20 ± 1.16	546.20 ± 0.72
12	551.20 ± 0.38	551.60 ± 1.67	539.80 ± 1.35	544.60 ± 0.26

Subject 12 / Week	area1 (H = control)	area2 (product E)	area3 (product F)	area4 (product G)
0	579.40 ± 1.22	587.00 ± 0.89	584.40 ± 1.24	587.60 ± 0.44
1	574.40 ± 1.62	573.00 ± 0.82	566.00 ± 1.02	577.20 ± 1.25
2	569.00 ± 0.35	578.80 ± 0.80	565.00 ± 0.68	571.40 ± 0.48
3	555.80 ± 0.69	571.20 ± 1.05	563.20 ± 1.03	564.60 ± 0.56
4	569.40 ± 0.44	574.00 ± 0.61	575.40 ± 0.66	575.60 ± 0.60
5	560.00 ± 1.26	568.40 ± 1.52	558.00 ± 0.54	566.20 ± 0.43
6	553.60 ± 0.70	559.80 ± 0.38	561.00 ± 0.35	565.40 ± 0.60
7	563.60 ± 0.33	567.40 ± 0.16	554.60 ± 0.33	565.20 ± 0.13
8	567.40 ± 0.39	564.20 ± 0.55	560.80 ± 0.24	563.20 ± 0.47
9	569.00 ± 0.70	571.40 ± 0.26	570.80 ± 0.66	568.40 ± 0.56
10	568.20 ± 1.95	567.60 ± 0.81	561.00 ± 1.77	563.80 ± 1.41
11	561.60 ± 0.73	565.20 ± 0.88	564.40 ± 0.78	565.60 ± 0.53
12	563.20 ± 0.63	564.80 ± 1.35	558.60 ± 0.72	563.60 ± 1.13

PART 4 Absolute erythema values of the individual subjects after application of the three

body products for different periods, (Data = mean $\pm$ S.E.M.., N = 5)

Subject 1 / Week	area1 (product E)	area2 (product F)	area3 (product G)	area4 (H = control)
0	620.20 $\pm$ 1.20	619.60 $\pm$ 0.95	618.20 $\pm$ 1.11	608.80 $\pm$ 0.92
1	624.20 $\pm$ 1.47	623.00 $\pm$ 1.24	624.20 $\pm$ 1.68	618.60 $\pm$ 0.72
2	634.00 $\pm$ 0.84	632.40 $\pm$ 0.56	629.20 $\pm$ 1.20	619.80 $\pm$ 0.90
3	630.20 $\pm$ 1.38	627.00 $\pm$ 1.24	626.60 $\pm$ 0.93	618.40 $\pm$ 0.75
4	616.80 $\pm$ 1.16	621.40 $\pm$ 0.95	615.40 $\pm$ 1.01	603.20 $\pm$ 0.83
5	616.60 $\pm$ 1.51	622.40 $\pm$ 1.88	614.60 $\pm$ 1.97	599.80 $\pm$ 0.69
6	619.20 $\pm$ 1.52	620.00 $\pm$ 1.06	627.00 $\pm$ 0.74	621.60 $\pm$ 0.53
7	614.40 $\pm$ 1.93	615.60 $\pm$ 0.83	620.80 $\pm$ 1.86	612.20 $\pm$ 0.55
8	604.60 $\pm$ 0.66	610.80 $\pm$ 1.13	611.60 $\pm$ 1.48	602.20 $\pm$ 1.03
9	610.60 $\pm$ 1.62	614.80 $\pm$ 0.90	609.40 $\pm$ 0.90	617.20 $\pm$ 0.55
10	608.80 $\pm$ 1.17	615.80 $\pm$ 1.55	618.00 $\pm$ 0.79	615.80 $\pm$ 1.36
11	620.80 $\pm$ 0.32	630.40 $\pm$ 0.63	621.60 $\pm$ 1.62	613.20 $\pm$ 1.45
12	616.00 $\pm$ 0.46	619.80 $\pm$ 0.38	613.00 $\pm$ 1.40	613.00 $\pm$ 1.53

Subject 2 / Week	area1 (product F)	area2 (product G)	area3 (H =control)	area4 (product E)
0	640.00 $\pm$ 1.87	632.00 $\pm$ 0.46	628.80 $\pm$ 0.52	634.80 $\pm$ 0.32
1	651.20 $\pm$ 0.82	640.00 $\pm$ 0.61	636.20 $\pm$ 1.27	641.00 $\pm$ 1.26
2	648.60 $\pm$ 1.45	635.00 $\pm$ 1.77	636.80 $\pm$ 0.47	638.80 $\pm$ 0.49
3	638.60 $\pm$ 0.93	636.80 $\pm$ 0.38	637.60 $\pm$ 1.11	639.20 $\pm$ 0.55
4	636.60 $\pm$ 0.48	622.40 $\pm$ 0.44	623.40 $\pm$ 1.48	630.80 $\pm$ 1.49
5	640.40 $\pm$ 0.48	637.00 $\pm$ 0.98	633.20 $\pm$ 0.95	636.60 $\pm$ 1.50
6	627.00 $\pm$ 1.40	625.60 $\pm$ 1.24	632.80 $\pm$ 0.90	635.80 $\pm$ 1.30
7	643.00 $\pm$ 0.74	637.20 $\pm$ 1.67	640.80 $\pm$ 0.85	647.40 $\pm$ 0.56
8	637.80 $\pm$ 1.25	636.00 $\pm$ 0.74	634.20 $\pm$ 0.90	648.00 $\pm$ 1.29
9	644.80 $\pm$ 0.66	644.40 $\pm$ 0.83	638.00 $\pm$ 0.96	638.20 $\pm$ 1.07
10	636.80 $\pm$ 0.38	628.00 $\pm$ 0.46	632.00 $\pm$ 1.08	634.00 $\pm$ 0.54
11	641.20 $\pm$ 1.03	633.00 $\pm$ 1.21	648.00 $\pm$ 1.08	641.80 $\pm$ 0.32
12	633.80 $\pm$ 0.63	636.00 $\pm$ 1.32	641.80 $\pm$ 0.90	632.20 $\pm$ 1.47

Subject 3 / Week	area1 (product G)	area2 (H=control)	area3 (product E)	area4 (product F)
0	632.40 ± 0.33	632.00 ± 0.21	631.80 ± 0.52	627.80 ± 0.24
1	643.00 ± 1.65	634.80 ± 0.55	639.80 ± 1.63	631.40 ± 0.33
2	644.20 ± 1.22	628.40 ± 0.60	636.20 ± 0.55	629.20 ± 1.56
3	635.40 ± 1.74	627.20 ± 1.47	631.20 ± 1.30	622.60 ± 0.66
4	633.60 ± 1.22	625.20 ± 0.75	628.20 ± 1.01	618.00 ± 1.54
5	631.60 ± 1.95	626.40 ± 0.66	624.40 ± 0.97	618.80 ± 1.70
6	633.20 ± 1.93	625.00 ± 0.74	635.40 ± 1.29	627.20 ± 2.13
7	615.00 ± 1.10	613.00 ± 1.24	619.40 ± 1.81	621.60 ± 0.70
8	631.20 ± 1.53	632.40 ± 0.88	626.80 ± 1.77	621.80 ± 1.52
9	627.00 ± 1.83	623.20 ± 1.55	624.60 ± 1.81	615.21 ± 1.60
10	620.80 ± 1.82	621.20 ± 1.03	619.20 ± 1.25	616.60 ± 0.86
11	625.20 ± 0.38	623.00 ± 1.68	623.80 ± 0.95	618.20 ± 0.97
12	616.80 ± 0.95	620.20 ± 0.24	613.00 ± 0.68	610.80 ± 1.60

Subject 4 / Week	area1 (H =control)	area2 (product E)	area3 (product F)	area4 (product G)
0	622.40 ± 0.60	623.20 ± 0.38	613.40 ± 1.17	612.20 ± 0.77
1	619.00 ± 1.37	618.00 ± 0.74	610.20 ± 0.69	612.20 ± 1.63
2	613.60 ± 1.68	616.20 ± 0.95	617.40 ± 1.20	608.00 ± 0.84
3	613.80 ± 1.44	617.60 ± 1.77	612.20 ± 1.56	612.00 ± 0.46
4	608.40 ± 1.22	606.80 ± 0.97	608.00 ± 1.58	610.80 ± 1.07
5	608.40 ± 1.68	611.40 ± 1.36	604.20 ± 1.32	606.60 ± 0.95
6	615.20 ± 1.82	609.80 ± 1.16	609.20 ± 1.16	611.80 ± 1.71
7	607.00 ± 1.04	607.20 ± 1.42	603.20 ± 0.85	608.00 ± 1.29
8	603.00 ± 0.84	607.40 ± 1.32	594.40 ± 0.97	604.00 ± 0.79
9	606.00 ± 1.02	614.80 ± 1.91	613.00 ± 0.96	613.20 ± 1.09
10	609.20 ± 1.55	604.40 ± 0.97	602.00 ± 1.43	608.20 ± 1.91
11	606.00 ± 1.53	606.60 ± 0.97	611.20 ± 1.32	605.60 ± 1.03
12	602.60 ± 1.15	606.40 ± 0.75	604.60 ± 0.33	607.60 ± 1.20

Subject 5 / Week	area1 (product E)	area2 (product F)	area3 (product G)	area4 (H=control)
0	612.60 ± 0.44	606.20 ± 1.18	603.60 ± 1.25	607.60 ± 1.32
1	618.40 ± 1.15	614.80 ± 1.97	620.20 ± 1.45	622.40 ± 1.30
2	613.40 ± 0.60	609.40 ± 0.78	611.80 ± 1.75	609.80 ± 0.55
3	610.80 ± 1.16	615.60 ± 0.93	616.00 ± 0.54	621.00 ± 0.41
4	633.60 ± 1.38	612.20 ± 0.97	614.80 ± 1.42	617.20 ± 1.11
5	617.60 ± 1.55	609.40 ± 0.63	610.00 ± 0.79	617.40 ± 0.52
6	615.00 ± 1.10	613.00 ± 1.24	619.40 ± 1.81	621.60 ± 0.86
7	609.00 ± 1.58	620.80 ± 1.28	610.80 ± 1.44	623.00 ± 0.65
8	610.80 ± 0.97	609.80 ± 1.93	604.00 ± 1.57	610.00 ± 1.37
9	613.80 ± 0.88	612.40 ± 1.97	615.80 ± 1.56	620.80 ± 0.55
10	612.80 ± 1.74	614.80 ± 0.85	615.00 ± 0.46	620.40 ± 1.85
11	615.40 ± 0.66	616.20 ± 0.77	603.60 ± 0.60	624.20 ± 0.92
12	610.40 ± 0.93	616.40 ± 1.72	610.80 ± 1.11	612.00 ± 1.10

Subject 6 / Week	area1 (product F)	area2 (product G)	area3 (H=control)	area4 (product E)
0	602.80 ± 0.38	608.20 ± 0.24	613.60 ± 0.33	616.80 ± 0.38
1	610.40 ± 0.88	617.20 ± 1.77	617.80 ± 1.95	614.40 ± 1.30
2	621.20 ± 2.02	620.20 ± 0.92	623.80 ± 1.77	615.00 ± 1.17
3	621.60 ± 0.66	618.20 ± 1.68	630.20 ± 0.43	623.00 ± 1.10
4	614.20 ± 1.18	621.60 ± 1.30	612.80 ± 1.09	612.80 ± 1.09
5	609.20 ± 1.01	620.00 ± 1.14	621.00 ± 0.91	622.80 ± 0.69
6	606.80 ± 0.72	606.60 ± 1.68	607.80 ± 1.47	621.80 ± 0.52
7	620.40 ± 1.69	623.80 ± 1.94	620.40 ± 0.44	619.80 ± 0.90
8	620.00 ± 0.46	622.20 ± 0.55	626.00 ± 0.74	611.60 ± 0.78
9	608.80 ± 0.80	613.20 ± 0.99	614.00 ± 1.67	606.20 ± 1.66
10	606.00 ± 1.82	614.40 ± 0.78	619.40 ± 0.60	607.20 ± 1.27
11	604.20 ± 0.75	618.80 ± 0.90	606.40 ± 0.83	615.40 ± 1.37
12	613.40 ± 0.48	616.20 ± 1.76	606.60 ± 0.33	609.20 ± 1.01

Subject 7 / Week	area1 (product G)	area2 (H=control)	area3 (product E)	area4 (product F)
0	624.80 ± 1.18	626.80 ± 1.58	624.40 ± 1.51	618.20 ± 1.47
1	620.80 ± 1.25	617.60 ± 0.86	628.00 ± 1.31	622.60 ± 1.32
2	623.20 ± 1.39	616.60 ± 1.24	612.20 ± 1.75	616.60 ± 1.63
3	618.20 ± 1.53	617.20 ± 1.91	611.20 ± 0.75	613.00 ± 0.96
4	623.20 ± 1.75	618.60 ± 1.25	620.00 ± 1.53	627.80 ± 0.88
5	627.80 ± 0.95	629.60 ± 0.70	621.00 ± 0.54	618.80 ± 0.90
6	608.40 ± 1.40	625.20 ± 1.20	609.80 ± 1.48	617.80 ± 1.38
7	629.00 ± 0.98	615.20 ± 1.27	613.40 ± 1.60	618.20 ± 0.55
8	615.00 ± 1.06	623.20 ± 1.14	619.00 ± 1.56	618.00 ± 1.65
9	619.60 ± 0.44	623.80 ± 1.18	611.80 ± 1.47	622.20 ± 1.01
10	620.00 ± 1.14	630.00 ± 1.40	620.80 ± 0.75	614.60 ± 1.75
11	612.80 ± 1.69	627.80 ± 0.75	623.20 ± 0.95	620.80 ± 2.14
12	621.20 ± 1.22	623.00 ± 0.46	614.40 ± 0.66	626.00 ± 1.19

Subject 8 / Week	area1 (H=Control)	area2 (product E)	area3 (product F)	area4 (product G)
0	606.00 ± 0.79	600.80 ± 1.39	606.40 ± 0.73	606.60 ± 0.78
1	621.20 ± 1.11	608.60 ± 0.60	620.20 ± 1.18	613.80 ± 1.25
2	617.00 ± 1.43	613.80 ± 1.82	620.00 ± 1.99	626.40 ± 1.92
3	612.00 ± 1.75	611.80 ± 0.38	616.20 ± 0.69	613.80 ± 1.28
4	609.20 ± 1.77	609.00 ± 1.26	620.80 ± 1.07	616.20 ± 1.90
5	607.40 ± 0.44	614.80 ± 1.42	625.80 ± 1.28	609.80 ± 1.20
6	614.80 ± 1.30	610.00 ± 0.46	617. 00 ± 0.65	613.20 ± 1.55
7	606.40 ± 1.17	606.20 ± 1.64	605.20 ± 1.03	606.60 ± 1.87
8	607.60 ± 1.79	607.80 ± 0.95	604.20 ± 1.52	615.20 ± 0.99
9	607.80 ± 1.28	602.60 ± 1.11	610.00 ± 1.47	601.80 ± 2.00
10	596.80 ± 1.44	606.60 ± 1.99	605.40 ± 1.27	608.60 ± 1.97
11	612.20 ± 0.55	608.40 ± 1.56	609.20 ± 0.95	612.60 ± 1.73
12	619.80 ± 1.59	606.20 ± 1.05	612.00 ± 0.46	600.20 ± 1.84

Subject 9 / Week	area1 (product E)	area2 (product F)	area3 (product G)	area4 (H=control)
0	624.80 ± 1.18	626.80 ± 1.58	624.40 ± 1.51	618.20 ± 1.47
1	634.60 ± 0.78	644.00 ± 1.39	638.80 ± 1.07	641.20 ± 0.55
2	651.00 ± 1.53	647.80 ± 1.20	643.80 ± 0.83	650.00 ± 1.93
3	637.80 ± 1.74	634.80 ± 1.53	632.20 ± 0.88	635.20 ± 0.99
4	624.80 ± 0.75	619.60 ± 0.83	613.40 ± 0.75	627.20 ± 0.75
5	630.00 ± 0.74	631.40 ± 1.79	632.80 ± 1.60	633.60 ± 0.88
6	621.00 ± 1.34	620.60 ± 1.80	623.40 ± 1.09	624.80 ± 1.82
7	624.80 ± 1.11	634.20 ± 1.32	628.60 ± 0.70	627.00 ± 0.65
8	628.40 ± 1.54	620.00 ± 0.90	627.40 ± 1.13	621.20 ± 0.75
9	620.80 ± 1.95	623.20 ± 0.90	628.40 ± 1.97	631.00 ± 0.68
10	611.00 ± 0.91	616.20 ± 1.25	613.60 ± 1.27	626.20 ± 1.01
11	629.80 ± 0.24	635.00 ± 1.75	622.20 ± 1.63	623.40 ± 1.15
12	624.80 ± 1.38	630.60 ± 1.56	628.20 ± 0.52	632.20 ± 1.86

Subject 10 / Week	area1 (product F)	area2 (product G)	area3 (H=control)	area4 (product E)
0	616.60 ± 1.42	612.60 ± 1.55	607.80 ± 0.24	608.60 ± 0.78
1	632.40 ± 0.66	615.60 ± 0.88	618.20 ± 0.72	619.60 ± 0.95
2	616.60 ± 0.93	622.00 ± 0.46	617.20 ± 0.95	624.00 ± 0.91
3	616.20 ± 0.66	619.20 ± 0.75	615.80 ± 1.60	623.60 ± 0.73
4	609.00 ± 1.06	610.60 ± 1.85	603.00 ± 1.04	610.80 ± 1.60
5	596.40 ± 1.34	602.00 ± 0.84	600.80 ± 0.43	606.40 ± 0.44
6	605.40 ± 1.11	610.60 ± 0.66	604.20 ± 0.24	607.60 ± 1.56
7	608.20 ± 1.75	610.00 ± 1.42	611.80 ± 1.03	611.20 ± 1.41
8	604.60 ± 0.93	609.60 ± 1.05	601.60 ± 0.33	605.60 ± 1.58
9	602.00 ± 0.61	599.40 ± 0.86	598.60 ± 1.48	607.20 ± 1.05
10	600.60 ± 1.68	612.80 ± 1.48	611.20 ± 1.60	614.60 ± 1.35
11	608.60 ± 0.44	623.40 ± 0.60	611.60 ± 1.75	615.40 ± 1.34
12	615.40 ± 0.44	615.20 ± 1.47	612.20 ± 0.47	613.80 ± 0.88

Subject 11 / Week	area1 (product G)	area2 (H =control)	area3 (product E)	area4 (product F)
0	619.40 ± 1.45	620.40 ± 1.48	615.80 ± 1.09	613.60 ± 1.29
1	630.20 ± 1.79	629.40 ± 1.15	627.80 ± 0.55	626.80 ± 0.99
2	619.40 ± 1.40	624.80 ± 0.75	622.40 ± 1.80	628.00 ± 1.61
3	631.80 ± 1.28	628.40 ± 0.33	628.00 ± 0.46	621.00 ± 1.40
4	624.80 ± 1.01	617.80 ± 1.53	619.00 ± 1.37	615.80 ± 1.20
5	628.60 ± 1.77	622.80 ± 0.75	622.20 ± 1.60	624.20 ± 1.18
6	620.40 ± 1.13	616.20 ± 0.77	618.40 ± 1.38	618.00 ± 1.23
7	618.40 ± 0.78	618.80 ± 1.77	614.40 ± 1.60	621.20 ± 0.99
8	622.00 ± 1.08	622.20 ± 0.55	611.00 ± 1.34	608.20 ± 0.88
9	621.60 ± 1.35	623.20 ± 1.23	616.20 ± 1.36	622.20 ± 0.77
10	618.00 ± 0.71	622.20 ± 0.46	620.20 ± 0.83	620.20 ± 0.92
11	621.00 ± 0.46	618.40 ± 0.93	620.00 ± 1.56	617.00 ± 1.02
12	615.00 ± 0.89	623.80 ± 1.20	613.00 ± 0.46	617.00 ± 0.91

Subject 12 / Week	area1 (H=control)	area2 (product E)	area3 (product F)	area4 (product G)
0	615.20 ± 1.76	625.20 ± 1.76	616.40 ± 1.13	619.40 ± 1.17
1	613.20 ± 0.97	622.40 ± 1.47	623.60 ± 1.86	632.60 ± 0.97
2	620.20 ± 1.47	621.40 ± 1.20	624.20 ± 0.85	625.80 ± 0.77
3	620.60 ± 0.60	633.00 ± 1.49	620.80 ± 0.47	628.40 ± 1.63
4	609.60 ± 1.09	617.80 ± 1.63	617.00 ± 1.49	617.80 ± 0.99
5	619.00 ± 1.14	621.80 ± 1.25	613.20 ± 1.55	620.20 ± 1.35
6	622.80 ± 1.38	615.80 ± 1.45	620.40 ± 0.53	621.80 ± 1.68
7	615.60 ± 1.24	625.20 ± 0.66	614.00 ± 1.12	623.40 ± 0.93
8	620.00 ± 1.14	612.60 ± 1.54	617.20 ± 1.65	616.60 ± 1.15
9	619.00 ± 1.49	620.60 ± 1.69	622.00 ± 0.91	623.00 ± 0.65
10	623.00 ± 1.96	623.20 ± 0.69	622.80 ± 1.62	624.80 ± 1.35
11	617.80 ± 1.36	621.20 ± 0.24	622.40 ± 1.27	628.20 ± 1.52
12	616.60 ± 0.44	624.20 ± 1.16	618.20 ± 0.88	622.20 ± 0.59

APPENDIX II

PART 1 Comparison of the extent of melanin decrease (difference from initial values) among the three face products and control after application for different periods.

PART 2 Comparison of the extent of erythema values (difference from initial values) among the three face products and control after application for different periods.

PART 3 Comparison of the extent of melanin decrease (difference from initial values) among the three body products and control after application for different periods.

PART 4 Comparison of the extent of erythema values (difference from initial values) among the three body products and control after application for different periods.

PART 1   Comparison of the extent of melanin decrease (difference from initial values)   among the three face products and control after application for different periods.

(Negative values indicate an increase in the absolute melanin values after application).

Week	Subject	Treatment			
		A	B	C	D (Control)
1	1	6.40	2.60	-5.00	-7.40
	2	-1.40	6.80	5.80	5.60
	3	13.40	8.00	16.20	11.20
	4	5.60	4.80	3.40	4.80
	5	4.20	7.60	7.80	-1.20
	6	2.80	0.60	-1.40	8.20
	7	2.40	12.40	12.60	2.60
	8	1.40	1.00	0.80	3.20
	9	4.60	5.40	0.20	4.60
	10	5.40	-3.60	-2.40	-3.60
	11	1.00	-4.20	0.40	3.20
	12	2.80	5.60	7.40	0.00
	Mean±S.E.M.	4.05 ± 1.06	3.92 ± 1.40	3.82 ± 1.83	2.60 ± 1.46

Week	Subject	Treatment			
		A	B	C	D (Control)
2	1	2	-2.00	-1.60	-9.80
	2	-1.00	0.20	6.20	5.20
	3	7.20	9.60	10.00	3.20
	4	4.60	-2.20	-4.80	-2.20
	5	3.80	1.20	7.40	-2.00
	6	5.40	2.20	4.40	-3.80
	7	11.60	10.20	9.80	1.40
	8	5.60	1.60	5.40	1.80
	9	2.00	8.00	0.60	1.00
	10	0.60	-5.00	-3.00	-4.20
	11	3.60	2.20	1.20	3.40
	12	5.00	3.20	10.00	0.20
	Mean±S.E.M.	4.20 ± 0.95	2.43 ± 1.37	3.80 ± 1.51	-0.48 ± 1.20

Week	Subject	Treatment			
		A	B	C	D (Control)
3	1	8.20	-3.00	2.20	-3.40
	2	4.60	9.20	4.60	-0.40
	3	11.00	13.00	15.20	8.60
	4	2.60	-5.00	0.00	-5.00
	5	4.40	7.20	5.40	-1.20
	6	6.60	4.40	5.00	3.00
	7	12.20	6.80	10.00	3.60
	8	5.40	0.00	2.60	1.00
	9	7.40	11.00	4.20	4.80
	10	4.40	-3.00	-2.60	-6.40
	11	2.60	2.00	1.80	4.40
	12	5.40	4.20	13.00	0.40
	Mean±S.E.M.	6.23 ± 0.88	3.90 ± 1.68	5.12 ± 1.51	0.78 ± 1.27

Week	Subject	Treatment			
		A	B	C	D (Control)
4	1	10.40	5.40	0.60	-8.00
	2	7.80	15.00	6.80	7.60
	3	19.80	13.40	16.40	6.20
	4	1.60	-5.20	1.00	-5.20
	5	7.60	5.80	13.00	3.80
	6	9.40	-1.60	3.40	-1.00
	7	10.40	5.80	9.80	-0.20
	8	3.00	-1.60	-1.40	-1.40
	9	5.60	9.60	5.60	4.20
	10	2.60	1.00	-0.80	-4.00
	11	4.20	4.60	8.40	5.20
	12	10.20	7.40	12.00	0.60
	Mean±S.E.M.	7.72 ± 1.44	4.97 ± 1.76	6.23 ± 1.69	0.65 ± 1.41

Week	Subject	Treatment			
		A	B	C	D (Control)
5	1	9.40	14.00	7.20	-1.80
	2	3.80	8.40	5.00	2.60
	3	17.00	16.60	15.20	10.80
	4	6.20	3.00	1.00	3.00
	5	5.00	6.60	11.80	-0.20
	6	7.40	6.80	2.00	4.20
	7	15.00	3.80	17.80	1.00
	8	2.60	-0.40	3.60	1.40
	9	7.00	11.60	9.20	8.00
	10	6.20	2.00	8.40	0.80
	11	-1.00	1.80	-0.60	0.00
	12	8.40	10.20	16.80	0.80
	Mean±S.E.M.	7.25 ± 1.43	7.03 ± 1.53	8.12 ± 1.81	2.55 ± 1.04

Week	Subject	Treatment			
		A	B	C	D (Control)
6	1	11.20	10.20	15.20	0.00
	2	10.80	14.60	14.20	5.60
	3	13.60	14.00	11.00	10.60
	4	1.40	-0.40	-0.40	-0.40
	5	8.60	5.40	5.20	-1.00
	6	10.20	7.60	5.60	9.00
	7	14.40	14.00	16.80	0.20
	8	5.60	3.40	5.20	-0.40
	9	8.80	10.80	9.40	1.80
	10	5.40	7.00	1.40	-3.20
	11	4.20	2.60	2.00	-0.20
	12	10.80	9.40	15.00	1.00
	Mean±S.E.M.	8.75 ± 1.13	8.22 ± 1.40	8.38 ± 1.74	1.92 ± 1.22

Week	Subject	Treatment			
		A	B	C	D (Control)
7	1	16.80	9.20	12.40	-2.80
	2	12.00	21.20	16.00	7.40
	3	11.80	24.60	17.20	7.60
	4	0.80	-0.20	4.00	-0.20
	5	6.20	7.80	10.20	-2.20
	6	4.00	6.40	2.20	5.20
	7	12.20	10.80	18.40	1.60
	8	6.20	2.40	3.60	1.20
	9	6.20	5.80	6.00	3.80
	10	-1.40	0.60	1.60	-3.20
	11	5.20	10.40	6.60	0.40
	12	14.60	10.80	19.60	0.40
	Mean±S.E.M.	7.88 ± 1.61	9.15 ± 2.16	9.82 ± 1.93	1.60 ± 1.07

Week	Subject	Treatment			
		A	B	C	D (Control)
8	1	9.20	10.80	9.40	1.40
	2	6.80	19.40	9.40	0.80
	3	15.60	19.20	16.40	6.20
	4	8.60	1.00	11.20	1.00
	5	0.60	-5.60	7.00	-3.20
	6	7.20	6.80	7.00	11.60
	7	20.40	17.80	14.20	1.20
	8	6.80	5.80	4.20	1.80
	9	4.00	7.20	7.00	4.40
	10	1.80	1.80	1.20	-2.40
	11	6.60	9.20	8.60	4.80
	12	9.20	11.40	18.80	0.60
	Mean±S.E.M.	8.07 ± 1.58	8.73 ± 2.21	9.56 ± 1.46	2.35 ± 1.15

Week	Subject	Treatment			
		A	B	C	D (Control)
9	1	12.00	11.20	12.00	-3.80
	2	4.40	5.20	0.80	-0.60
	3	8.60	13.80	17.80	3.00
	4	8.00	-0.40	12.40	-0.40
	5	2.40	4.40	11.20	-2.60
	6	11.00	11.00	8.80	5.20
	7	17.80	16.00	17.80	5.20
	8	4.40	4.80	1.80	-0.40
	9	5.60	10.20	12.00	3.20
	10	5.20	4.80	8.40	1.00
	11	1.40	3.20	3.80	-4.20
	12	16.40	18.00	27.20	2.20
	Mean±S.E.M.	8.10 ± 1.53	8.52 ± 1.64	9.75 ± 2.22	0.65 ± 0.93

Week	Subject	Treatment			
		A	B	C	D (Control)
10	1	17.20	16.40	16.80	-2.40
	2	4.00	12.00	8.40	0.20
	3	15.20	23.40	16.40	7.00
	4	10.00	-0.8	8.80	-0.80
	5	7.40	11.40	13.60	-2.20
	6	11.80	8.00	12.00	7.80
	7	23.40	17.00	20.80	0.40
	8	5.80	4.60	8.00	0.60
	9	5.20	10.40	9.60	1.40
	10	6.40	6.20	8.00	-7.40
	11	5.40	3.00	0.80	-4.00
	12	15.40	14.20	25.80	-0.80
	Mean±S.E.M.	10.60 ± 1.75	10.48 ± 1.96	12.42 ± 1.94	-0.02 ± 1.22

Week	Subject	Treatment			
		A	B	C	D (Control)
11	1	13.20	13.80	17.60	0.40
	2	6.60	18.40	13.80	2.40
	3	16.40	17.60	16.40	7.60
	4	8.80	-3.60	11.40	-3.60
	5	9.20	11.40	11.40	-1.80
	6	10.40	10.80	13.60	5.80
	7	29.00	13.80	26.20	0.00
	8	12.60	10.40	8.60	2.40
	9	9.80	15.80	14.80	3.00
	10	6.00	7.20	10.60	-4.80
	11	5.40	7.40	7.80	0.40
	12	15.00	15.60	25.60	1.20
	Mean±S.E.M.	11.87 ± 1.86	11.55 ± 1.73	14.82 ± 1.72	1.08 ± 1.03

Week	Subject	Treatment			
		A	B	C	D (Control)
12	1	11.00	16.60	16.60	-4.00
	2	7.20	11.40	6.80	0.00
	3	13.40	17.60	17.60	8.00
	4	10.60	2.40	9.00	2.40
	5	9.80	11.60	10.20	-1.20
	6	7.60	7.20	14.00	3.80
	7	23.60	14.40	25.40	0.60
	8	6.80	8.40	6.00	1.80
	9	10.00	12.20	11.80	-2.00
	10	7.00	7.20	7.80	-5.60
	11	4.20	3.40	5.00	-3.60
	12	11.40	15.80	22.40	0.20
	Mean±S.E.M.	10.22 ± 1.42	10.68 ± 1.45	12.72 ± 1.91	0.03 ± 1.08

PART 2   Comparison of erythema values (difference from initial values) among the three
face products and control after   application for different periods. (Negative
values indicate an increase in the absolute erythema values after application).

Week	Subject	Treatment			
		A	B	C	D (Control)
1	1	1.40	-18.60	-7.40	-17.80
	2	-12.20	3.40	0	2.00
	3	6.60	6.20	5.60	-2.40
	4	10.40	3.60	-4.60	3.80
	5	-0.80	-0.20	-7.00	-4.80
	6	-3.40	0.60	1.00	-1.00
	7	0.40	1.00	-1.20	-6.60
	8	6.20	6.20	-7.60	0.20
	9	6.00	9.20	-5.40	-4.40
	10	2.00	-4.00	-17.60	-8.60
	11	10.40	-3.80	3.40	1.80
	12	2.20	18.60	17.60	-6.80
	Mean ± S.E.M.	2.43 ± 1.82	1.85 ± 2.57	-1.93 ± 2.51	-3.72 ± 1.71

Week	Subject	Treatment			
		A	B	C	D (Control)
2	1	-6.80	-9.00	-12.00	-17.80
	2	-11.00	-9.40	-10.60	-15.80
	3	-5.40	1.00	-5.00	-3.60
	4	12.80	-1.60	-9.00	-2.40
	5	1.40	-2.80	-2.20	-4.80
	6	-8.80	-14.40	-7.20	-2.20
	7	-5.60	5.80	-16.20	-6.40
	8	5.00	-7.40	-4.20	-2.60
	9	1.00	3.00	-8.80	-11.40
	10	-4.00	-1.00	-4.60	-10.20
	11	-1.80	4.00	-2.00	3.40
	12	2.20	0.80	-5.00	-6.40
	Mean ± S.E.M.	-1.75 ± 1.92	-2.58 ± 1.79	-7.23 ± 1.23	-6.68 ± 1.77

Week	Subject	Treatment			
		A	B	C	D (Control)
3	1	4.20	-8.20	-3.60	-12.00
	2	-12.60	-5.00	-20.20	-14.60
	3	13.60	-0.20	-1.00	-3.80
	4	6.60	-1.60	-8.40	3.20
	5	-2.40	-4.40	-2.20	-2.40
	6	-6.20	-4.40	-6.60	-4.40
	7	0.00	-2.40	-6.40	-1.40
	8	9.40	-5.20	-1.00	0.20
	9	8.80	4.8	-3.80	10.80
	10	-1.40	-2.40	-4.20	-9.60
	11	6.80	6.00	6.00	8.00
	12	5.00	15.20	10.80	3.20
	Mean ± S.E.M.	2.65 ± 2.14	-0.65 ± 1.86	-3.38 ± 2.19	-1.90 ± 2.22

Week	Subject	Treatment			
		A	B	C	D (Control)
4	1	3.00	2.60	6.20	2.00
	2	-2.20	4.20	2.60	6.80
	3	6.60	10.00	-1.60	-1.20
	4	7.00	-7.80	-10.60	-5.00
	5	-2.40	-2.00	-4.20	-6.40
	6	-1.00	-3.80	2.80	1.60
	7	-2.00	-2.0	-10.00	-0.60
	8	4.60	-8.80	-5.20	-7.40
	9	7.00	6.60	3.20	3.80
	10	1.00	-2.60	-7.40	-5.60
	11	-7.6	-1.2	3.60	5.20
	12	1.4	16.00	5.40	3.00
	Mean ± S.E.M.	1.28 ± 1.32	0.93 ± 2.10	-1.27 ± 1.74	-0.32 ± 1.39

Week	Subject	Treatment			
		A	B	C	D (Control)
5	1	4.20	1.00	4.00	-9.40
	2	-7.00	-3.40	-1.00	-4.60
	3	14.00	5.80	-0.60	1.80
	4	16.40	-4.80	-3.80	-0.20
	5	0.40	3.60	-7.60	-12.20
	6	-1.20	-2.20	-0.20	-0.80
	7	-4.60	-2.80	2.00	-1.60
	8	3.40	-5.80	-2.60	-9.00
	9	9.80	11.80	0.40	3.80
	10	-5.00	-6.60	-25.40	-12.20
	11	-7.60	3.80	-3.80	0.40
	12	2.60	12.60	11.00	-0.20
	Mean ± S.E.M.	2.12 ± 2.30	1.08 ± 1.89	-2.30 ± 2.49	-3.68 ± 1.62

Week	Subject	Treatment			
		A	B	C	D (Control)
6	1	5.00	2.40	-13.20	-19.20
	2	-10.80	-3.20	-3.00	-4.60
	3	1.80	6.40	-3.40	1.00
	4	11.40	-5.00	-10.60	-1.80
	5	9.20	1.40	1.60	1.60
	6	-5.80	-7.00	2.00	1.20
	7	9.80	-2.40	-3.20	-10.20
	8	11.00	-1.40	-2.00	-7.20
	9	5.00	4.00	-0.60	-4.60
	10	5.00	1.20	-0.40	-11.40
	11	-3.20	8.80	5.80	-1.60
	12	-0.40	7.60	0.60	-3.20
	Mean ± S.E.M.	3.17 ± 2.04	1.07 ± 1.46	-2.20 ± 1.52	-5.00 ± 1.78

Week	Subject	Treatment			
		A	B	C	D (Control)
7	1	2.40	3.60	5.00	-12.60
	2	-9.00	7.80	0.20	-3.60
	3	12.20	9.80	13.40	11.00
	4	23.00	3.20	-3.60	-2.80
	5	4.20	5.00	3.60	-2.20
	6	-9.80	1.80	7.20	4.60
	7	4.40	0.20	-8.00	-2.80
	8	11.60	-8.00	-5.40	4.60
	9	10.60	10.40	1.60	-1.40
	10	6.20	1.60	-0.40	-1.80
	11	0.80	5.60	1.40	-1.60
	12	5.00	12.20	9.60	5.80
	Mean $\pm$ S.E.M.	5.13 $\pm$ 2.60	4.43 $\pm$ 1.58	2.05 $\pm$ 1.79	-0.23 $\pm$ 1.73

Week	Subject	Treatment			
		A	B	C	D (Control)
8	1	7.40	11.80	16.00	0.80
	2	-1.00	8	3.20	-3.60
	3	16.60	12.60	10.00	11.60
	4	20.80	3.40	3.00	-3.80
	5	11.80	15.80	-0.60	0.60
	6	-4.00	-4.40	10.20	3.00
	7	-1.20	-2.00	-6.00	7.80
	8	14.60	-2.00	-3.20	1.20
	9	14.20	10.20	2.60	-4.80
	10	-2.40	-1.20	-6.60	-9.00
	11	-7.60	-13.20	0.60	-2.80
	12	4.20	13.60	16.40	10.60
	Mean $\pm$ S.E.M.	6.12 $\pm$ 2.71	4.38 $\pm$ 2.60	3.80 $\pm$ 2.26	0.97 $\pm$ 1.84

Week	Subject	Treatment			
		A	B	C	D (Control)
9	1	0.40	0.80	7.60	-12.60
	2	-9.80	1.40	-1.80	-0.20
	3	12.00	11.20	10.00	9.00
	4	2.40	-6.40	-9.00	-4.80
	5	6.40	6.80	4.20	-4.40
	6	-0.20	2.20	5.80	10.20
	7	3.80	0.00	8.60	12.00
	8	7.40	-11.60	-7.60	-6.00
	9	11.60	6.80	3.80	1.60
	10	3.40	4.60	5.40	-11.20
	11	-5.20	-2.00	2.00	0.80
	12	8.20	15.00	13.80	8.60
	Mean ± S.E.M.	3.37 ± 1.87	2.40 ± 2.10	3.57 ± 1.97	0.25 ± 2.42

Week	Subject	Treatment			
		A	B	C	D (Control)
10	1	-1.20	-0.20	5.00	-14.60
	2	-6.00	4.80	-0.60	5.20
	3	-1.60	6.40	7.60	5.40
	4	12.00	-2.00	-2.40	-2.80
	5	13.00	13.20	7.40	0.00
	6	-2.40	-1.20	11.40	-5.20
	7	1.40	-9.00	-8.20	-3.80
	8	-0.60	-18.20	-12.20	-13.00
	9	0.60	4.20	-0.60	-5.00
	10	-0.80	6.00	-1.60	-5.60
	11	-5.20	-2.00	3.20	0.80
	12	6.80	10.60	18.80	1.00
	Mean ± S.E.M.	1.33 ± 1.77	1.05 ± 2.49	2.32 ± 2.45	-3.13 ± 1.80

Week	Subject	Treatment			
		A	B	C	D (Control)
11	1	0.20	3.40	9.00	-13.00
	2	3.60	6.20	2.40	7.20
	3	10.20	10.60	16.20	1.20
	4	14.20	-5.20	-1.60	1.40
	5	8.60	2.20	4.80	11.00
	6	-2.20	1.60	-4.80	8.40
	7	-5.00	1.60	-0.80	11.40
	8	3.60	-11.20	-3.40	3.20
	9	5.40	3.80	9.80	-4.40
	10	-1.60	2.20	8.20	-7.60
	11	-0.80	6.40	10.20	7.20
	12	-0.80	19.80	17.80	-1.00
	Mean ± S.E.M.	2.95 ± 1.66	3.45 ± 2.19	5.65 ± 2.15	2.08 ± 2.19

Week	Subject	Treatment			
		A	B	C	D (Control)
12	1	-4.80	4.00	11.60	-18.00
	2	-3.00	2.80	-2.00	0.80
	3	1.60	3.80	17.00	15.60
	4	11.00	-5.80	-4.20	8.80
	5	14.20	14.40	11.40	-5.40
	6	-1.60	-7.20	7.60	7.80
	7	6.80	7.60	4.80	11.60
	8	7.20	-0.60	0.00	1.00
	9	20.60	15.60	7.00	0.00
	10	2.80	-2.20	-6.60	-4.40
	11	-0.60	-0.80	7.40	2.80
	12	11.80	19.80	17.60	8.40
	Mean ± S.E.M.	5.50 ± 2.25	4.28 ± 2.48	5.97 ± 2.28	2.42 ± 2.61

PART 3 Comparison of the extent of melanin decrease (difference from initial values) among the three body products and control after application for different periods.
(Negative values indicate an increase in the absolute melanin values after application).

Week	Subject	Treatment			
		E	F	G	H (Control)
1	1	15.0	13.80	10.40	13.60
	2	12.60	3.80	14.00	15.60
	3	1.60	8.80	2.80	3.80
	4	3.60	9.60	12.40	0.40
	5	11.80	9.60	4.80	3.00
	6	12.00	6.00	4.40	10.00
	7	-0.60	4.20	3.00	1.40
	8	16.80	13.80	15.40	10.60
	9	10.20	10.00	8.00	11.40
	10	12.20	14.60	13.00	13.40
	11	22.40	17.80	7.60	7.20
	12	14.00	18.40	10.40	5.00
	Mean± S.E.M.	10.97 ± 1.89	10.87 ± 1.41	8.85 ± 1.27	7.95 ± 1.49

Week	Subject	Treatment			
		E	F	G	H (Control)
2	1	5.20	11.20	2.00	5.60
	2	9.20	13.80	10.00	3.40
	3	6.20	8.00	-1.00	5.00
	4	8.20	7.60	6.80	7.40
	5	16.00	16.80	9.80	7.00
	6	6.80	-0.40	-0.40	4.00
	7	11.40	12.60	8.20	8.00
	8	8.00	10.60	8.80	8.00
	9	6.40	6.80	6.60	4.00
	10	6.80	15.40	9.20	10.40
	11	12.40	7.00	20.40	19.00
	12	8.20	19.40	16.20	10.40
	Mean±S.E.M.	8.73 ± 0.90	10.73 ± 1.55	8.05 ± 1.79	7.68 ± 1.23

Week	Subject	Treatment			
		E	F	G	H (Control)
3	1	10.20	10.60	9.20	13.60
	2	13.60	13.80	17.20	7.00
	3	10.20	12.60	5.80	4.20
	4	4.80	7.60	6.20	5.60
	5	15.20	12.80	8.60	2.60
	6	9.40	0.40	2.60	1.40
	7	5.40	5.20	1.80	-2.60
	8	14.60	5.20	10.20	13.00
	9	15.60	16.20	12.20	14.40
	10	12.00	19.20	16.20	16.00
	11	20.80	17.40	12.00	14.00
	12	23.00	23.60	15.80	21.20
	Mean±S.E.M.	12.90 ± 1.58	12.05 ± 1.92	9.82 ± 1.48	9.20 ± 2.06

Week	Subject	Treatment			
		E	F	G	H (Control)
4	1	9.60	6.60	6.60	10.80
	2	10.60	11.00	15.80	17.60
	3	8.80	7.00	2.60	3.60
	4	7.60	11.60	10.40	11.40
	5	11.00	13.60	13.00	6.20
	6	2.00	-3.60	-10.80	-2.00
	7	5.60	6.00	2.80	8.20
	8	15.00	8.20	11.60	11.00
	9	6.40	8.20	6.40	3.80
	10	2.00	6.80	5.00	5.60
	11	18.60	15.00	9.00	13.40
	12	13.00	9.00	12.00	10.00
	Mean±S.E.M.	9.18 ± 1.43	8.28 ± 1.36	7.03 ± 2.01	8.30 ± 1.51

Week	Subject	Treatment			
		E	F	G	H (Control)
5	1	14.40	13.00	11.20	13.80
	2	13.00	10.60	12.20	13.60
	3	9.40	6.80	5.00	6.60
	4	3.40	10.40	9.80	6.60
	5	14.80	12.80	13.40	4.20
	6	4.00	-0.60	0.60	4.20
	7	15.00	13.00	10.00	7.00
	8	16.40	7.20	13.00	10.00
	9	19.80	18.20	17.00	15.00
	10	2.80	13.20	9.20	1.40
	11	21.40	14.20	10.60	13.80
	12	18.60	26.40	21.40	19.40
	Mean±S.E.M.	12.75 ± 1.86	12.10 ± 1.88	11.12 ± 1.52	9.63 ± 1.56

Week	Subject	Treatment			
		E	F	G	H (Control)
6	1	18.20	15.60	14.80	11.40
	2	14.80	15.80	18.40	14.00
	3	11.80	11.40	7.40	6.80
	4	4.00	7.00	3.00	1.40
	5	21.00	15.20	11.40	3.20
	6	7.80	0.20	-2.60	8.20
	7	13.80	10.40	15.80	2.40
	8	24.00	21.20	22.20	17.20
	9	22.20	19.40	16.80	15.00
	10	3.600	16.20	13.20	10.80
	11	26.00	21.80	20.80	19.80
	12	27.20	23.40	22.20	25.80
	Mean±S.E.M.	16.20 ± 2.38	14.80 ± 1.94	13.62 ± 2.23	11.33 ± 2.15

Week	Subject	Treatment			
		E	F	G	H (Control)
7	1	22.80	17.80	15.40	15.00
	2	18.60	15.60	19.80	18.80
	3	16.80	19.80	9.60	10.20
	4	7.40	13.20	9.80	1.20
	5	20.60	17.40	18.20	5.00
	6	9.20	-0.20	0.80	4.80
	7	10.60	10.40	13.20	8.20
	8	18.00	15.60	16.60	12.20
	9	19.00	17.40	16.00	10.60
	10	5.00	12.60	9.40	8.60
	11	26.00	18.40	21.40	20.40
	12	19.60	29.80	22.40	15.80
	Mean±S.E.M.	16.13 ± 1.89	15.65 ± 2.01	14.38 ± 1.79	10.90 ± 1.68

week	subject	Treatment			
		E	F	G	H (Control)
8	1	23.20	21.40	16.80	14.20
	2	15.00	21.80	21.80	19.00
	3	15.00	13.40	15.00	12.60
	4	3.40	12.40	7.40	7.00
	5	18.00	7.20	14.00	3.20
	6	13.00	8.60	4.60	1.60
	7	10.80	8.00	13.20	1.60
	8	13.00	21.40	21.20	21.80
	9	21.20	22.40	21.60	18.00
	10	9.40	15.80	19.00	15.60
	11	19.80	12.80	13.20	15.40
	12	22.80	23.60	24.40	12.00
	Mean±S.E.M.	15.38 ± 1.72	15.73 ± 1.78	15.98 ± 1.72	11.83 ± 2.01

Week	Subject	Treatment			
		E	F	G	H (Control)
9	1	27.20	22.00	21.40	18.80
	2	20.40	19.40	17.40	14.20
	3	16.60	13.80	19.80	11.40
	4	8.00	8.40	8.00	10.80
	5	23.20	16.40	13.20	2.80
	6	12.40	5.20	-0.40	4.00
	7	10.60	8.20	11.00	5.40
	8	23.20	20.20	23.60	15.40
	9	31.00	24.60	20.40	20.00
	10	11.60	18.40	14.20	14.00
	11	30.40	19.60	19.60	20.20
	12	15.60	13.60	19.20	10.40
	Mean±S.E.M.	19.18 ± 2.28	15.82 ± 1.75	15.62 ± 1.97	12.28 ± 1.73

Week	Subject	Treatment			
		E	F	G	H (Control)
10	1	22.20	17.00	14.40	15.20
	2	10.00	3.20	15.60	6.40
	3	20.60	17.80	26.20	17.00
	4	11.00	14.20	10.20	3.80
	5	23.20	20.00	17.60	4.60
	6	11.60	4.20	1.60	2.40
	7	11.40	10.60	14.00	7.60
	8	19.20	24.00	22.40	28.40
	9	22.00	20.40	17.40	17.00
	10	6.40	16.60	7.60	11.40
	11	27.20	19.80	27.80	16.00
	12	19.40	23.40	23.80	11.20
	Mean±S.E.M.	17.02 ± 1.90	15.93 ± 1.97	16.55 ± 2.25	11.75 ± 2.15

Week	Subject	Treatment			
		E	F	G	H (Control)
11	1	17.60	8.80	11.00	15.20
	2	14.80	18.60	17.20	11.40
	3	19.80	16.60	26.20	12.00
	4	9.00	11.00	6.60	9.80
	5	24.80	20.20	18.40	2.60
	6	11.40	4.20	0.60	11.20
	7	8.20	9.20	14.60	3.80
	8	23.40	21.40	22.60	23.00
	9	21.80	14.20	20.60	14.60
	10	8.20	17.40	15.00	11.00
	11	26.40	21.80	25.80	21.00
	12	21.80	20.00	22.00	17.80
	Mean±S.E.M.	17.27 ± 1.95	15.28 ± 1.66	16.72 ± 2.23	12.78 ± 1.76

Week	Subject	Treatment			
		E	F	G	H (Control)
12	1	16.20	11.00	10.80	9.60
	2	14.40	14.00	15.60	11.60
	3	21.00	19.00	26.40	10.80
	4	11.60	13.00	8.40	8.00
	5	23.60	18.40	20.00	7.20
	6	15.60	6.20	3.40	8.80
	7	11.80	8.00	15.20	7.00
	8	25.00	22.20	23.20	16.40
	9	16.20	16.80	11.60	7.40
	10	0.20	13.00	10.20	10.20
	11	33.80	23.40	24.40	21.20
	12	22.20	25.80	24.00	16.20
	Mean±S.E.M.	17.63 ± 2.43	15.90 ± 1.77	16.10 ± 2.15	11.20 ± 1.29

PART 4   Comparison of erythema values (difference from initial values) among the three body
products and control after application for different periods.

(Negative values indicate an increase in the absolute erythema values after application).

Week	Subject	Treatment			
		E	F	G	H (Control)
1	1	-4.00	-3.40	-6.00	-9.80
	2	-6.20	-11.20	-8.00	-7.40
	3	-8.00	-3.60	-10.60	-2.80
	4	5.20	3.20	0.00	3.40
	5	-5.80	-8.60	-16.60	-14.80
	6	2.40	-7.60	-9.00	-4.20
	7	-3.60	-4.40	4.00	9.20
	8	-7.80	-13.80	-7.20	-15.20
	9	-9.80	-17.20	-14.40	-23.00
	10	-11.00	-15.80	-3.00	-10.40
	11	-12.00	-13.20	-10.80	-9.00
	12	2.80	-7.20	-13.20	2.00
	Mean± S.E.M.	-4.82 ± 1.63	-8.57 ± 1.73	-7.90 ± 1.73	-6.83 ± 2.59

Week	Subject	Treatment			
		E	F	G	H (Control)
2	1	-13.80	-12.80	-11.00	-11.00
	2	-4.00	-8.60	-3.00	-8.00
	3	-4.40	-1.40	-11.80	3.60
	4	7.00	-4.00	4.20	8.80
	5	-0.80	-3.20	-8.20	-2.20
	6	1.80	-18.40	-12.00	-10.20
	7	12.20	1.60	-2.40	10.20
	8	-13.00	-13.60	-19.80	-11.00
	9	-26.20	-21.00	-19.40	-31.80
	10	-15.40	0.00	-9.40	-9.40
	11	-6.60	-14.40	0.00	-4.40
	12	3.80	-7.80	-6.40	-5.00
	Mean± S.E.M	-4.95 ± 3.12	-8.63 ± 2.15	-8.27 ± 2.10	-5.87 ± 3.19

Week	Subject	Treatment			
		E	F	G	H (Control)
3	1	-10.00	-7.40	-8.40	-9.60
	2	-4.40	1.40	-4.80	-8.80
	3	0.60	5.20	-3.00	4.80
	4	5.60	1.20	0.20	8.60
	5	1.80	-9.40	-12.40	-13.40
	6	-6.20	-18.80	-10.00	-16.60
	7	13.20	5.20	6.60	9.60
	8	-11.00	-9.80	-7.20	-6.00
	9	-13.00	-8.00	-7.80	-17.00
	10	-15.00	0.40	-6.60	-8.00
	11	-12.20	-7.40	-12.40	-8.00
	12	-7.80	-4.40	-9.00	-5.40
	Mean ± S.E.M.	-4.87 ± 2.48	-4.32 ± 2.07	-6.23 ± 1.57	-5.82 ± 2.60

Week	Subject	Treatment			
		E	F	G	H (Control)
4	1	3.40	-1.80	2.80	5.60
	2	4.00	3.40	9.60	5.40
	3	3.60	9.80	-1.20	6.80
	4	16.40	5.40	1.40	14.00
	5	-21.00	-6.00	-11.20	-9.60
	6	4.00	-11.40	-13.40	0.80
	7	4.40	-9.60	1.60	8.20
	8	-8.20	-14.40	-9.60	-3.20
	9	0.00	7.20	11.00	-9.00
	10	-2.20	7.60	2.00	4.80
	11	4.80	-2.20	7.60	2.00
	12	7.40	-0.60	1.60	5.60
	Mean ± S.E.M.	1.38 ± 2.63	1.05 ± 2.32	0.18 ± 2.29	2.62 ± 2.01

Week	Subject	Treatment			
		E	F	G	H (Control)
5	1	3.60	-2.80	3.60	9.00
	2	-1.80	-0.40	-5.00	-4.40
	3	7.40	9.00	0.80	5.60
	4	11.80	9.20	5.60	14.00
	5	-5.00	-3.20	-6.40	-9.80
	6	-6.00	-6.40	-11.80	-7.40
	7	3.40	-0.60	-3.00	-2.80
	8	-14.00	-19.40	-3.20	-1.40
	9	-5.20	-4.60	-8.40	-15.40
	10	2.20	20.20	10.60	7.00
	11	-6.40	-10.60	-9.20	-2.40
	12	3.40	3.20	-0.80	-3.80
	Mean±S.E.M.	-0.55 ± 2.06	-0.53 ± 2.95	-2.27 ± 1.90	-0.98 ± 2.44

Week	Subject	Treatment			
		E	F	G	H (Control)
6	1	1.00	-0.40	-8.80	-12.80
	2	-1.00	13.00	6.40	-4.00
	3	-3.60	0.60	-0.80	7.00
	4	13.40	4.20	0.40	7.20
	5	-2.40	-6.80	-15.80	-14.00
	6	-5.00	-4.00	1.60	5.80
	7	14.60	0.40	16.40	1.60
	8	-9.20	-10.60	-6.60	-8.80
	9	3.80	6.20	1.00	-6.60
	10	-4.40	11.20	2.00	3.60
	11	-2.60	-4.40	-1.00	4.20
	12	9.40	-4.00	-2.40	-7.60
	Mean±S.E.M.	1.17 ± 2.20	0.45 ± 2.06	-0.63 ± 2.29	-2.03 ± 2.26

Week	Subject	Treatment			
		E	F	G	H (Control)
7	1	5.80	4.00	-2.60	-3.40
	2	-12.60	-3.00	-5.20	-12.00
	3	12.40	6.20	17.40	19.00
	4	16.00	10.20	4.20	15.40
	5	3.60	-14.60	-7.20	-15.40
	6	-3.00	-17.60	-15.60	-6.80
	7	11.00	0.00	-4.20	11.60
	8	-5.40	1.20	0.00	-0.40
	9	0.00	-7.40	-4.20	-8.80
	10	-2.60	8.40	2.60	-4.00
	11	1.40	-7.60	1.00	1.60
	12	0.00	2.40	-4.00	-0.40
	Mean±S.E.M.	2.22 ± 2.34	-1.48 ± 2.55	1.12 ± 2.31	-0.3 ± 3.10

Week	Subject	Treatment			
		E	F	G	H (Control)
8	1	15.60	8.80	6.60	6.60
	2	-13.20	2.20	-4.00	-5.40
	3	5.00	6.00	1.20	-0.40
	4	15.80	19.00	8.20	19.40
	5	1.80	-3.60	-0.40	-2.40
	6	5.20	-17.20	-14.00	-12.40
	7	5.40	0.20	9.80	3.60
	8	-7.00	2.20	-8.60	-1.60
	9	-3.60	6.80	-3.00	-3.00
	10	3.00	12.00	3.00	6.20
	11	4.80	5.40	-2.60	-1.80
	12	12.60	-0.80	2.80	-4.80
	Mean±S.E.M.	3.78 ± 2.51	3.42 ± 2.58	-0.08 ± 2.00	0.33 ± 2.30

Week	Subject	Treatment			
		E	F	G	H (Control)
9	1	9.60	4.80	8.80	-8.40
	2	-3.40	-4.80	-12.40	-9.20
	3	7.20	12.60	5.40	8.80
	4	8.40	0.40	-1.00	16.40
	5	-1.20	-6.20	-12.20	-13.20
	6	10.60	-6.00	-5.00	-0.40
	7	12.60	-4.00	5.20	3.00
	8	-1.80	-3.60	4.80	-1.80
	9	4.00	3.60	-4.00	-12.8
	10	1.40	14.60	13.20	9.20
	11	-0.40	-8.60	-2.20	-2.80
	12	4.60	-5.60	-3.60	-3.80
	Mean±S.E.M.	4.30 ± 1.56	-0.23 ± 2.20	-0.25 ± 2.29	-1.25 ± 2.67

Week	Subject	Treatment			
		E	F	G	H (Control)
10	1	-18.60	12.20	12.20	7.00
	2	0.80	3.20	4.00	-3.20
	3	12.60	11.20	11.60	10.80
	4	18.80	11.40	4.00	13.20
	5	-0.20	-8.60	-11.40	-12.80
	6	9.60	-3.20	-6.20	-5.80
	7	3.60	3.60	4.80	-3.20
	8	-5.80	1.00	-2.00	9.20
	9	13.80	10.60	10.80	-8.00
	10	-6.00	16.00	-0.20	-3.40
	11	-4.40	-6.60	1.40	-1.80
	12	2.00	-6.40	-5.40	-7.80
	Mean±S.E.M.	2.18 ± 3.01	3.70 ± 2.47	1.97 ± 2.16	-0.48 ± 2.43

Week	Subject	Treatment			
		E	F	G	H (Control)
11	1	-0.60	-10.80	-3.40	-4.40
	2	-7.00	-1.20	-1.00	-19.20
	3	8.00	9.60	7.20	9.00
	4	16.60	2.20	6.60	16.40
	5	-2.80	-10.00	0.00	-16.60
	6	1.40	-1.40	-10.60	7.20
	7	1.20	-2.60	12.00	-1.00
	8	-7.60	-2.80	-6.00	-6.20
	9	-5.00	-8.20	2.20	-5.20
	10	-6.80	8.00	-10.80	-3.80
	11	-4.20	-3.40	-1.60	2.00
	12	4.00	-6.00	-8.80	-2.60
	Mean±S.E.M.	-0.23 ± 2.07	-2.21 ± 1.85	-1.18 ± 2.10	-2.03 ± 2.90

Week	Subject	Treatment			
		E	F	G	H (Control)
12	1	4.20	-0.20	5.20	-4.20
	2	2.60	6.20	-4.00	-13.00
	3	18.80	17.00	15.60	11.80
	4	16.80	8.80	4.60	19.80
	5	2.20	-10.20	-7.20	-4.40
	6	7.60	-10.60	-8.00	7.00
	7	10.00	-7.80	3.60	3.80
	8	-5.40	-5.60	6.40	-13.80
	9	0.00	-3.80	-3.80	-14.00
	10	-5.20	1.20	-2.60	-4.40
	11	2.80	-3.40	4.40	-3.40
	12	1.00	-1.80	-2.80	-1.40
	Mean±S.E.M.	4.62 ± 2.19	-0.85 ± 2.36	0.95 ± 1.98	-1.35 ± 3.02

APPENDIX III

ANOVA FOR LATIN SQUARE

PART 1 Comparison of mean melanin values (difference from initial values) among three face products and control after application at various periods.

PART 2 Comparison of mean erythema values (difference from initial values) among three face products and control after application at various periods.

PART 3 Comparison of mean melanin values (difference from initial values) among three body products and control after application at various periods.

PART 4 Comparison of mean erythema values (difference from initial values) among three body products and control after application at various periods.

PART 1 Comparison of mean melanin values (difference from initial values) among three
face products and control after application at various periods.

ANOVA for Latin square after one – week application ($X_0 - X_1$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	602.17	54.74	3.26	2.13	Sig
area	3	27.70	9.23	0.55	2.92	NS
product	3	16.20	5.40	0.32	2.92	NS
error	30	503.73	16.79			
total	47	1149.80				

ANOVA for Latin square after two – week application ($X_0 - X_2$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	540.76	49.16	4.81	2.13	Sig
area	3	7.68	2.56	0.25	2.92	NS
product	3	161.81	53.94	5.27	2.92	Sig
error	30	306.78	10.23			
Total	47	1017.03				

ANOVA for Latin square after three – week application ($X_0 - X_3$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	700.84	63.71	7.34	2.13	Sig
area	3	25.47	8.49	0.98	2.92	NS
product	3	199.10	66.37	7.64	2.92	Sig
error	30	260.43	8.68			
Total	47	1185.84				

ANOVA for Latin square after four – week application ($X_0 - X_4$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	939.64	85.42	6.97	2.13	Sig
area	3	7.04	2.35	0.19	2.92	NS
product	3	333.34	111.11	9.06	2.92	Sig
error	30	367.74	12.26			
total	47	1647.76				

ANOVA for Latin square after five – week application ($X_0 - X_5$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	698.18	63.47	4.28	2.13	Sig
area	3	7.42	2.47	0.17	2.92	NS
product	3	225.45	75.15	5.07	2.92	Sig
error	30	444.84	14.83			
total	47	1375.89				

ANOVA for Latin square after six – week application ($X_0 - X_6$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	739.91	67.26	7.43	2.13	Sig
area	3	8.61	2.87	0.32	2.92	NS
product	3	385.95	128.65	14.20	2.92	Sig
error	30	271.77	9.06			
total	47	1406.22				

ANOVA for Latin square after seven - week application($X_0 - X_7$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	1101.30	100.12	6.42	2.13	Sig
area	3	33.83	11.28	0.72	2.92	NS
product	3	509.35	169.78	10.89	2.92	Sig
error	30	467.59	15.59			
total	47	2112.07				

ANOVA for Latin square after eight - week application ($X_0 - X_8$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	855.77	77.80	4.51	2.13	Sig
area	3	50.19	16.73	0.97	2.92	NS
product	3	384.79	128.26	7.43	2.92	Sig
error	30	517.97	17.27			
total	47	1808.72				

ANOVA for Latin square after nine - week application($X_0 - X_9$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	982.04	89.28	6.90	2.13	Sig
area	3	13.56	4.52	0.35	2.92	NS
product	3	733.76	244.59	18.89	2.92	Sig
error	30	388.40	12.95			
total	47	2117.76				

ANOVA for Latin square after ten - week application ($X_0 - X_{10}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA Result
subject	11	1030.29	93.66	4.99	2.13	Sig
area	3	6.78	2.26	0.12	2.92	NS
product	3	1153.81	384.60	20.50	2.92	Sig
error	30	562.88	18.76			
total	47	2753.76				

ANOVA for Latin square after eleven - week application($X_0 - X_{11}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA result
subject	11	790.89	71.90	3.75	2.13	Sig
area	3	9.74	3.25	0.17	2.92	NS
product	3	1301.73	433.91	22.65	2.92	Sig
error	30	574.67	19.16			
total	47	2677.04				

ANOVA for Latin square after twelve - week application($X_0 - X_{12}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	ANOVA Result
subject	11	734.54	66.78	4.77	2.13	Sig
area	3	22.10	7.37	0.53	2.92	NS
product	3	1165.78	388.59	27.73	2.92	Sig
error	30	420.42	14.01			
total	47	2342.83				

NS = non - significant among three face products and control.

Sig = significant among three face products and control.

PART 2 Comparison of mean erythema values (difference from initial values) among three face products and control after application at various periods.

ANOVA for Latin square after one week application($X_0 - X_1$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1112.92	101.17	2.25	2.13	Sig
area	3	57.63	19.21	0.43	2.92	NS
product	3	317.14	105.71	2.35	2.92	NS
error	30	1351.03	45.03			
total	47	3838.72				

ANOVA for Latin square after two week application($X_0 - X_2$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	724.90	65.90	3.10	2.13	Sig
area	3	155.08	51.69	2.43	2.92	NS
product	3	281.50	93.83	4.42	2.92	Sig
error	30	637.61	21.25			
total	47	1799.09				

ANOVA for Latin square after three week application($X_0 - X_3$)

Source of errors	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1602.17	145.65	6.13	2.31	Sig
area	3	25.19	8.40	0.35	2.92	NS
product	3	237.68	79.23	3.34	2.92	Sig
error	30	712.58	23.75			
total	47	2577.62				

ANOVA for Latin square after four - week application($X_0 - X_4$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	699.68	63.61	2.68	2.13	Sig
area	3	54.70	18.23	0.77	2.92	NS
product	3	49.47	16.45	0.69	2.92	NS
error	30	712.79	23.76			
total	47	1516.64				

ANOVA for Latin square after five - week application($X_0 - X_5$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1247.49	113.41	3.30	2.13	Sig
area	3	54.19	18.07	0.53	2.92	NS
product	3	270.89	90.30	2.63	2.92	NS
error	30	1030.63	34.35			
total	47	2603.20				

ANOVA for Latin square after six - week application($X_0 - X_6$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	384.34	34.94	1.00	2.13	NS
area	3	116.04	38.68	1.10	2.92	NS
product	3	465.66	155.22	4.43	2.92	Sig
error	30	1051.76	35.06			
total	47	2017.76				

ANOVA for Latin square after seven - week application($X_0 - X_7$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	692.21	62.93	1.82	2.13	NS
area	3	309.02	103.06	2.98	2.92	Sig
product	3	214.41	71.47	2.07	2.92	NS
error	30	1036.86	34.56			
total	47	2252.50				

ANOVA for Latin square after eight - week application($X_0 - X_8$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1491.89	135.63	3.86	2.13	Sig
area	3	424.49	141.50	4.02	2.92	Sig
product	3	164.81	54.94	1.56	2.92	NS
error	30	1055.44	35.18			
total	47	3136.63				

ANOVA for Latin square after nine - week application($X_0 - X_9$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1298.38	118.03	4.84	2.13	Sig
area	3	290.92	96.97	3.98	2.92	Sig
product	3	83.02	27.67	1.13	2.92	NS
error	30	731.67	24.39			
total	47	2403.96				

ANOVA for Latin square after ten - week application ($X_0 - X_{10}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1324.40	120.40	4.20	2.13	Sig
area	3	262.23	87.40	3.05	2.92	Sig
product	3	209.42	69.81	2.44	2.92	NS
error	30	859.87	28.66			
total	47	2655.92				

ANOVA for Latin square after eleven - week application ($X_0 - X_{11}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	592.67	53.88	1.01	2.13	NS
area	3	44.33	14.78	0.28	2.92	NS
product	3	83.16	27.72	0.52	2.92	NS
error	30	1606.27	53.54			
total	47	2326.43				

ANOVA for Latin square after twelve - week application ($X_0 - X_{12}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1312.56	119.32	2.66	2.13	NS
area	3	404.27	134.76	3.01	2.92	Sig
product	3	90.38	30.13	0.67	2.92	NS
error	30	1344.31	44.81			
total	47	3151.52				

NS = non - significant among three face products and control.

Sig = significant among three face products and control.

PART 3 Comparison of mean melanin values (difference from initial values) among three body products and control after application at various periods.

ANOVA for Latin square after one – week application ($X_0 - X_1$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	709.16	64.47	4.38	2.13	Sig
area	3	91.76	30.59	2.08	2.92	NS
product	3	80.92	26.97	1.83	2.92	NS
error	30	441.43	14.71			
total	47					

ANOVA for Latin square after two – week application ($X_0 - X_2$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	600.46	54.59	3.74	2.13	Sig
area	3	7.21	2.40	0.16	2.92	NS
product	3	66.62	22.21	1.52	2.92	NS
error	30	438.19	14.61			
total	47	1112.48				

ANOVA for Latin square after three – week application ($X_0 - X_3$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1310.25	119.11	10.48	2.13	Sig
area	3	14.00	4.67	0.41	2.92	NS
product	3	112.23	37.41	3.29	2.92	Sig
error	30	341.03	11.37			
total	47	1777.51				

ANOVA for Latin square after four – week application ($X_0 - X_4$)

source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1051.62	95.60	10.37	2.13	Sig
area	3	18.51	6.17	0.67	2.92	NS
product	3	28.14	9.38	1.02	2.92	NS
error	30	276.45	9.21			
total	47	1394.72				

ANOVA for Latin square after five – week application ($X_0 - X_5$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1198.68	108.97	9.66	2.13	Sig
area	3	21.51	7.17	0.64	2.92	NS
product	3	66.16	22.05	1.96	2.92	NS
error	30	338.29	11.28			
total	47	1624.64				

ANOVA for Latin square after six– week application ($X_0 - X_6$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	2050.78	186.43	14.27	2.13	Sig
area	3	65.99	22.00	1.68	2.92	NS
product	3	152.85	50.95	3.90	2.92	Sig
error	30	391.93	13.06			
total	47	2661.55				

ANOVA for Latin square after seven – week application ($X_0 - X_7$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1357.95	123.45	9.38	2.13	Sig
area	3	42.89	14.30	1.09	2.92	NS
product	3	200.96	66.98	5.09	2.92	Sig
error	30	394.96	13.17			
total	47	1996.75				

ANOVA for Latin square after eight – week application ($X_0 - X_8$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1212.56	110.23	7.37	2.13	Sig
area	3	69.32	23.11	1.55	2.92	NS
product	3	137.76	45.92	3.07	2.92	Sig
error	30	448.53	14.95			
total	47	1868.16				

ANOVA for Latin square after nine – week application ($X_0 - X_9$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1585.33	144.12	12.40	2.13	Sig
area	3	61.39	20.46	1.76	2.92	NS
product	3	285.90	95.30	8.20	2.92	Sig
error	30	348.63	11.62			
total	47	2281.25				

ANOVA for Latin Square after ten – week application ($X_0 - X_{10}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1628.70	148.06	7.81	2.13	Sig
area	3	61.82	20.61	1.09	2.92	NS
product	3	210.15	70.05	3.70	2.92	Sig
error	30	568.60	18.95			
total	47					

ANOVA for Latin Square after eleven – week application ($X_0 - X_{11}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1318.64	119.88	8.25	2.13	Sig
area	3	171.98	57.33	3.94	2.92	Sig
product	3	144.34	48.11	3.31	2.92	Sig
error	30	435.99	14.53			
total	47	2070.95				

ANOVA for Latin Square after twelve – week application ($X_0 - X_{12}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1483.81	134.89	12.62	2.13	Sig
area	3	31.41	10.47	0.98	2.92	Sig
product	3	426.73	142.24	13.31	2.92	Sig
error	30	320.55	10.69			
total	47	2262.50				

NS = non significant among three face products and control.

Sig = significant among three face products and control.

PART4 Comparison of mean erythema values (difference from initial values) among three body products and control after application at various periods.

ANOVA for Latin square after one – week application ($X_0 - X_1$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1330.69	120.97	6.64	2.13	Sig
area	3	143.75	47.92	2.63	2.92	NS
product	3	96.67	32.22	1.77	2.92	NS
error	30	546.81	18.23			
total	47	2117.92				

ANOVA for Latin square after two – week application ($X_0 - X_2$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	2840.25	258.20	8.85	2.13	Sig
area	3	116.87	32.56	1.12	2.92	NS
product	3	972.52	38.96	1.34	2.92	NS
error	30	874.84	29.16			
total	47	3929.64				

ANOVA for Latin square after three – week application ($X_0 - X_3$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1952.18	177.47	9.14	2.13	Sig
area	3	51.98	17.33	0.89	2.92	NS
product	3	27.51	9.170	0.47	2.92	NS
error	30	582.81	19.43			
total	47	2614.48				

ANOVA for Latin square after four – week application ($X_0 - X_4$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1691.57	153.78	4.42	2.13	Sig
area	3	103.78	34.59	1.00	2.92	NS
product	3	89.31	29.77	0.86	2.92	NS
error	30	1042.78	34.76			
total	47	2927.43				

ANOVA for Latin square after five – week application ($X_0 - X_5$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	2213.71	201.25	8.39	2.13	Sig
area	3	35.03	11.68	0.49	2.92	NS
product	3	23.97	7.99	0.33	2.92	NS
error	30	719.76	23.99			
total	47	2992.47				

ANOVA for Latin square after six – week application ($X_0 - X_6$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1335.18	121.38	4.77	2.13	Sig
area	3	459.93	153.31	6.03	2.92	Sig
product	3	69.88	23.29	0.92	2.92	NS
error	30	762.78	25.43			
total	47	2627.77				

ANOVA for Latin square after seven – week application ($X_0 - X_7$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	2497.46	227.04	8.64	2.13	Sig
area	3	241.01	80.34	3.06	2.92	NS
product	3	109.54	36.51	1.39	2.92	NS
error	30	788.80	26.29			
total	47	3636.81				

ANOVA for Latin square after eight – week application ($X_0 - X_8$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	2000.44	181.86	6.02	2.13	Sig
area	3	22.89	7.63	0.25	2.92	NS
product	3	146.76	48.92	1.62	2.92	NS
error	30	905.85	30.19			
total	47	3075.93				

ANOVA for Latin square after nine– week application ($X_0 - X_9$)

Source of variations	df	SS	MS = $\dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1489.80	135.45	4.36	2.13	Sig
area	3	167.54	55.85	1.79	2.92	NS
product	3	222.27	74.01	2.38	2.92	NS
error	30	933.81	31.13			
total	47	2813.60				

ANOVA for Latin square after ten – week application ($X_0 - X_{10}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	2003.43	182.13	7.06	2.13	Sig
area	3	327.12	109.04	4.22	2.92	Sig
product	3	219.81	73.27	2.84	2.92	NS
error	30	774.67	25.82			
total	47	3325.03				

ANOVA for Latin square after eleven – week application ($X_0 - X_{11}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1457.95	132.54	3.78	2.13	Sig
area	3	196.30	65.43	1.87	2.92	NS
product	3	29.70	9.90	0.29	2.92	NS
error	30	1051.80	35.06			
total	47	2735.75				

ANOVA for Latin square after twelve – week application ($X_0 - X_{12}$)

Source of variations	df	SS	$MS = \dfrac{SS}{df}$	F_{cal}	F_{tab}	Sig
subject	11	1973.52	179.41	5.21	2.13	Sig
area	3	74.23	24.74	0.72	2.92	NS
product	3	263.13	87.71	2.55	2.92	NS
error	30	1032.77	34.43			
total	47	3343.68				

NS = non significant among three face products and control

Sig = significant among three face products and control

APPENDIX IV

PART 1   Duncan's new multiple range test of melanin values among the three face
products and control after application for different periods.

PART 2   Duncan's new multiple range test of erythema values among the three face
products and control after application for different periods.

PART 3   Duncan's new multiple range test of melanin values among the three body
products and control after application for different periods.

PART 1   Duncan's new multiple range test of melanin values among the three face products and

               control after application for different periods.

At two – week (X_0 - X_2) after application.

MS Error = 10.2262	df Error = 30	Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	2.6679
LSR where p = 3 - - - - -	3.2125
LSR where p = 4 - - - - -	3.5448

Means

Mean # 1 = -0.4830	(control)
Mean # 2 = 2.4300	(b)
Mean # 3 = 3.8000	(c)
Mean # 4 = 4.2000	(a)

Result : control < b < c < a

At three – week (X_0 – X_3) after application.

MS Error = 8.6811	df Error = 30	Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	2.4581
LSR where p = 3 - - - - -	2.9599
LSR where p = 4 - - - - -	3.2661

Means

Mean # 1 = 0.7833	(control)
Mean # 2 = 3.9000	(b)
Mean # 3 = 5.1166	(c)
Mean # 4 = 6.2300	(a)

Result : control < b < c < a

At four – week $(X_0 – X_4)$ after application.

MS Error = 12.2580   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -   2.9209

LSR where p = 3 - - - - -   3.5172

LSR where p = 4 - - - - -   3.8811

Means

Mean # 1 = 0.6166   (d)

Mean # 2 = 5.0333   (b)

Mean # 3 = 5.2333   (c)

Mean # 4 = 7.5000   (a)

Result : control < <u>b < c < a</u>

At five – week $(X_0 – X_5)$ after application.

MS Error = 14.8279   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -   3.2125

LSR where p = 3 - - - - -   3.8684

LSR where p = 4 - - - - -   4.2686

Means

Mean # 1 = 2.5500   (d)

Mean # 2 = 7.0333   (b)

Mean # 3 = 7.2500   (a)

Mean # 4 = 8.1166   (c)

Result : control < <u>b < a < c</u>

At six – week ($X_0 - X_6$) after application.

MS Error = 9.0589 df Error = 30 Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - - 2.5110

LSR where p = 3 - - - - - 3.0236

LSR where p = 4 - - - - - 3.3364

Means

Mean # 1 = 1.9167 (control)

Mean # 2 = 8.2167 (b)

Mean # 3 = 8.3833 (c)

Mean # 4 = 8.7500 (a)

Result : control < b < c < a

At seven – week ($X_0 - X_7$) after application.

MS Error = 15.5864 df Error = 30.0000 Significance level = 0.0500

Least Significant Ranges

LSR where p = 2 - - - - - 3.2937

LSR where p = 3 - - - - - 3.9661

LSR where p = 4 - - - - - 4.3764

Means

Mean # 1 = 1.6000 (control)

Mean # 2 = 7.3667 (a)

Mean # 3 = 9.1500 (b)

Mean # 4 = 9.8167 (c)

Result : control < a < b < c

At eight – week ($X_0 – X_8$) after application.

MS Error = 17.2657   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -   3.4666

LSR where p = 3 - - - - -   4.1743

LSR where p = 4 - - - - -   4.6061

Means

Mean # 1 = 2.3500   (control)

Mean # 2 = 8.0660   (a)

Mean # 3 = 8.7330   (b)

Mean # 4 = 9.5330   (c)

Result : control < a < b < c

At nine – week ($X_0 – X_9$) after application.

MS Error = 12.9500   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -   3.0022

LSR where p = 3 - - - - -   3.6151

LSR where p = 4 - - - - -   3.9891

Means

Mean # 1 = 0.6500   (d)

Mean # 2 = 8.1000   (a)

Mean # 3 = 8.5200   (b)

Mean # 4 = 9.7500   (c)

Result : control < a < b < c

At ten – week ($X_0 - X_{10}$) after application.

MS Error = 18.7625   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -   3.6137

LSR where p = 3 - - - - -   4.3514

LSR where p = 4 - - - - -   4.8016

Means

Mean # 1 = -0.0167   (control)

Mean # 2 = 10.4830   (b)

Mean # 3 = 10.6000   (a)

Mean # 4 = 12.4170   (c)

Result : control < b < a < c

At eleven – week ($X_0 - X_{11}$) after application.

MS Error = 19.1558   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -   3.6514

LSR where p = 3 - - - - -   4.3968

LSR where p = 4 - - - - -   4.8517

Means

Mean # 1 = 1.0830   (control)

Mean # 2 = 11.5500   (b)

Mean # 3 = 11.8660   (a)

Mean # 4 = 14.8167   (c)

Result : control < b < a < c

At twelve – week ($X_0 - X_{12}$) after application.

| MS Error = 14.0139 | df Error = 30 | Significance level = 0.05 |

Least Significant Ranges

LSR where p = 2 - - - - -   3.1231

LSR where p = 3 - - - - -   3.7607

LSR where p = 4 - - - - -   4.1497

Means

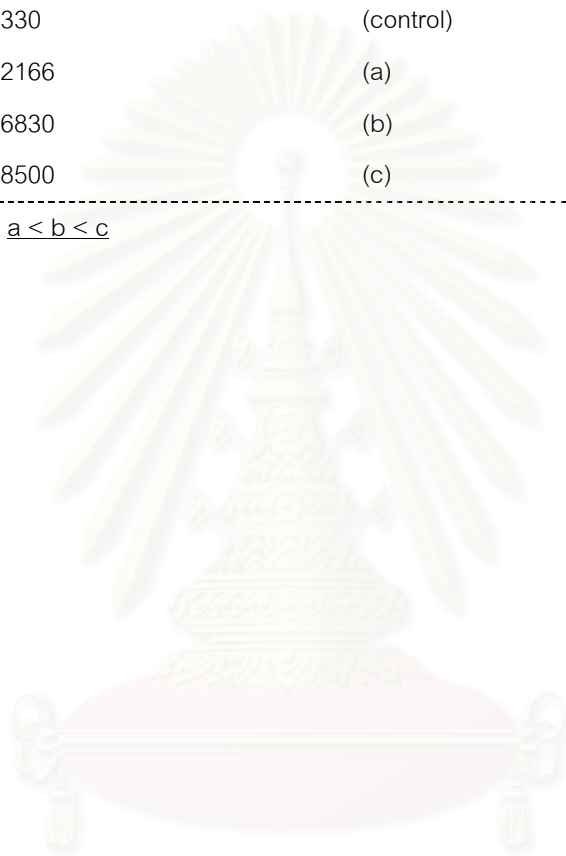---

Mean # 1 = 0.0330   (control)

Mean # 2 = 10.2166   (a)

Mean # 3 = 10.6830   (b)

Mean # 4 = 10.8500   (c)

Result : control < <u>a < b < c</u>

PART 2   Duncan's new multiple range test of erythema values among the three face   products

and control after application for different periods.

At two – week (X_0 - X_2) after application.

MS Error = 21.2500   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	3.8458
LSR where p = 3 - - - - -	4.6309
LSR where p = 4 - - - - -	5.1100

Means	Product
Mean # 1 = -7.2300	(c)
Mean # 2 = -6.6800	(control)
Mean # 3 = -2.5800	(b)
Mean # 4 = -1.7500	(a)

Result : c < control < b < a

At three – week (X_0 – X_3) after application.

MS Error = 23.7500   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	4.0657
LSR where p = 3 - - - - -	4.8958
LSR where p = 4 - - - - -	5.4022

Means

Mean # 1 = -3.3800	(c)
Mean # 2 = -1.9000	(control)
Mean # 3 = -0.6500	(b)
Mean # 4 = 2.6500	(a)

Result : c < control < b < a

At six – week ($X_0 - X_6$) after application.

| MS Error = 35.0600 | df Error = 30 | Significance level = 0.05 |

Least Significant Ranges

LSR where p = 2 - - - - -   4.9398

LSR where p = 3 - - - - -   5.9483

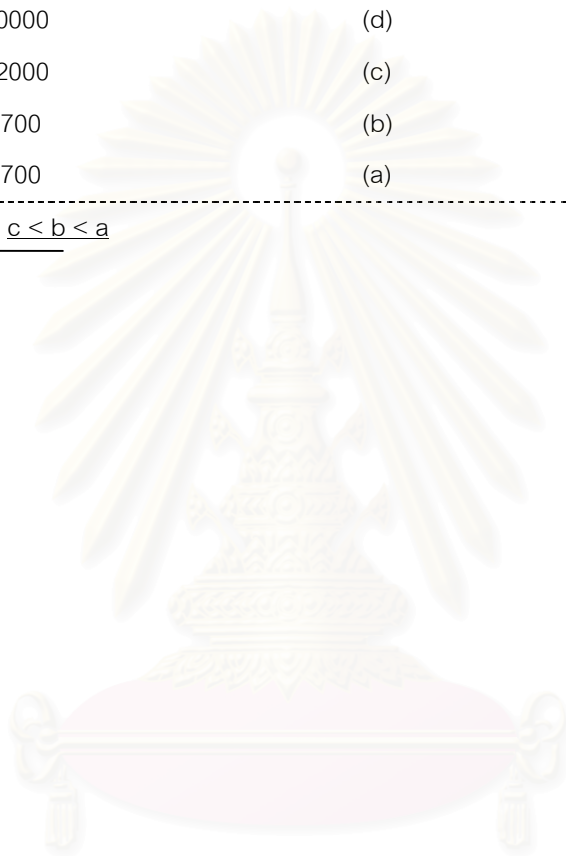LSR where p = 4 - - - - -   6.5637

Means

Mean # 1 = -5.0000   (d)

Mean # 2 = -2.2000   (c)

Mean # 3 = 1.0700   (b)

Mean # 4 = 3.1700   (a)

Result : control < c < b < a

PART 3   Duncan's new multiple range test of melanin values among the three body products and control after application for different periods.

At three – week ($X_0 – X_3$) after application.

MS Error = 11.3677   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	2.8128
LSR where p = 3 - - - - -	3.3871
LSR where p = 4 - - - - -	3.7375

Means

Mean # 1 = 9.2000	(D)
Mean # 2 = 9.8167	(C)
Mean # 3 = 12.0500	(B)
Mean # 4 = 12.9000	(A)

Result : control < C < B < A

At six – week ($X_0 – X_6$) after application.

MS Error = 13.0643   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	3.0154
LSR where p = 3 - - - - -	3.6310
LSR where p = 4 - - - - -	4.0067

Means

Mean # 1 = 11.3333	(control)
Mean # 2 = 13.6167	(c)
Mean # 3 = 14.8000	(b)
Mean # 4 = 16.2000	(a)

Result : control < c < b < a

At seven – week ($X_0 - X_7$) after application.

MS Error = 13.1654   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	3.0271
LSR where p = 3 - - - - -	3.6451
LSR where p = 4 - - - - -	4.0221

Means

Mean # 1 = 9.9830	(control)
Mean # 2 = 14.3800	(c)
Mean # 3 = 15.6500	(b)
Mean # 4 = 16.1300	(a)

Result : control < c < b < a

At eight – week ($X_0 - X_8$) after application.

MS Error = 14.9510   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -	3.2258
LSR where p = 3 - - - - -	3.8844
LSR where p = 4 - - - - -	4.2862

Means

Mean # 1 = 11.8333	(control)
Mean # 2 = 15.3830	(a)
Mean # 3 = 15.7333	(b)
Mean # 4 = 16.0166	(c)

Result : control < a < b < c

At nine – week ($X_0 – X_9$) after application.

MS Error = 11.6211   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2   - - - - -   2.8440

LSR where p = 3   - - - - -   3.4246

LSR where p = 4   - - - - -   3.7789

Means

Mean # 1   =   12.2833   (control)

Mean # 2   =   15.6167   (c)

Mean # 3   =   15.8167   (b)

Mean # 4   =   19.1833   (a)

Result : control < c < b < a

At ten – week ($X_0 – X_{10}$) after application.

MS Error = 18.9533   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2   - - - - -   3.6320

LSR where p = 3   - - - - -   4.3735

LSR where p = 4   - - - - -   4.8260

Means

Mean # 1   =   11.7500   (control)

Mean # 2   =   15.9330   (b)

Mean # 3   =   16.5500   (c)

Mean # 4   =   17.0166   (a)

Result : control ≤ b < c < a

At eleven – week ($X_0 – X_{11}$) after application.

MS Error = 14.5330   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2 - - - - -   3.1804

LSR where p = 3 - - - - -   3.8297

LSR where p = 4 - - - - -   4.2259

Means

Mean # 1 = 12.7830   (control)

Mean # 2 = 15.2830   (b)

Mean # 3 = 16.7167   (c)

Mean # 4 = 17.2667   (a)

Result : control < b < c < a

At twelve – week ($X_0 – X_{12}$) after application.

MS Error = 10.6850   df Error = 30   Significance level = 0.05

Least Significant Ranges

LSR where p = 2   - - - - -   2.7271

LSR where p = 3   - - - - -   3.2838

LSR where p = 4   - - - - -   3.6235

Means

Mean # 1 = 11.2000   (control)

Mean # 2 = 15.9000   (b)

Mean # 3 = 16.1000   (c)

Mean # 4 = 17.6330   (a)

Result : control < b < c < a

VITA

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