APPLICATION OF PHYTANDIOLAMINE IN COSMETIC FIELD

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Introduction

1. As a powerful anti-acne agent

Acne is a frequently occurring inflammatory disease or disorder generally developed at sebum gland in hair follicle of skin. Many reagents have been developed for treatment of this disorder. But excellent reagent for treatment of this disorder was in rare case because a reagent which has powerful efficacy is not compatible to human body, and a compatible agent is not effective. So, many researches have continually focused on better compatibility and efficacy to human body.

Our new synthetic materials, phytandiol amine derivatives, are good for developing anti-acne product in cosmetic fields. The phytandiol amine derivatives of this study can be produced from phytantriol and phytol, which are commercially available. To test the anti-acne activity, we measured a MIC(minimum inhibitory concentration) of phytandiol amine derivatives against the bacteria causing acne. Those results showed that phytandiol amine derivatives are more effective than erythromycin-antibiotics to inhibit acne-causing bacteria.

2. As a precursor for synthetic pseudoceramide

It is generally understood that ceramides play an important role in the production and maintenance of the water permeability barrier of the skin. But the application of natural ceramide in formulation is limited because of low solubility, high melting point, and bacterial contamination. In order to overcome these problems, synthetic ceramides called pseudoceramides, which are similar to natural ceramides, have been proposed. The purpose of our study was to synthesize novel pseudoceramides via effective and economical pathway.

Materials and Reagents

1> The synthesis of Phytandiol amine & Pseudoceramide

- Phytantriol, Pytol, *p*-Tolunesolfonic chloride, Triethylamine, Pyridine, Sodium azide, Palladium 10 wt% on activated carbon, Stearic acid.
- We purchased these reagents from Aldrich Co.

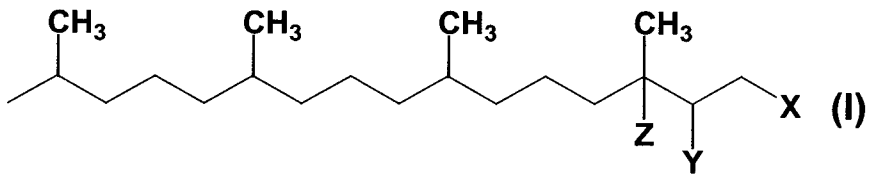
2> Measurement of Minimum Inhibitory Concentration of various reagents against acne-causing anaerobic bacteria

- reinforced clostridial agar medium (Difco 218081(1808-17))
- Anaerobic system(Difco 219521(1952-24-8))
- Erythromycin(SIGMA E-6376(114-07-8))
- Benzoyl peroxide(SIGMA 17,998-1(94-36-0)

Procedure and results

1. The formula of Phytandiol amine

A phytandiol amine derivative is represented by the following formula (I):



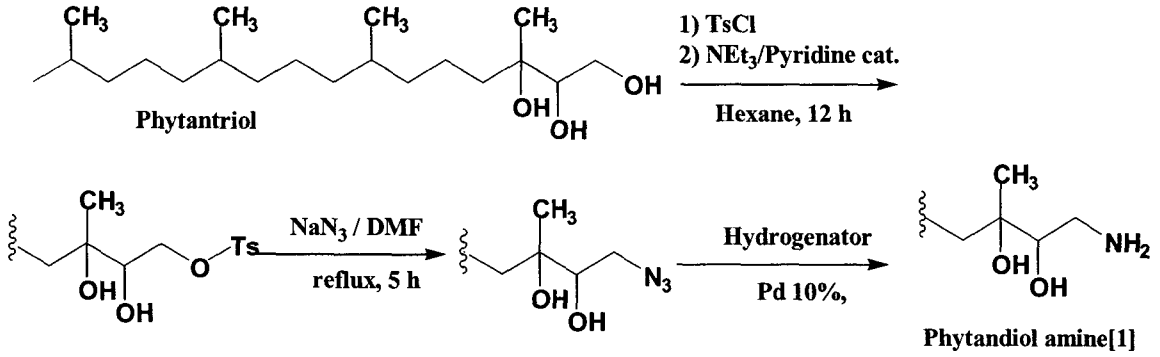
(I)

wherein Phytandiol amine[1] each of Y and Z is OH with the proviso that X is NH_2.

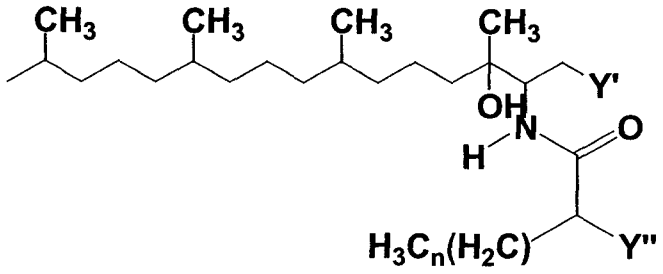
Phytandiol amine[2] X and Z is OH with the proviso that Y is NH_2.

Phytandiol amine[3] X and Y is OH with the proviso that Z is NH_2.

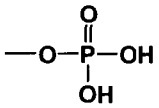
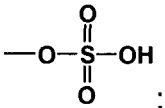
2.The synthesis of Phytandiol amine[1]



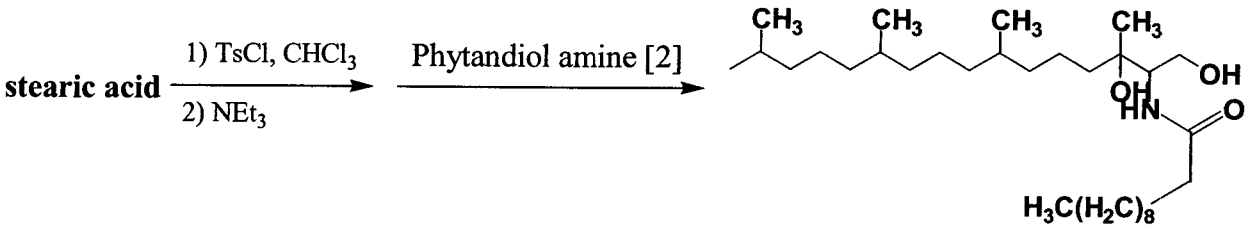
3. The example formula of Pseudoceramide



(II)

wherein Y' represents –OH,  or  ; Y" represents H or –OH; and is 0 or an integer of from 1 to 47.

4. The example scheme of pseudoceramide synthesis



5. Measurement of Minimum Inhibitory Concentration

To evaluate the antibiotic activity of the phytandiol amine against acne pathogen, the minimum inhibitory concentration (hereinafter referred to as "MIC") of the samples shown in Table 1 was measured as follows:

The sample to be tested was added to reinforced clostridial agar medium (available from Difco Co.) in the amount of 0.001-0.1%, followed by solidification of the medium. The suspension of acne pathogenic bacteria shown in Table 1 was streaked on the surface of the medium and the medium was incubated for 3 days at 35℃ under anaerobic condition. The MIC was measured by the determination of the minimum concentration to completely inhibit the growth of the acne pathogenic bacteria, of which results are indicated in Table 1.

Table 1. Minimum Inhibitory Concentration(MIC) of various agents against three acne-causing bacteria

(Unit: %(W/V))

Pathogen	*P. acnes* ATCC 6919	*P. acne* ATCC 11828	*P. avidum* ATCC 25577
Phytandiol amine[1]	0.002	0.002	0.002
Phytandiol amine[2]	0.002	0.002	0.002
Phytandiol amine[3]	0.003	0.004	0.003
Erythromycin	0.02	0.02	0.02
chitosan	0.2	0.2	0.2
Benzoyl peroxide	0.1	0.1	0.1
Tea tree oil	1.0	0.2	1.0

As demonstrated in Table 1, the phytandiol amine derivatives of this study represent antibiotic activity against acne pathogens 10-50 times greater than those of erythromycin and benzoyl peroxide which are conventionally used as a therapeutic agent for acne. Furthermore, the phytandiol amine derivatives of this study are improved in terms of workability and skin-compatibility, thereby leading to little side effects.

6. Examination of moisture-retaining capacity

In a constant temperature and humidity room at a temperature of 22℃ under relative humidity of 45%, each of cosmetic compositions(0.03 g/16 ㎠) was topically applied on the inward region of the forearm of 30 persons and then well scrubbed. Water content of the skin treated was measured prior to application, and, 1 hr, and 2 hr after application. The measurement apparatus used is corneometer CM820 (Conrage + Khazaka), measuring the electric

capacity of skin varied depending on water content, and the results are indicated in Table 2. The formula I(Form I) contained pseudoceramide[II] at 1.0% and The formula of Com Form II not contained the pseudoceramide.

Table 2 The moisture-retaining capacity of pseudoceramide

(Arbitrary unit)

Electrical conductivity	Form.I	Com.Form.II
Prior to application	50	50
1 hr after application	105	77
2 hr after application	86	63

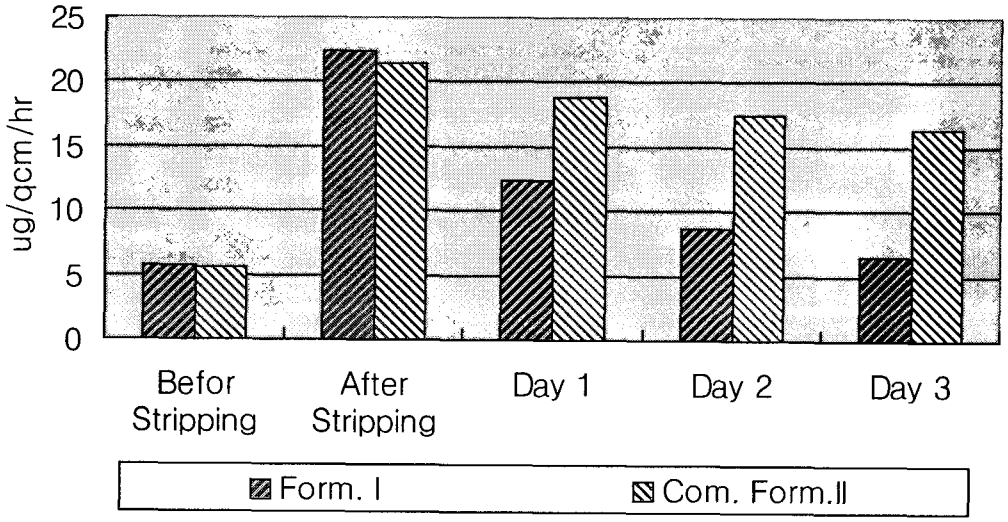
As demonstrated in Table 2, the cosmetic compositions comprising the pseudoceramide of this study exhibit excellent moisture-retaining capacity as compared to the cosmetic compositions without the pseudoceramide.

7. Measurement of transepidermal water loss

By means of tape stripping on the inward region of the forearm, the protective barrier of skin was damaged. Thereafter, in a constant temperature and humidity room at a temperature of 22℃ under relative humidity of 45%, each of cosmetic compositions (0.03 g/16 ㎠) was topically applied on the inward region of the forearm of 30 persons and then well scrubbed. The amount of transepidermal water loss was measured every 8 hours with TEWL meter

(Koln-Germany). The respective measurement was performed 5 times at an interval of 5 min and the mean value was calculated, of which results are indicated in Table 3.

Figure 1. The trans epidermal water loss of pseudoceramide



As indicated in Figure 1, the cosmetic compositions comprising the pseudoceramide of this study show significantly lower transepidermal water loss as compared to the cosmetic compositions without the pseudoceramide.

8. Physical property

Table 3. The Physical properties of psedoceramide and natural ceramide.

	Natural ceramide	Pseudoceramide [II]
Solubility(1,3-BG)	10 mg/ ml	100 mg/ ml
MP(Melting point)	98 ~102 °C	45~48 °C

When we use some raw materials in cosmetic fomula, their physical properties are very important, because their physical properties are closely related to the stability of the cosmetic formula. In this aspect, our pseudoceramide has good physical properties for cosmetic formulation. The solubility of pseudoceramide is higher than natural ceramide and the melting point of that is lower. The cosmetic formula containing pseudoceramide is more stable than the fomula using natural ceramide, because the properties of pseudoceramide are more compatible with cosmetic formula.

Conclusion

1> The phytandiol amine derivatives of this study can be excellent agents for treating acne and the compositions comprising the same are also expected to exhibit a remarkable treatment effect to acne.

2> Our sythetic pseudoceramide, which is derived from phytandiol amine, has good physical properties for application as a substitution for natural ceramide in cosmetic formula.

3> And the moisture-retaining capacity and the recovery of TEWL in the skin applied the cosmetic formula containing pseudoceramide are similar to those using natural ceramide.

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