Acta Pharmaceutica Turcica
XLI (2) (86-92) 1999

PRE-FORMULATION AND SOME STABILITY STUDIES ON COSMETIC EMULSIONS PREPARED WITH ALPHA-HYDROXY ACIDS

ALFA-HİDROKSİ ASİTLERLE HAZIRLANAN KOZMETİK EMÜLSİYONLARDA ÖN-FORMÜLASYON VE BAZI STABİLİTE ÇALIŞMALARI

GÖKHAN ERTAN, ÖZGEN ÖZER, ZEYNEP B. SARÇIN

Ege University, Faculty of Pharmacy, Department of Pharmaceutical Technology
35100 Bornova, İzmir,TURKEY

In this study emulsions used for cosmetic purposes considered as pharmaceutical forms were prepared by developing different formulations and their stabilities were examined. Comparisons were done by investigating the stabilities of the cosmetic emulsion formulations prepared by the combinations of two different surfactants and three different active substances.

α - Hydroxy acids (AHAs) are popular natural compounds found in almost every kind of cosmetic product. They have special effects on the skin such as improving skin texture, firmness and brightness, decreasing wrinkling and pigmentation. AHAs are incorporated into cosmetic products for different purposes. The type and concentration of AHAs are very important points in the cosmetic formulations. We used three active substances from this class in our formulations and decided to investigate the stabilities of the cosmetic emulsions prepared.

Results showed that decomposition of emulsions was directly propotional with time and an increase in pH and in particle size was observed related to time. It was seen that the formulations which were stable in the organoleptic controls were also stable in the centrifuge tests. Besides, it was observed that the emulsions prepared with PEG 55 propylene glycol oleat (PEG 55 PGO) were more stable compared with the ones prepared with PEG 80 sorbitan laurate (PEG 80 SL), so we decided to use PEG 55 PGO in the preparations of the emulsions.

Bu çalışmada farmasötik şekil olarak kozmetik amaçla kullanılan emülsiyonlar ele alındı ve değişik formülasyonlar geliştirilerek stabiliteleri incelendi. İki ayrı emülgatör ve üç ayrı etken maddenin kombinasyonlarıyla oluşturulan kozmetik emülsiyon formülasyonlarının stabilitelerinin incelenmesi suretiyle karşılaştırma yapıldı.

α-Hidroksi asitler (AHA'lar) doğal bir bileşik sınıfındandır ve deri yapısını, parlaklığını ve sıkılığını düzeltmek, kırışıklığı ve pigmentasyonu azaltmak gibi özel etkiler oluştururlar. Son yıllarda kozmetik preparatlarda güncel olarak kullanılması nedeniyle, formülasyonlarımızda bu sınıftan üç etken madde kullanıldı ve hazırlanan kozmetik emülsiyonların stabilitesinin incelenmesi amaçlandı.

Sonuçta, sıcaklığın artmasıyla orantılı olarak emülsiyon dayanıklılığının bozulduğu, zamana bağlı olarak partikül büyüklüğünün ve pH'ın da genelde arttığı gözlendi. Organoleptik kontrollerle santrifüj denemelerinin uyum içinde olduğu görüldü. İlaveten PEG 55 propilen glikol oleat (PEG 55 PGO) ile yapılan emülsiyonların PEG 80 sorbitan laurat (PEG 80 SL) ile yapılan emülsiyonlara göre daha dayanıklı olduğu, dolayısıyla emülsiyon yapımında PEG 55 PGO'ın kullanılmasının uygun olduğuna karar verildi.

Keywords : *Cosmetic emulsion; α-Hydroxy acids; PEG 55 PGO; PEG 80 SL; Stability tests*

Anahtar kelimeler : *Kozmetik emülsiyon; α-hidroksi asitler; PEG 55 PGO; PEG 80 SL; Stabilite testleri*

Introduction

"AHAs" refer to a group of weak hygroscopic acids which contain a hydroxy function in the alpha position relative to the carbon atom bearing the carboxyl function (1). These acids were reported for cosmetic use in 1974 for the

first time, are considered as renaissance materials. However their long-term usage and formulations are still debated. AHAs such as glycolic, lactic, tartaric, citric, malic, mandelic, benzylic and gluconic were introduced into cosmetic products either alone or as a complex (2,3). AHAs are involved in a range of cellular processes including glucose metabolism, energy production, redox potential and glycosaminoglycan synthesis (3). They are used at low concentrations for the long-term control of dry skin, ichtiyosis, acne, age spots and superficial wrinkles and for increasing the elasticity of the skin (4).

The AHAs are clearly effective in the management of various dry skin conditions, particularly hyperkeratotic disorders such as ichthyosis (3). AHAs reduce the thickness of hyperkeratotic stratum corneum by decreasing corneocyte cohesion when used topically (5). One of the properties of the AHAs is their ability to plasticize the stratum corneum, thereby making the skin more flexible and less vulnerable to cracking. They can improve the extensibility (or elasticity) of the stratum corneum without increasing the water content (3,6).

Various acids were examined for their ability to increase cell renewal at various pHs, and similar results were observed for all the acids tested. As pH increased, the ability to stimulate cell renewal diminished. Additionally, for all the acids tested, a maximal stimulation of renewal at a pH of about 3 was observed (7).

Several enzymes (phosphatases, lipases, transforming growth factor beta etc.) have maximum activity at pH 5 or lower values and it is possible that an acid environment may activate these mechanisms (4,8). It is impossible to market a raw material or a drug without any stability test. It should be stored without any decrease in its chemical, physical and therapeutic properties during the storage (9). Emulsions are thermo dynamically unstable systems and may undergo some changes after aging. The aim of this study was to prepare cosmetic emulsions by using different surfactants and different active substances as citric, tartaric and lactic acids and to evaluate the stabilities of these systems.

Materials and Methods

Materials and Apparatus

Almond oil (Galenic Pharmaceutical Wholesale Store), tartaric acid (Horasan Chemistry Co. Ltd.), lactic acid (C. H. Boehringer - suitable to DAB 7), citric acid monohydrate (Uparc), sodium – carboxymethyl-cellulose (CMC) (Sigma), methyl paraben, propyl paraben, PEG - 55 PGO, PEG - 80 SL (Johnson & Johnson Ltd.) and distilled water were used in the preparation of the emulsions

Apparatus: Mechanic mixer (Janke and Kungel), centrifuge (Heraeus Sepatech Minifuge, Model RF), microscope (OMO), mechanic shaker (B. Braun), balance (Sartorius Basic and Shimadzu Libror EB-3200 H), pH-meter (Nel mod. 821), water bath (BÜCHI 461), refrigerator (Arçelik), deep-freeze (Uğur),ovens (Nüve, Hereaus, Dedeoğlu, Electro-mag).

Methods

Active substance	5	g
Almond oil	20	g.
Surfactant	15	g.
Sodium - CMC	2	g.
Methyl paraben	0.10	g.
Propyl paraben	0.05	g.
Distilled water	57.85	g.

According to the formulation given above, emulsions were prepared by using different active substances and surfactants. Citric, tartaric and lactic acids were used as active substances and PEG 55 PGO and PEG 80 SL as surfactants. O/W emulsions were perpared having the following combinations:

PEG 55 PGO - citric acid
PEG 55 PGO - lactic acid
PEG 55 PGO - tartaric acid
PEG 80 SL - citric acid
PEG 80 SL - lactic acid
PEG 80 SL - tartaric acid

7 different emulsions were prepared for each formulation and 6 of these were used for duration tests and 1 for the temperature variation test. Totally 42 emlusions were subjected to various analiysis.

Preparation of the emulsions :

"Surfactant in water" method was utilized when preparing the o/w emulsions (10). 2 g. of sodium - CMC was swollen in 57.85 g. of distilled water. 20 g. of almond oil for each formulation were heated to 70 °C on a water-bath. 15 g surfactant, 5 g active substance and 0.1 g methyl paraben were dissolved in the water phase. 0.05 g propyl paraben was dissolved in almond oil and the oil phase was mixed with the water phase gently at 800 rpm. by using a mechanical mixer. The mixing process was continued until the temperature of the emulsion dropped to room temperature. These emulsions were transferred to 100 cc bottles

Stability tests

These tests were carried on the 6 of the 7 emulsions prepared as mentioned above and the temperatures were : a) -24 °C (deep - freeze) b) - 5 °C c)Room temperature (20°C) and dark cabin (11), d) 37°C e) 45°C f) 50°C

Temperature variation test was applied to the 7th formulation. It was kept at -5°C and at 40°C for 24 hours for a period of three weeks. Triplicate measurements were done for each emulsion.

Control methods :

Stability tests performed were: Duration, temperature variation and centrifugal analysis. Organoleptic and particle size controls and pH measurements were done at certain time intervals for each emulsion.

1. Duration Tests (12)

The investigations were done on the emulsions stored;

1) for 24 hrs. under -24 °C.
2) for 1 week under -5 °C.
3) at room temperature and dark after 3 weeks time interval.
4) At 37 °C on the 3rd day each week for 3 weeks .
5) under 45 °C after each week of the 3 weeks time interval and also on the 3rd day of the storage.
6) under 50 °C after the 1st, 3rd, 7th days of the 1 week time interval.

2. Temperature variation test (13)

The emulsions were stored for 24 hrs. under -5 °C and 40 °C. The test is continued for 3 weeks in this order and at the end of the 3rd week the position of the samples were both observed and examined.

3. Centrifuge test (3)

5 g. of each emulsion was transferred into test tubes. The centrifugation process was performed at room temperature and 3000 rpm. for 30 mins. and the samples were observed for decomposition or phase separation.

4. Organoleptic controls (13)

The color, odor and the physical appearance of the emulsions were examined. The occurrance of any phase separation was observed. The examinations were evaluated under 5 groups :

1) Stable position
2) The light decomposition of the homogenity (Slight inhomogenity)
3) Beginning of the separation. (Creaming, lifting)
4) Certain separation (Marked separation)
5) Complete separation of the phases (Total separation)

5. Measurement of the pH (12)

The continuous phases of the emulsions were water and their pHs were measured freshly and after preparation at certain time intervals.

6. Measurement of the particle size

0.1 ml of each emulsion was transferred into a test tube and 1ml of distilled water was added. After stirring for 5 mins with a mechanical mixer the particle sizes were examined in a sufficient amount of sample under a microscope. Average particle size and the physical appearances of the emulsions were predicted after ten consecutive measurements.

Results and Discussion

The stability of fortytwo different cosmetic emulsions was investigeted by developing various formulations. Tests carried out included; Duration, temperature variations, centrifugal and organoleptic controls, pH and particle size analysis.

Stabilities of the emulsion systems depend mainly on the preparation method, apparatus used, oil and surfactants selected and their concentration, the sizes of the globules obtained and the temperature used, along with other conditions.

Emulsions must be tested at varying temperatures in order to ensure their stability at all possible environmental conditions. (14). For this reason duration tests were performed at various temperatures.

In this study, the emulsions appearance were checked every day for phase separation or microbial contamination. All the emulsions prepared had a homogenous appearance with good consistency. Macroscopically they were white and odourless cream.

The pH of the medium should be between 1.0-5.5 in the products containing AHA. The most suitable pH interval is between 3.0-5.0. By the application of low pH products on stratum corneum the bonds between the keratinized cells break off and thus the effectiveness of the product increases (15). Therefore the pH's of the emulsions should be adjusted both for the appropriateness of the product to the users skin and for its stability. In this work after examining the pHs of the emulsions initially and at the end of the durations in different temperatures, measurements showed that initial pHs were 2,48-3.08 and the final pHs were 2,50-3.16. The pHs of the emulsions should be adjusted to 3.0-5.0 before application for optimum cutaneus tolerance (2,11).

Centrifugation gives a definite idea about the stability of a simple emulsion. The cream volume or the separation of phases at a given time was taken as a measure of the physical stability of the emulsion. To accelerate the effect of gravity, the emulsion was centrifuged at a speed not below 2000 rpm (16). The centrifugation was carried on at room temperature at 3000 rpm. for 30 minutes. Proceeding the centrifuge studies, it was observed that the emulsions prepared with PEG 55 PGO were stable while the ones prepared with PEG 80 SL decomposed. In addition, PEG 55 PGO-L.A and PEG 55 PGO-C.A were stable while the others decomposed in temperature variation tests.

The thermal tests give a general information about the stability of the emulsions during aging. Cosmetic products which are exposed to varying climates are significantly influenced by temperature. To test the thermal stability of freshly prepared emulsions, they were subjected to different temperatures (C) as:-24°, -5°, room temperature (20°), 37°, 45°, 50°. The results are given in Table 1. According to this table, it can be seen that the results of the thermal stability tests and centrifuge tests were in accordance.

The method of manufacture has an effect on the particle size and stability of the emulsion. As a general rule, each emulsifier shoul be added to the phase where it is easily soluble (14).

The particle sizes of the emulsions intended for cosmetic use are expected to

Table 1- The results of the investigations done on the emulsions stored for 24 hrs. under -24 °C.

Type of emulsion	organoleptic control int.	fin.	pH i.pH	f.pH	particle size int.	fin.	centrifuge
PEG 55 PGO-L.A.	(1)wc,o.	(1)wc,o.	3.10	3.13	3.25 μm	3.90 μm	stable
PEG 55 PGO-C.A.	(1)wc,o.	(1)wc,o.	2.78	3.08	4.20 μm	4.30 μm	stable
PEG 55 PGO-T.A.	(1)wc,o.	(1)wc,o.	2.32	2.61	3.70 μm	4.20 μm	stable
PEG 80 SL-L.A.	(1)wc,o.	(1)wc,o.	3.07	3.14	2.50 μm	2.70 μm	phase separation
PEG 80 SL-C.A.	(1)wc,o.	(2)wc,o.	2.78	2.87	2.80 μm	4.00 μm	phase separation
PEG 80 SL-T.A.	(1)wc,o.	(2)wc,o.	2.47	2.64	1.70 μm	3.70 μm	phase separation

i, int : initial
f, fin : final
wc : white-cream
o : odorless

LA : Lactic acid
CA : Citric acid
TA : Tartaric acid

(1) : Stable position
(2) : The light decomposition of the homogenity

Table 2- The results of the investigations done on the emulsions stored for 1 week under -5 °C.

Type of emulsion	organoleptic control int.	fin.	pH i.pH	f.pH	particle size int.	fin.	centrifuge
PEG 55 PGO-L.A.	(1)wc,o.	(1)wc,o.	3.10	3.17	3.25 μm	4.00 μm	stable
PEG 55 PGO-C.A.	(1)wc,o.	(1)wc,o.	2.78	3.01	4.20 μm	4.80 μm	stable
PEG 55 PGO-T.A.	(1)wc,o.	(1)wc,o.	2.71	2.54	4.10 μm	4.50 μm	stable
PEG 80 SL-L.A.	(1)wc,o.	(3)wc,o.	3.07	3.26	2.50 μm	4.80 μm	phase separation
PEG 80 SL-C.A.	(1)wc,o.	(3)wc,o.	2.78	2.98	2.80 μm	5.30 μm	phase separation
PEG 80 SL-T.A.	(1)wc,o.	(3)wc,o.	2.47	2.47	2.50 μm	3.80 μm	phase separation

i, int : initial
f, fin : final
wc : white-cream
o : odorless

LA : Lactic acid
CA : Citric acid
TA : Tartaric acid

(1) : Stable position
(3) : Beginning of the separation

be 0.5-10 μm (16). In the present study they were found to be 1.7-6.4 μm and an increase in the particle sizes was observed related to time and temperature. It is seen from the graphics that PEG 55 PGO-C.A is the most stable one at all temperatures. Besides PEG 80 SL- T.A was also found to be stable at 37°C. The results of theparticle size are presented at Tables 2,3 and Figs. 1-4.

The role of the polymeric surfactant in stabilizing the emulsion interfaces is a very important point in the stability of the system. The type of the surfactant could also be related the mechanical stability of the W/O emulsion. It must be reflected as a change in droplet size of the W/O emulsion with time. PEG 55 PGO seems to have a little influence on the stability of the emulsion systems we formulated. Emulsion stability decreases at high temperatures with PEG 80 SL. It seems that PEG 80 SL does not form a network within he aquaeus phases of this system.

Low-viscosity grades of methyl cellulose, hydroxypropyl cellulose, and/or hydroxyethyl cellulose having inverse water solubility with respect to temperature provide a lubricious, dense, stable, voluminous foam. Sodium-CMC was used in 2% concentration in our study (17).

All constituents in the emulsion system are open to microbial contamination. This contamination may lead to several undesired effects such as influencing the physical and and chemical stability changing the normal functions of the skin applied (3). To prevent the contamination of the

Table 3- The results of the investigations done on the emulsions stored under room temperature and dark conditions after each week of the 3 weeks time interval.

Type of emulsion	time	organoleptic control	pH	particle size	centrifuge
PEG 55 PGO - L.A.	int.	(1)wc,o.	3.10	3.25 μm	stable
	1st week	(1)wc,o.	3.19	4.50 μm	stable
	2nd week	(1)wc,o.	3.06	4.60 μm	stable
	3rd week	(1)wc,o.	3.15	4.60 μm	stable
PEG 55 PGO- C.A.	int.	(1)wc,o.	2.78	4.20 μm	stable
	1st week	(1)wc,o.	3.01	4.20 μm	stable
	2nd week	(1)wc,o.	2.68	4.50 μm	stable
	3rd week	(1)wc,o.	2.77	4.70 μm	phase separation
PEG 55 PGO- T.A.	int.	(1)wc,o.	2.71	4.10 μm	stable
	1st week	(1)wc,o.	2.45	4.30 μm	stable
	2nd week	(1)wc,o.	2.53	4.50 μm	stable
	3rd week	(1)wc,o.	2.50	4.70 μm	stable
PEG 80 SL- L.A.	int.	(1)wc,o.	3.07	2.50 μm	stable
	1st week	(1)wc,o.	3.07	3.00 μm	stable
	2nd week	(1)wc,o.	3.11	3.40 μm	stable
	3rd week	(1)wc,o.	3.08	3.80 μm	stable
PEG 80 SL- C.A.	int.	(1)wc,o.	2.78	2.80 μm	stable
	1st week	(3)wc,o.	2.89	5.70 μm	phase separation
	2nd week	(3)wc,o.	2.77	5.80 μm	phase separation
	3rd week	(4)wc,o.	2.88	5.80 μm	phase separation
PEG 80 SL- T.A.	int.	(1)wc,o.	2.47	2.50 μm	stable
	1st week	(3)wc,o.	2.70	3.40 μm	phase separation
	2nd week	(3)wc,o.	2.53	4.10 μm	phase separation
	3rd week	(4)wc,o.	2.52	6.20 μm	phase separation

int : initial
wc : white-cream
o : odorless

LA : Lactic acid
CA : Citric acid
TA : Tartaric acid

(1) : Stable position
(3) : Beginning of the separation
(4) : Certain separation

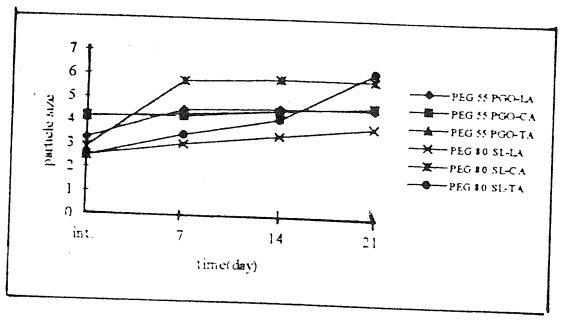

Fig. 1. Changing of the particle size of the emulsions versus time at room temperature (20°C)

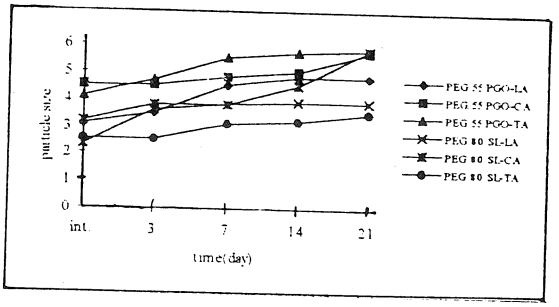

Fig.2. Changing of the particle size of the emulsions versus time at 37°C

emulsion system, methyl paraben and propyl paraben were introduced into the emulsions. The effects of antimicrobial agents to the system were confirmed by other authors, aswell (2,11,18,19)

AHAs may have a physiological influence on the qualitative character of the stratum corneum. Topical application of these acids can return disordered hyperkera-tinized skin to a nearly normal appearance by influencing the casting off of old stratum corneum cells and a return to normal rates and patterns

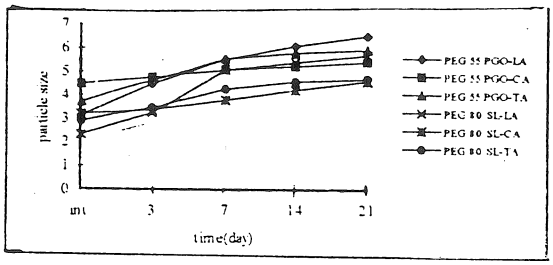

Fig.3. Changing of the particle size of the emulsions versus time at 45°C

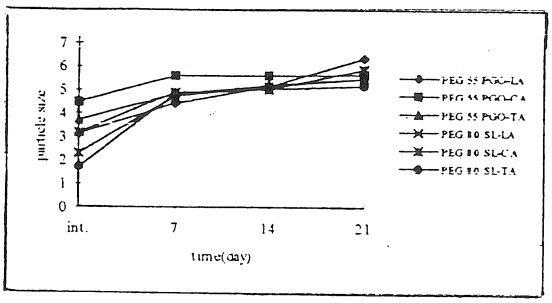

Fig. 4. Changing of the particle size of the emulsions versus time at 50°C

of cell formation, cohesion and shedding (7). AHAs in high and low concentrations, in solutions, lotions, creams and gels provide new treatment options for a range of conditions, including dry skin and its variants, acne "age spots" and actinic keratoses, warts and wrinkles and for skin peeling. High concentrations of AHA have more penetrating, more profound but perhaps less specific effects (20). AHAs are usually used at low consenrations (4-12%) in cosmetic products (2,12). We also used AHA in 5% concentration in the present study.

As a result of all these studies, it was observed that the stability of the emulsions decrease as the temperature increases. Also it can be said that the particle size and the pH increases by time. It was also observed that the emulsions prepared with PEG 55 PGO were more stable than the emulsions preapared with PEG 80 SL.

References

1. Siegfried, R.W.: DCI, May (1995)
2. Yazan, Y., Seiller,M., Arslan, K.: Drug and Cosm. Ind. 160, 30 (1997)
3. Bartolone, J. "Mechanism of action of AHAs unclear yet effective, in dry skin treatment" Proc. of the New Generation of Skin Care Science Symposium, Bermuda, April 22-25, p. 13-14, 1993
4. Smith, W.P.: Cosm. Toilet. 109, 41 (1994)
5. Berardesca, E., Maibach, H.: Cosm. Toilet. 110, 30 (1995)
6. Takahashi, M., Machida, Y., Tsuda, Y.: J. Soc. Cosmet. Chem. 36, 177 (1985)
7. Idson, B.: DCI, May (1995)
8. Berardesca, E., Distante, F.: Euro. Cosmetics 4, 13 (1995)
9. Öner, F.: Proc. of the 1st Int. Cosmetic Symp. (ICoS) Eskisehir, October 4-7 pp. 134, 1993
10. Güven, K.C., Bergişadi, N., Sel, İ.: Eczacılık Teknolojisi-1, pp. 82-100 Modern Reprodüksiyon, İstanbul 1987
11. Idson, B.: Pharmaceutical Dosage Forms: Disperse Systems-1 Ed. H.A. Lieberman, M.M. Rieger, G.S. Banker, Marcel Dekker INC. pp 199-243, 1988
12. Wittern, K.P., Ansmann, A., Hüttingert, R., Billek, D., Charlet, E., Hoenen, L., Kuczera, K., Motitschke, L., Quack, J., Seib, K., Umbach, I., Wolff, G.: Cosm. Toilet. 100, 33 (1985)
13. Tarımcı, N.: SEGEM (Sınai Eğitim ve Geliştirme Merkezi Genel Müdürlüğü) Kozmetik Yapımlarda Kalite Kontrol ve Denetim, Ankara 1987
14. Klein, K.: Cosmet.Toilet. 99, 121 (1984)
15. Tarımcı, N.: Kozmetoloji Günleri-1, pp. 75 Ankara, June 3, 1996
16. Kaş, H.S.: Ibid. pp. 41, Ankara, June 3, 1996
17. Fox, C.: Cosm. Toilet. 107, 91 (1992)
18. Bhargava, H.N.: Drug Dev. Ind. Pharm. 13, 2363 (1987)
19. Soytürk, B., Yıldız, S., Tarımcı, N.: Proc. of the 5th Int. Symp. on Phar. Sci., Ankara, June 24-27 pp. 122, 1997
20. Van Scott, E.J., Yu, R. J.: The Canadian J.Dermatology 1, 108 (1989)
21. Klein, K.: Cosm. Toilet. 109, 63 (1994)

Accepted: 07.12.1998