journal of applied cosmetology

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OFFICIAL JOURNAL OF

international society of cosmetic dermatology

INTERNATIONAL EDIEMME

Volume 11 - Number 1
January/March 1993
ISSN 0392-8543 Sped. abb. post. gr. IV° 70

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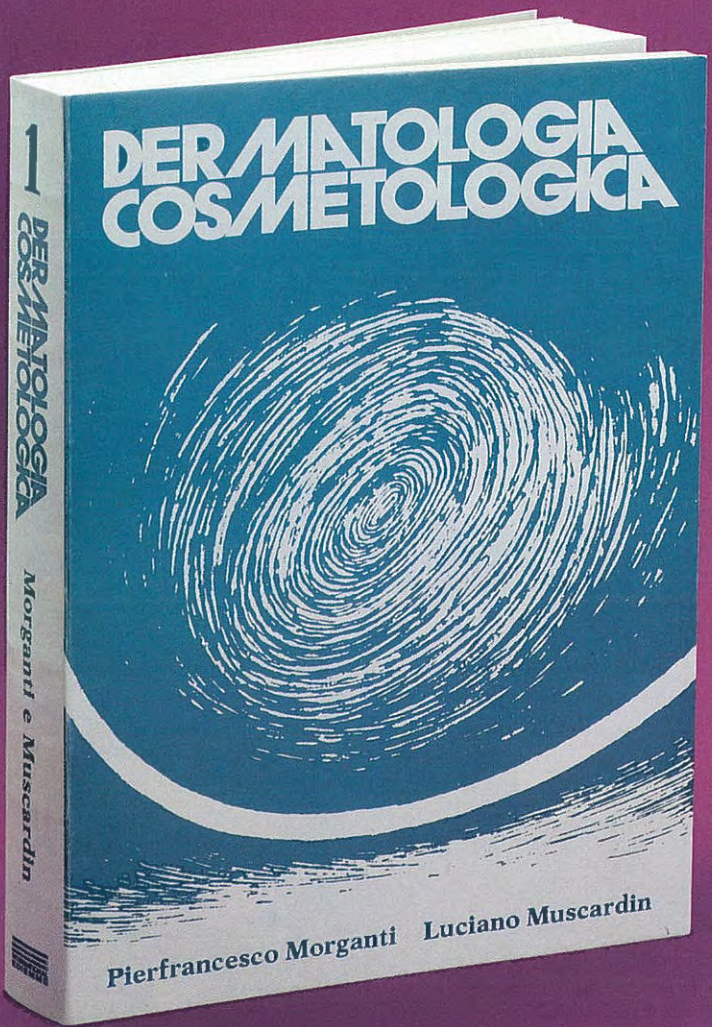

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DERMATOLOGIA COSMETOLOGICA

A cura di P. Morganti e L. Muscardin
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Volume 2
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J. Appl. Cosmetol. 11, 1-22 (January - March 1993)

DERMATOLOGICAL EVALUATION OF COSMETIC PRODUCTS FOR SKIN DETERGENCY

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Work developed into P.F. Chimico Fine CNR.

Receveid: *10 January, 1993*

Key words: *Safety, Efficacy, Cleansing.*

Synopsis

In this study the Authors evaluated, on the dermatological and cosmetological point of view, a panel of sexteen products of cutaneous cleasing, through the utilization of standardized methods. Today is still necessary to execute codified tests of high reliability to establish the safety and efficacy use of cosmetic products.
These tests were conducted both by Dermatologists and Cosmetologists.

Riassunto

In questo studio gli Autori valutano sotto l'aspetto cosmetologico e dermatologico un gruppo di sedici prodotti detergenti utilizzando metodiche standard. E' necessario, infatti, utilizzare test codificanti che stabiliscono la sicurezza e l'efficacia nell'uso dei prodotti cosmetici.
Questi test sono stati condotti da Dermatologi e Cosmetologi.

Introduction

Cleasing of the skin without altering its physiological aspects is the goal of all those who work in the field of cosmetology. The habits of modern-day life have resulted in an increased use of skin cleansers, but, fortunately, advances in technology have rendered these products less aggressive to the skin. Dermatologists know that cleansing of the skin is extremely important to keep it in good condition. It is also essential to the health of the skin. When the skin is not cleaned regularly, microorganisms and tissue debris accumulate, and infection can occur. On the other hand, overly aggressive or frequent cleansing will inevitably lead to alterations in the cutaneous defense system.

Although water is the most common means of cleansing the skin, its use is not without risks.

Water removes the hydrolipid film from the skin, as well as the dirt that is attached to it. When surfactants are added, complete delipidization of the skin and alterations of the horny layer cells can occur. It is important, then, to understand the structures and mechanisms at the base of the cutaneous defense system and to utilize products that not only provide satisfactory cleansing, but also respect the physiological needs of the skin.

Dermatological problems caused by skin cleansing

The principal effects of skin cleansing can be summarized as follows:

- delipidization
- modification of the pH
- alteration of the microbial flora
- alteration of the stratum corneum
- dehydration and increased transepidermal water loss
- irritation
- sensitization

These effects are all inter-related. The alterations touched off by cleansing initiate a chain of reactions which produce structural damage with multiple effects. For simplicity's sake, however, we will discuss each effect independently. (1-15,50)

Delipidization

Use of water alone for cleansing can cause a 25% reduction in the lipidic film that protects the skin. The reduction is obviously greater when soaps or other surface-active substances are used.

Delipidization can become almost total if repeated cleansing occurs. This risk is especially high for persons who are forced to wash their hands often for professional reasons (health care workers or those employed in the chemical industry) but the same situation often occurs with housewives.

Delipidization results in the removal of substances that are dispersed within the hydrolipid film of the skin barrier and alteration of the functions performed by these substances. Reduction of the skin's protective barrier increases the risk of damage to the underlying stratum corneum and the removal of the chemical substances contained in both the epidermal and sebaceous lipids also leads to changes in the skin's pH. The effect that these lipids, especially those of the epidermis, have in keeping the stratum corneum pliant, is thus lost.

It is important to remember that loss of the lipid film also leads to loss of water and can facilitate drying. Tactile sensitivity is also reduced when this microfilm is removed.

Since certain fatty acids, unsaturated (C12, C22) and saturated (C9, C15), have been shown to exert bacteriostatic and antimycotic actions in the skin, it is clear that modification of the skin's normal flora will also occur with removal of skin lipids. This situation can, at least in theory, predispose the skin to attack by pathogens. (2-20)

Modification of pH

Changes in skin pH are caused by loss of the lipid layer, as we have already seen, as well as by the use of products with pHs that are different from that of normal skin. The effects on pH exerted by traditional soaps and synthetic deter-

gents are, in this latter respect, quite different. Soaps traditionally have alkaline pHs while synthetic detergents do not. The most important factors involved in the modification of cutaneous pH are the amount of time the detergent substance remains in contact with the skin, the amount of delipidization that occurs and the frequency with which the substance is used.
Although soaps are often better tolerated than synthetic detergents, the former undoubtedly cause greater changes in skin pH. Recent studies have shown that the time needed for normalization of the cutaneous pH is significantly longer when alkaline products are used.
The pH has a marked effect on the bacterial flora of the skin, and modification of the latter, especially in areas subject to maceration or pseudoanaerobiosis, can lead to fungal or bacterial infections. (2-20)

Changes in the microbial flora of the skin

We have already mentioned that certain fatty acids exert a powerful fungicidal effect. These are tbe saturated fatty acids C9 and C15.
Bactericidal effects are produced by the unsaturated fatty acids C12 and C22.
Delipidization, then, along with pH alterations, is the principal cause of alterations in the skin's microbial flora. (21) Ronchi and others have shown that, after cleansing with Marseille soap, skin pH does not return to normal for at least two hours.
Regions of the skin that are rich in sebaceous and apocrine glands (e.g. tbe axillae or pubic zone) and which consequently host a potentially pathogenic flora are particularly threatened by this effect of cleansing. (4)

Alteration of the stratum corneum

These changes are caused by a) keratin swelling, b) the direct action of hard water in the presence of soaps, c) delipidization, d) dehydration and e) absorption of tensioactive substances. Each of these mechanisms has effects on the cells of the horny layer. (3,5,25,26)
Deposition on the skin of fatty acid Ca and Mg salts, which are insoluble in water, causes occlusion of the openings of the hair follicles and sweat glands, which leads to irritation.
The phenomenon of dehydration causes the stratum corneum to lose its flexibility. At their isoelectric points, the proteins of the stratum corneum absorb water poorly. The isoelectric point of keratin is 4.1. During washing, the alkalinity of the soap and the actions of the anionic surface-sctive substances cause breakage of the hydrogen bonds of the interchain peptides and the stratum corneum thus becomes more absorbent.
Absorption of the surfactants that are left on the skin also alters the skin harrier allowing increased absorption of water and an influx of ions and other substances. These surfactants also dissolve the hydrolipid film. Some surface-active substances, such as the alkyl sulfates and the alkyl-benzene-sulfates, bind to the proteins of the horny layer where they damage the keratin by tranforming the alpha helixes into beta helixes. (27)

Dehydration and increased trans-epidermal water loss

Delipidization, alterations in the stratum corneum, breakdown of the keratin alpha helixes and removal of the natural moisturizing factor all contribute to a reduction in the water-binding capacity of the stratum corneum and an increase in the trans-epidermal water loss (TEWL).
Delipidization alone increases normal TEWL by 10%. (4,5,11,23)

Irritation

All of the mechanisms that we have mentioned thus far ultimately lead to a breakdown of the horny layer, which allows the surface-active

substances themselves to penetrate through to the vital layers of the epidermis. Short-chain fatty acids contained in detergents are more irritating than long-chain saturated fatty acids. The irritating effect of the fatty acids increase up to C12 and then diminish as the length of the chain increases. Sodium laurate is, thus, quite irritating to the skin while sodium stearate, even though it has a higher pH, is better tolerated.
For these reasons, protein hydrolysates are often added to soaps or synthetic detergents to bind the free short-chain fatty acids and decrease the irritant potential of the product. It is important to remember that, in addition to the irritating effects of the surfactants, the other negative effects of cleansing work together to bring about severe irritation and even irritative contact dermatitis. (3,5,11-13,25,28,29)

Sensitization

As the cutaneous barrier weakens, haptens and allergens penetrate the skin and reach the vital layers of the epidermis. Here immunocompetent cells initiate a process of defense which, after repeated contact, results in allergic contact dermatitis. (30-33)

Experimental work

Introduction

We attempted to evaluate several skin cleansing products currently on the market to determine how well they were tolerated and how acceptable they were from cosmetic points of view.
These products included both traditional soaps and synthetic detergents. The term "soap" is hereafter used to refer not only to traditional, alkaline soaps but also to those synthetic detergents sold in bar form.
Sixteen soaps, either traditional or synthetic, were selected for this study and each was assigned a number. The choice of products was based on sales data and reflects the common belief that all products used for cleansing of the skin are soaps.
The products were tested on a total of 150 healthy volunteers. The subjects were randomly assigned to groups which were similar in make-up.
Informed consent was obtained from all participants. The study lasted six months.
Evalutation of patient tolerance and cosmetic acceptability involved the difficult task of standardizing our methods and parameters of evaluation. The first parameters that had to be considered were the aggressivity of the product and the patient's cutaneous tolerance of it. In addition, the products were also evaluated from cosmetic points of view, i.e. moisturizing, smoothing and softening effects, etc. For This reason we decided to subject the products to a battery of tests to compare their effects and identify the characteristics of each. The tests included:
- Draize test for cutaneous irritation
- Soap chamber test
- Measurement of cutaneous pH
- Measurement of sebum levels
- Measurement of stratum corneum water content
- Scotch tape test
- Half-face test
- Flex wash test
- Cutaneous imprints

Cutaneous irritation test

The purpose of this test was to evaluate the irritative potential of the product when applied to the skin. The most effective method for determining the incidence of irritative contact dermatitis due to use of topical drugs or cosmetics is patch testing, which was first introduced by Jadassohn and Block. Since its introduction, it has been standardized according to the indications of numerous investigators. (31-35)

Materials

The products must remain in contact with the skin for a certain period of time if its irritative potential is to be evaluated. The "patches" used to maintain this contact must be made from ma-

terials that are, themselves, non-sensitizing.
They must also be able to absorb the test substance and, finally, to isolate the test area from the rest of the skin.
According to specific needs the following products can be used:
1. Dermotest diagent: this patch consists of a small sheet of aluminium foil covering a layer of polyethylene. In the center of the polyethylene sheet is a small cellulose disk upon which the test substance is applied.
2. Finn Chambers: A hypoallergenic adhesive strip with two rows of aluminium chambers attached to one side. Cellulose disks can be inserted into the chambers if liquid substances are to be tested.
3. Covertest diagent: this adhesive strip does not contain any of the haptens that are present in normal tapes. It can be used to secure either the Dermotest patches or Finn chambers.
4. Dermographic ink: used to mark the skin areas being tested so that they can be checked after the patches have been removed.
5. Micropore tape: used to attach strips containing test substances to the skin.
6. Whatmann paper filter disks (nos. 1 and 3): useful for absorbing liquid substances to be tested.
7. Non-occlusive patch tests: a porous, non-occlusive adhesive strip with a Whatmann paper disk (no. 1) attached. These strips are designed for use with products that might cause skin damage if applied with an occlnsive cover.

Study methods

The method used to determine the irritant potential of the cleansing products tested was a modification of the Draize test. (34) This test was originally designed for use in animals but over the years minor modifications have been made, mostly in the interpretation of the results, and it has now been used for many years to test both strong and weak irritants in man.
The method involves direct application of the test substance on the skin of the subject. In order to safeguard the subject, all substances have previously been tested in animals. Although these preliminary studies do not permit us to predict the human subject's reaction to a given substance, the investigator at least has an idea of the substance's irritative potential: strong, moderate or weak. All of the substances examined in the present study had been classidied as weak irritants on the basis of animal studies.

Modified Draize test Preparation of test substances

Samples that contain surfactants are generally tested at concentrations ranging from 1% to 10%. All of our samples were tested at a 2% dilution. Products must be diluted on the day of testing.

Application

The substances may be secured to the skin using either occlusive or non-occlusive adhesive strips. The former are generally used unless the test substance is known to be a strong irritant.

Preparation of Finn Chambers

In the present study aluminium Finn chambers containing product samples were attached to the subject's back using occlusive Covertest diagent. Whatmann no. 3 filter paper disks measuring 1 cm} were placed in Petri dishes to absorb the diluted, liquid test substance. Using tweezers the disks were pressed against the side of the dishes to squeeze out any excess liquid and inserted into the aluminum chambers.

Execution of the test

The skin of the subject's back is cleaned with a 70% solution of alcohol and the samples are applied in two rows, one on either side of the spine. The exact location of the strips will depend on the number of substances to be tested as well

as the presence of nevi or pre-existing areas of discoloration. The samples are left in place for 48 hrs and the subject is instructed to keep the area dry. At the end of this period the subject returns and the strips are removed.
Residual test substances are cleaned away and the contact point is circled with dermographic ink so that it can be read later.

Reading the results

Skin reactions are observed 15 min and 24 hr after the strips have been removed. The severity of the reaction is scored according to the following scale and any lesions or signs of toxic reactions are carefully examined.

Evaluation Scale

Erythema	
None	0
Barely visible	1
Visible	2
Moderate	3
Intense (possibly with slight crusting)	4
Edema	
None	0
Barely visible	1
Visible	2
Moderate (borders raised circa 1 mm)	3
Intense (edema outside the test area)	4

Scoring the results

At each reading (15 min, 24 hr) each application site is scored according to the above scale for erythema and for edema, and the sum of the two scores (erythema and edema) is calculated. The average of the final scores for all subjects was calculated for each product. The Final Results Table contains the average group scores at each reading for each product tested.

Classification of the products

Each product was classified as a non-irritant, a mild irritant, a moderate irritant or a strong irritant according to a modification of the scale originally proposed by Draize. This modified scale, which considers as non-irritants only those products with scores of less than 0.5, allows the investigator to distinguish more easily between mild, non-specific reactions and those that are due to the test substance itself.

Modified Draize Classification

Index	Classification
<0.5	Non-irritant
0.5-2.0	Mild irritant
2.0-5.0	Moderate irritant
5.0-8.0	Strong irritant

Selection of volunteers

The study was conducted on 40 healthy volunteers, male and female, between the ages of 18 and 65. Subjects were excluded from the study if they had: 1) dermatitis or positive histories for allergic tendencies, and / or 2) participated in a similar study within three months prior to the beginning of our study. The purpose of the study and the possible risks involved were explained to all subkects prior to obtaining their consent.

Results

Irritation skin test, conducted through occlusive patch-test methods, is helpful to point out moderate or strong irritants.
This test is usuitable to point out weak irritants, especially if used products potentially irritant but in low concentration as those normally emploied.
In other words Draize's test needs, to give positive results, higher concentrations than those normally used in the products.
In our study, evaluating some soaps, we used a 2% concentration, probably the same normally present during the use of a soap-bar.
Our results demonstrated that any soaps were able to induce, in that concentration and through emploied method, important skin irritation. (table 1).

Soap Chamber Test

This test allowed us to evaluate the irritant potential of repeated applications under stress of a 7% solution of each test substance. Each product was tested in this manner on 30 volunteers for seven days.

Selection of volunteers

Volunteers of both sexes between the ages of 20 and 65 were selected for these tests. Prior to testing, potential candidates were subjected to screening with the modified Draize technique to determine their tolerance of sodium lauryl sulfate. Those with positive results were excluded from the soap chamber test. This preliminary screening facilitated interpretation of the results of the latter test.

Preparation of samples

Aqueous 7% solutions of each product were used for testing. At this concentration, the solutions were excessively dense to be applied easily and had to be heated slightly to liquefy them.

Method of application

Substances were applied to the subject's skin using During chambers. The During chamber is an aluminum chamber 12 mm in diameter containing two layers of cotton which absorb a considerable quantity of the test substance. The chamber is applied with an occlusive dressing in order to demonstrate the irritant potential of the test substance under conditions of stress. (1,37,38,53)

Test execution:

1. The skin of the volar surfaces of both forearms was cleaned with a 70% alcohol solution. Because of the limited space available for testing, only eight samples were tested at a time: four on each forearm.

Table I

SKIN IRRITATION TEST: RESULTS

	IIM 15 (1)	IIM 24 (2)
01	0	0
02	0,1	0
03	0,1	0,06
04	0	0
05	0,1	0,06
06	0,06	0,06
07	0,1	0,1
08	0,1	0,06
09	0,1	0,06
10	0,06	0
11	0	0
12	0	0
13	0	0
14	0	0
15	0	0
16	0	0,06

2. The contact portion of the testing last for five days. On the first day of the test, the chambers were filled and applied to the skin where they remained for 24 hrs. The subject was instructed to refrain from wetting the test area. After 24 hrs the chamber was removed and refilled with the same quantity of the test substance. The chamber was reapplied to the same site and left in place for six hours. This process was repeated on days 3, 4 and 5. Contact during these last four days was limited to six hours each. The test areas were left unprotected during the hours between daily applications. The last application was removed on the fifth day of testing and the results were read 36 hrs later, i.e. on the seventh test day.
The initial application is left in place four times longer than the subsequent four. This serves to increase the permeability of the skin barrier.
The 18-hour periods between each subsequent application are aimed at reducing any acute inflammation that might occur and to allow the development of visible drying, wrinkling or desquamation.

Reading of the test results

The parameters of possible irritative reactions are:
- Erythema
- Desqnamation
- Fissure formation

Each is evaluated according to the following sclae:

Erythema

None	0
Slight (mottled or diffuse)	1
Moderate and uniform	2
Intense	3
Intense with edema	4

Desquamation

None	0
Fine	1
Moderate	2
Severe	3

Fissure formation

None	0
Fine	1
Superficial (single or multiple)	2
Deep with hemorrhage or exudate	3

Calculation of results

Each product was tested on 30 subjects. For organizational reasons, these subjects were divided into three groups of ten each.
As with the Draize test, the scores for each of the three parameters were added together to obtain the subject score for each substance. These individual scores were then averaged for each group of ten subjects. These mean indices are presented for each product in Table 2.

The average of these three group indices was then calculated for each product (mean irritant index).

Product Classification

Based on their mean irritant indices, the sixteen products tested were classified into four categories:
- non-irritants
- mild irritants
- moderate irritants
- strong irritants

The results of this classification are shown in Table 3.

Discussion

This classification system has been used in other studies like ours and obviously reflects the skin responses to the various products being examined. In fact, the soaps classified as moderately irritating cause moderately severe alterations of the skin and the sum of the scores assigned to these changes ranges from 3.0 to 4.5.
Below this level, in the score range of 1.0 to

Table II

SOAP CHAMBER TEST RESULTS

Mean values for erythema, desquamation and fissure formation

Product	Group 1*	Group 2*	Group 3*
01	0.5	0.4	0.6
02	3.8	3.9	4.1
03	3.6	3.4	3.7
04	4.5	4.7	4.6
05	4.6	4.7	4.8
06	6.3	6.1	6.0
07	6.6	6.4	6.3
08	6.6	6.5	6.4
09	3.9	3.8	3.4
10	4.1	4.1	4.3
11	2.1	3.1	3.2
12	2.7	2.5	2.9
13	2.6	2.3	2.7
14	2.4	3.1	2.8
15	2.6	2.3	2.4
16	2.5	2.2	2.3

* each group contained 10 subjects.

Table III

PRODUCT CLASSIFICATION BASED ON MEAN IRRITANT INDEX

Mean indices based on results of soap chamber test in 30 subjects.

Product	Mean index	Classification *
01	0.5	non-irritant *
16	2.3	moderate irritant *
15	2.4	"
13	2.5	"
12	2.7	"
14	2.8	"
11	3.0	"
03	3.6	"
09	3.7	"
02	3.9	"
10	4.2	"
04	4.6	"
05	4.7	"
06	6.1	strong irritant *
07	6.4	"
08	6.5	"

<0.5 = non irritant 0.5-2.0 = mild irritant
2.0-5.0 = moderate irritant 5.0-8.0 = strong irritant

3.0, products are classified as weak irritants. Scores less than 1.0 indicate that the product is a non-irritant. (1,37-40)
It is almost impossible not to provoke some form of cutaneous lesion with the method used here. For this reason, the classification of "non-irritant" is given to those products with mean irritant indices of less than 1.0. According to this classification, only product no. 01 met the criteria for a non-irritant.

Flex Wash Test

The Flex wash test, first introduced by Kligman et al., is one of the most useful and reliable tests available for evaluating the irritant capacity of a substance. The test was designed to determine, within a relatively brief period of time, whether a product can provoke cutaneous irritation. (1,47,48,49)

Materials and methods

Because of its sensitivity, the skin of the antecubital fossa is used for this test. The volunteer washes this area three times a day with a predetermined quantity of the product at a standardized concentration. The cleansing should be performed by delicately massaging the area with the fingers for approximately thirty seconds. The area is then thoroughly rinsed and patted dry.
The above routine is repeated for five days and the area is examined daily for signs of irritation. Tha test is determinated at the first sign of significant irritation.
Eighty subjects, divided into eight groups of ten each, were subjected to the flex wash test in the present study. The subjects of each group tested two products simultaneously, one on each arm.

Results

Since each group was composed of ten subjects, the results are expressed as percentages of subjects who had to interrupt the test, because of signs of irritation, before the five days were up.
Product no. 01 was associated with the lowest percentage of interruptions and therefore seems to be the least irritating even with excessively frequent use. The rank of the other fifteen products in terms of increasing irritant potential can be seen in Figure 1.
Since product no. 01 emerged from all of the previously described tests as the least irritating, we used it as a reference for comparison in all subsequent tests.

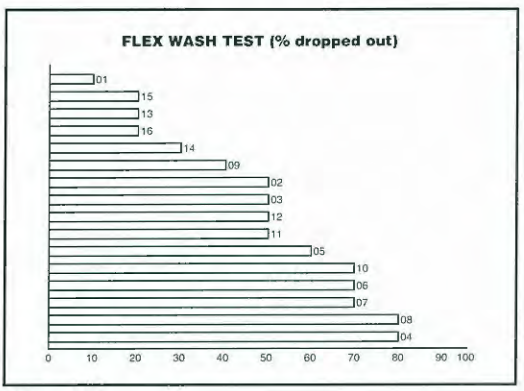

Fig. 1 -

Half-Face test

The most common problem encoutered when we attempt to study the effects of two or more cleansing products on the skin is that the objective reaction, non to mention the subjective evaluation of the effects, varies from subject to subject. The only way to eliminate this problem would be to test all of the products on the same subject using the same skin surface area for each test! Given the impracticality of such an approach, the value of the half-face test becomes obvious: it allows comparison of at least two products at the same time in one patient utilizing the same skin region.

Materials and methods

For this test, 150 volunteers between 18 and 55 years of age were selected. The study group included both males ond females. None had active lesions in the facial area and all denied history of allergic contact dermatitis.
The subjects were divided into 15 groups of ten. Each member of a given group was given two soaps, one of which was always product no. 01. In this way, each of the 15 products being compared with product no. 01 was tested in ten subjects.
The subject was instructed to wash one half of his/her face with product no. 01 and the other half with the comparison product. Cleansing was to be carried out twice a day for five consecutive days.
Before washing the face, the subject was instructed to wash his/her hands with a standard soap that contained no fragrances in order to eliminate possible contaminants from the hands which might interfere with our interpretation of the results.

The test was carried out as follows:
1. The hands were washed with one of the study products for 15 seconds.
2. One half of the face was gently washed with one of the study products or with product no. 01.
3. The face was rinsed and gently patted dry without rubbing.

The same procedure was then repeated for the other half of the face (using the second product).
At the beginning of the study each subject was given a form to fill out and return at the end of the study period. This form contained questions regarding the effects of cleansing with the two products.

The parameters to be evaluated with the questionnaire were:
- dryness
- moisture
- tightness
- softness
- roughness
- smoothness

The subject was asked to repond to each question with "yes", "no" or, in some cases, "I don't know".

The questionnaire is shown in the following table.

Half-Face test questionnaire

Subject no. _____ Product used on right side _____ Product used on left side _____

Questions

Does the right/left side of your face feel dry/moist/tight/soft/roug/smooth after washing?

1st washing: 2nd washing:

Which side feels drier/more moist/tighter/softer/rougher/smoother after washing?

Answers: Yes/No/Don't know

Surname and name/Tel./Address/Test Center

Results

Based on both the responses to the questionnaire and the objective evaluation of the abovementioned parameters, product no. 01 seemed to be superior to any of the other fifteen. For each parameter considered a graph was drawn that shows, together with the data in Table 4, the responses of the volunteers. The graphs show the percentage of positive responses to the questions on each parameter, i.e. affirming that use of the given product was associated with feelings of skin dryness, softness, etc. Since the parameters shown in Figure 2 (tightness), 3 (dryness) and 4 (roughness) are negative ones, the products in these graphs that received fewer affirmative responses are those that were judged more positively, while products with high percentages of affirmative responses in Figures 5 (moisturizing effect), 6 (softness) and 7 (smoothness) are the ones that made positive impressions on the volunteers.

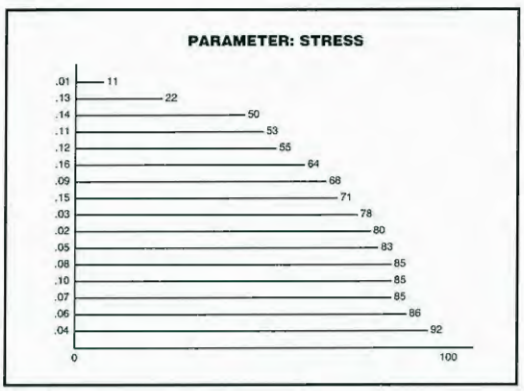

Fig. 2 -

Table IV

HALF FACE TEST: RESULTS

	01		13		01		06		01		14		01		15		01		07	
	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no
Dryness	3	97	24	76	17	83	60	40	10	90	40	60	21	79	43	57	5	95	57	43
Hydration	39	61	23	77	59	41	21	79	65	35	10	90	56	44	27	73	37	63	20	80
Stress	11	89	22	78	10	90	86	14	15	85	50	50	12	88	71	29	9	91	85	15
Tenderness	97	3	78	22	90	10	30	70	90	10	53	47	83	17	52	48	96	4	50	50
Roughness	1	99	5	95	2	98	56	44	8	92	42	58	5	95	12	88	3	97	38	62
Lenght	97	3	88	12	93	7	55	45	90	10	65	35	94	6	82	18	96	4	57	43
	01		05		01		03		01		09		01		12		01		04	
	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no
Dryness	18	82	62	38	21	79	54	46	16	84	58	42	15	85	55	45	9	91	66	34
Hydration	86	14	14	86	78	22	30	70	60	40	28	72	62	38	44	56	65	35	8	92
Stress	7	93	83	17	3	97	78	22	5	95	68	32	18	82	55	45	10	90	92	8
Tenderness	85	15	60	49	89	11	49	51	84	16	65	35	89	11	57	43	91	9	35	65
Roughness	6	94	65	35	9	91	49	51	1	99	45	55	3	97	50	50	-	100	67	43
Lenght	92	8	45	55	90	10	58	42	90	10	70	30	95	5	80	20	97	3	42	58
	01		08		01		11		01		02		01		16		01		10	
	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no	si	no
Dryness	12	88	61	39	20	80	41	59	15	85	52	48	6	94	45	55	22	78	68	32
Hydration	49	51	22	78	62	38	50	50	68	32	46	54	54	46	54	46	72	88	5	95
Stress	8	92	85	15	18	82	53	47	13	87	80	20	21	79	64	36	12	88	85	15
Tenderness	92	2	50	50	82	18	48	52	89	11	46	54	95	5	60	40	87	13	30	70
Roughness	-	100	47	53	11	89	38	62	3	97	42	58	2	98	56	44	7	93	60	40
Lenght	98	2	56	44	87	13	61	39	90	10	50	50	98	2	77	23	90	10	48	52

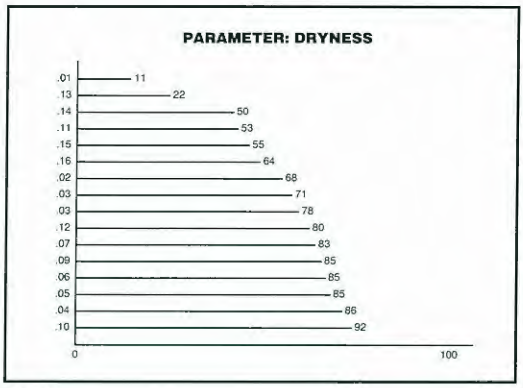

Fig. 3 -

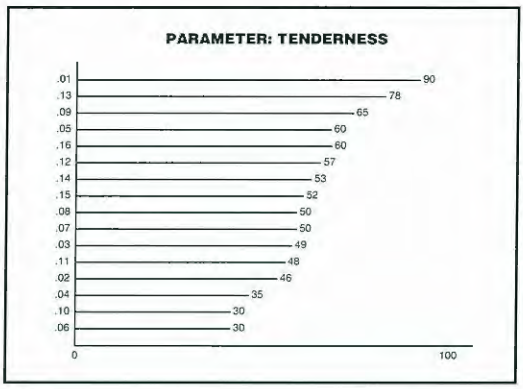

Fig. 6 -

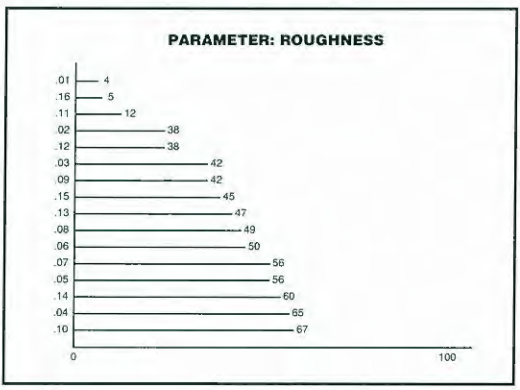

Fig. 4 -

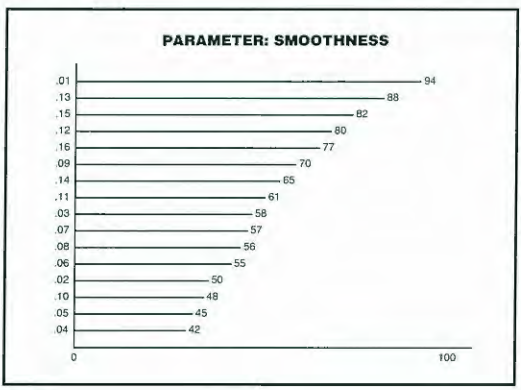

Fig. 7 -

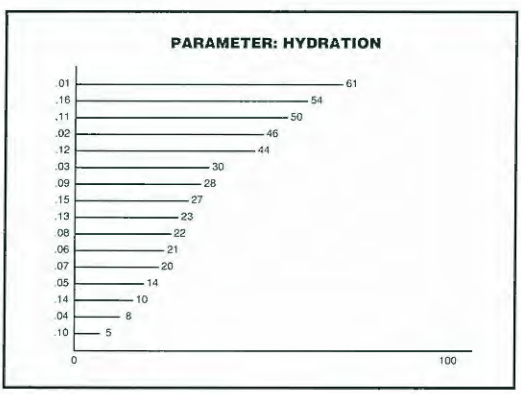

Fig. 5 -

For example, if we consider the parameter of skin tightness, product no. 04 emerges as the most unacceptable since 92% of the volunteers found that washing with this product left their skin feeling tight.

Product no. 01, in contrast, was considered the most acceptable from this point of view: only 11% of the volunteers indicated that skin tightness was associated with its use.

Measurement of sebum levels

The purpose of skin cleansing is that of removal of "dirt". However, the dirty portion of the skin is the hydrolipid barrier which contains not only environmental impurities but also epidermal tissue debris. The ideal skin cleanser must, then, remove al least part of the hydrolipid barrier but it should not deprive the skin completely of its protective covering. (2-5,42,43)

The skin of the face is one of the most delicate

areas of the body in which to test a product. Its anatomical structure is delicate, and certain parts of it are rich in sebaceous glands.
Facial skin is also one of the cutaneous areas most exposed to environmental aggression. This almost constant exposure, coupled with the sensitivity of facial skin to psychological and nervous factors, makes the skin of the face unique. (42-44,46)
For these reasons, the behavior of a cleansing product in this particular region is especially indicative and can serve as an index of its safety in other less delicate skin areas. In addition, testing on facial skin offers an excellent indication of the delipidizing effect of a cleansing product, which, as we have already seen, is one of the most important parameters to be considered in evaluating the irritant potential of these substances. We therefore decided to analyze the sebum levels of the faces of our volunteers to determine more precisely the delipidization potential of our test products.

Materials and methods

One hundred fifty subjects were divided into 15 groups of ten each. These groups were the same ones that were used in the half-face test and were later subjected to analysis of stratum corneum water content as well.
Baseline sebum levels were determined for each subject using the Schwarzhaupt SM 410 Sebometer.
Using a photometric method, this intrument measures the quantity of cutaneous oils deposited on a semitransparent tape which is pressed against the test area and held in place for 30 seconds.
Prior to testing, the instrument must be zeroed.
The spool of tape is advanced until an unused portion is covering the application head. The tape is inserted in a photoelectric cell chamber. Its presence causes closure of an electrical circuit which switches on a light. The beam is amplified with a mirror and transferred to an amperometer.
The tape becomes more and more transparent as more sebum is deposited on it and, consequently, more light can pass through it to reach the amperometer. The quantity of light that passess through the tape is reflected on a digital display. Higher values indicate that more light is passing through the tape which has become more transparentdue to a larger amount of sebum absorbed.
All of the subjects used product no. 01 on one half of their faces. Each group of ten subjects, (sex and age distribution were similar for all groups), used one of the other products on the other half of the face. On the day before test washing began, the baseline sebum levels were determined for each side of the subject's face.
Baseline values were based on five readings taken in adjacent areas of the facial skin. Measurements were made at the same hour of the day for allsubjects and not less than eight hours after routine facial cleansing in the morning. The exact same procedure was repeated after the subject had completed the required five days of the half-face test. These final values were then compared to baseline figures.

Results

Figure 8 shows the average baseline and final sebometric indices for each of the sixteen products tested. These values are averages of the values for the ten subjects testing each product. In Appendix no. 1, the average values, baseline and final, for each of the 150 subjects are shown.

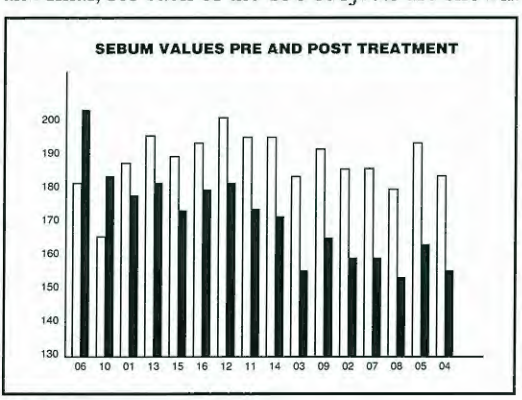

Fig. 8 -

Certain soaps, such as product no. 13, product no. 15 and product no. 16 were associated with values very similar to those of product no. 01, which caused very little change in the facial skin sebum levels. Once again, product no. 01 emerged as the superior product, although the differences between this product and the ones mentioned above were actually quite limited.
All of the other soaps tested, with the exception of products no. 06 and 10, significantly diminished the sebum levels in the subjects who used them. Products no. 06 and 10, in contrast, caused an increase in sebum levels with respect to baseline values which can be considered to be a rebound effect (Figure 9)

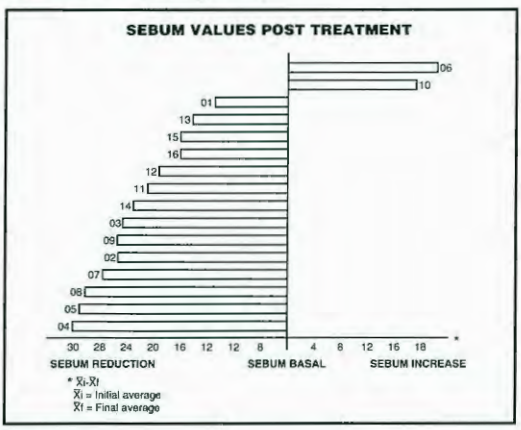

Fig. 9 -

Using these results, we can also make direct comparison between product no. 01 and each of the other 15 as far as their effects on each subject or each group are concerned.
Since, the aforementioned exhaustive analysis provided data only on product 01 compared to one other soap, it was decided to compare the difference in mean levels of sebum before and after five days of washing in the 15 groups of subjects who used various soaps on half their face with those of 150 subjects who used product 01 on half their face.

Some of these data are shown in Figure 9.

Measurement of stratum corneum water content

As pointed out earlier, one requisite for an acceptable skin cleanser is that it not alter the cutaneous barrier and therefore safeguard the integrity of the stratum corneum. Measurement of the level of hydration of this skin layer offers an indirect index of the aggressivity of a tensioactive substance since the skin becomes proportionally drier as alteration of the stratum corneum increases. We thus performed before and after corneometric examinations in the subjects who used the products being tested. (51,52)

Materials and methods

One hundred fifty subjects were used in this part of the study. Each washed one half of his/her face with product no. 01 and the other half with one of the other test products. Each of the latter products was tested in ten subjects, i.e. the same groups created for the half-face test and subjected to sebometric analysis. As with the latter approach, baseline values were determined before test washing began. These values were based on three consecutive readings taken from adjacent areas of the facial skin. Readings were made with a CM 420 corneometer made by Schwarzhaupt. This instrument uses a cutaneous probe to measure the capacitance induced by various quantities of water contained in the most superficial layers of the epidermis. After completion of the half-face test, final values were determined for both sides of each subject's face.

Results

The mean values, baseline and final, emerging from the corneometric analysis are shown in Figure 10. These figures indicate that only product no. 01 caused a significant increase in cutaneous hydration. All of the other products were

associated with modest increases or very slight decreases in cutaneous moisture levels. The significant increase associated with product no. 01 was seen in almost all of the 150 subjects who used it. Again these figure allow us to determine how each of the fifteen products compares with product no. 01 and to rank each product according to its effect on stratum corneum hydration. Appendix no. 2 contains the corneometric values for each of the fifteen test groups (expressed as group means); in the case of product no. 01, the values are the means of all 150 subjects who used this product.

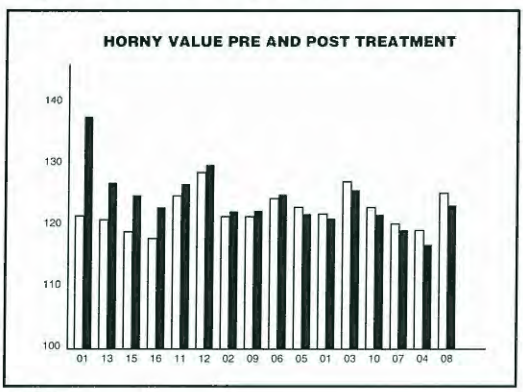

Fig. 10 -

In Figure 11, the sixteen products have been ranked in descending order according to the levels of cutaneous hydration reflected in the appendix figures.

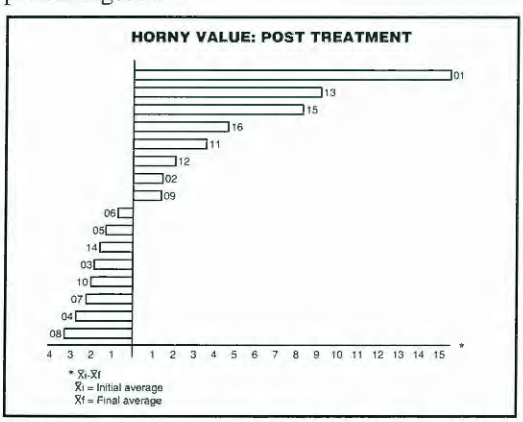

Fig. 11 -

Measurement of Cutaneous pH

The pH of the epidermal surface is determined by the biochemical and physical properties of the hydrolipid film that covers it. Skin pH varies with the area of the body being considered and is usually higher in those regions that contain apocrine sweat glands, such as the axillae or genital area, or where there is a buildup of epidermal cellular debris and sudoration products.

The average pH of skin is 5.5 although values between 4.5 and 6.0 are considered normal. (42,45,46)

The physiological pH contribues to skin homeostasis, inhibits the growth of pathogenic organisms and provides chemical defense of the skin depends primarily on the buffer system provided by the eccrine sweat glands. The secretions of these glands are able to restore the pH to physiological values within a relatively brief period of time.

Other substances present in the epidermis also contribute to this buffer system: amino acids, fatty acids, uric acid, lactic acid, SO~~and C1~ ions. These substances serve primarily to neutralize any excessive alkalinity. Cations, such as Na+, K+ and NH+, and other amino acids expert a buffering effect on excessive acidity. (4,42,46)

Cleansing is generally considered to be the most important factor involved in alterations of cutaneous pH. These alterations can facilitate the development of skin irritation which can then open the way to other pathological processess. It is thus important to evaluate the effect of any skin cleansing product on the pH of the skin. (42,47)

Materials and methods

Cutaneous pH was measured in 80 volunteers between the ages of 18 and 37. All subjects pre-

sented normal pH values in the regions tested prior to our measurements. Ten subjects were used for each test product.

The test period lasted for five days. Each day the subject used the product assigned to his/her group to wash the volar surface of one forearm in the morning and in the afternoon (not less than 8 hrs after the first washing). The other forearm was cleansed in the same way using product no. 01. The subjects used 1 ml of a 2% solution of the product and were instructed to use 30 seconds of manual massage of the area for each washing.

In the afternoon, 30 min. and 1 hr. after the second daily washing, the pH of the test areas were measured with a pH 900 PC skin pH-meter. Each value is a result of ten automatic measurements performed at two-second intervals.

Results

The baseline pH values in the study population varied from 4.0 to 5.5. In addition to the differences that emerge between soaps, synthetic detergents and products no 01, Figure 12 shows that the latter product produced less modification of the baseline pH than any of the other fifteen products. The group assigned product no. 01 had an average baseline pH of 5.2. At the end of the five days of washing, this average had risen to 3.35.

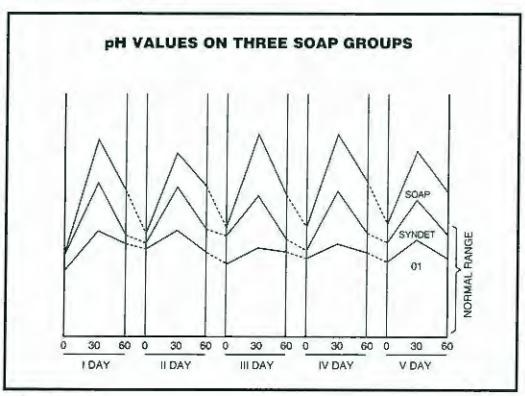

Fig. 12 -

This represent an extremely modest increase to levels that are still within normal limits.

The other products under study provoked much more significant modifications in the pH, as can be seen from Figure 13. Use of traditional alkaline soaps led to a full point increase in skin pH from a baseline mean of 5.5 to a final value of 6.5 which is clearly no longer within the normal range.

Figure 13 also shows the differences that emerged between product 01 and the other 15 tested.

One of the most important harmful effects of cleansing is the damage it causes to the stratum corneum. Adhesion between the keratin plaques disappears and they are shed. This situation leads to an increase in TEWL. In order to determine the degree of damage to the stratum corneum provoked by each of these products, we performed two more tests: the Scotch tape test and cutaneous imprints.

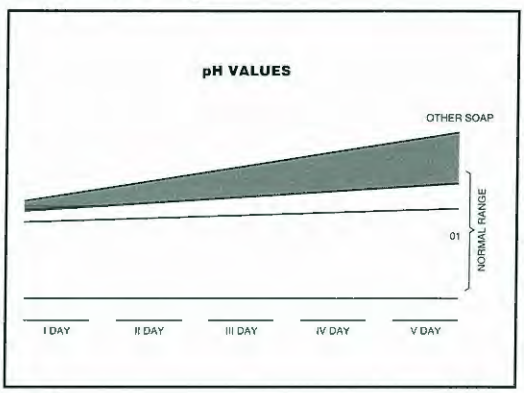

Fig. 13 -

The scotch tape test

This simple technique involves the application of an adhesive strip to the skin of the patient. When the strip is removed, a certain number of keratinocytes will come with it. The amount removed will be proportional to the degree of damage suffered by the stratum corneum.

In order to improve our evaluation of this para-

meter, the cells that were collected on the adhesive strip were examined under the electron microscope. The strip was attached to a cylindrical support (stub) 2.5 cm in diameter.
Even though application pressure has little effect on the number of keratinocytes that will be detached, we used a spring-activated device to standardize the pressure.
The scotch tape test was used on all 150 volunteers that participated in the half-face test.
Cells were collected before and after the five-day cycles of test washing. The specimens were metallicized directly using a Balzer instrument with a gold electrode. They were then examined with a Cambridge 180 Stereoscan electron microscope.

Results

The numbers of cells that were detached from the stratum corneum before and after the washing cycle were compared for each subject. It was not possible to make comparison between groups, since each individual presents his/her own desquamation pattern.
Our findings show that certain soaps were associated with greater desquamation after washing. Others produced little change in the desquamation.
Product no. 01 was found to reduce more significantly than the others the number of stratum corneum cells that were shed.

Skin imprints

This approach involves the use of an inert substance capable of reproducing a mirror image of the cutaneous surface. The material (Xanthopren - Bayer) is pressed against a skin surface where it fills all depressed areas (sulci, wrinkles, etc.).
These areas appear as ridges in the imprint. If the imprint is used as a mold and filled with another plastic material, the result will be a faithful reproduction of the skin surface. This method allows us to study the surface of a cutaneous area in vivo and to evaluate the changes induced by a cosmetic treatment or, in our case, a skin detergent.
We made imprints of the lateral periorbital and zygomatic areas of the subjects before and after the half-face test. The reproductions were metallicized with gold and examined with the Cambridge 180 Stereoscan electron microscope.

Results

The morphometric analysis of the cutaneous imprints allowed us to evaluate the damage to the stratum corneum induced bu each of the products we tested. Most of the products provoked modifications of the superficial corneocytes which appeared poorly linked to one another, irregular and in some cases desquamated. The products associated with these effects were nos. 04, 07, 09, 02, 10 and 12. More modest changes were found in the subjects who had used products no. 13, 16, 11 and 14. The differences were quantitative rather than qualitative and it would be impossible to rank the products according to these findings. Limited changes or even improvement in the superficial morphology of the skin were observed with the use of both product no. 15 and product no. 01 (Figures 14, 15, 16, 17). The findings are illustrated in the photographs.

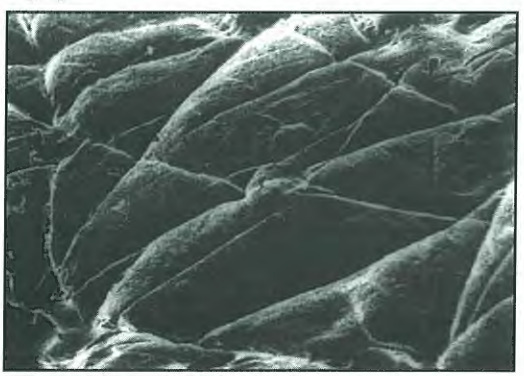

Fig. 14 - Skin imprint: S.E.M. before treatment with 01 soap (S.E.M. - Scanning Electronic Microscope)

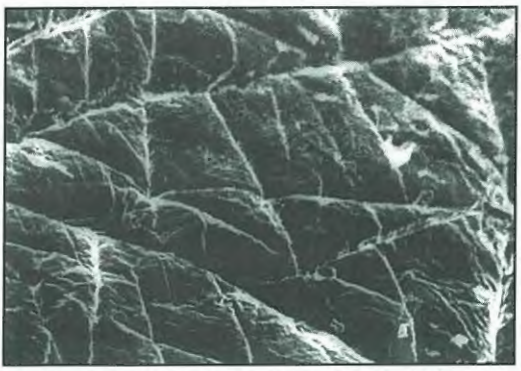

Fig. 15 - Skin imprint: S.E.M. after treatment with 01 soap (S.E.M. - Scanning Electronic Microscope)

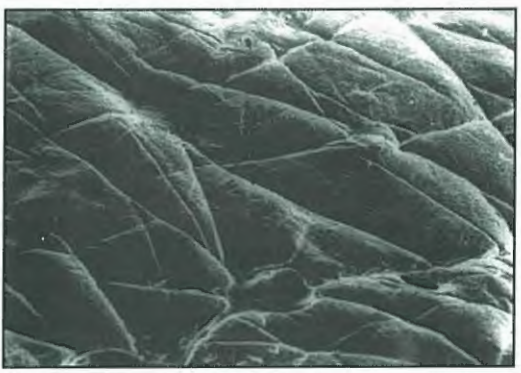

Fig. 16 - Skin imprint: S.E.M. before treatment with 15 soap (S.E.M. - Scanning Electronic Microscope)

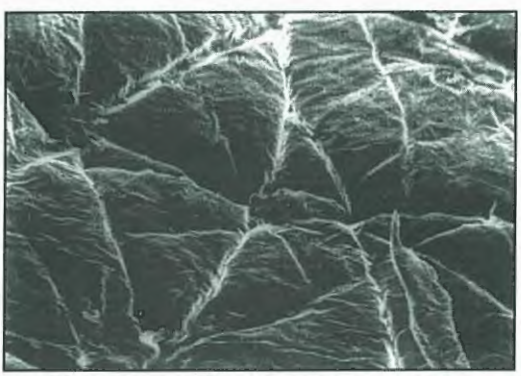

Fig. 17 - Skin imprint: S.E.M. after treatment with 05 soap (S.E.M. - Scanning Electronic Microscope)

Conclusions

Although the results of our studies allow us to define one product as superior to the other fifteen, this is not, in our opionion, the most important finding of our study. We would rather emphasize the utility of these approaches for the identification of products that are pontentially irritating or cosmetically unacceptable before they are placed on the market.

We found considerable differences among these products, but none of them was so irritating or cosmetically ineffective as to be judged in a completely negative manner. Overall, we found that several of the products we tested, some of them traditional soaps, others synthetic detergents, are well-tolerated and provide effective cosmetic improvement. In particular, products 01, 12, 13, 15 and 16 were all found to be weak irritants in our tests. Three of these products were synthetic, the other three were traditional soaps.

These findings were consistent with those that emerged from almost all of the tests we performed.

Product 01 consistently found to be the least aggressive and to produce the most cosmetically acceptable results. Between the two there were only very slight differences. Product no. 1 is a synthetic detergent.

This apparent similarity leads us to a general consideration. Cleansing of the skin is a complex and important problem. Choosing a product solely on the basis of whether it is a soap or a synthetic detergent is unwise. What matters more is that the formula upon which the product is based is a valid one, that the ingredients as well as the product itself are carefully controlled and that valid forms of quantitative testing are available to the manufacturer to help him to identify the product best suited to the consumers' needs as projected by the cosmetic industry. The cosmetological technician can carry out such tests and on the basis of the findings that emerge help identify the desired product.

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PEDIATRIC COSMETOLOGY: CURRENT AND FUTURE TRENDS

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Receveid: *October 30, 1991. Presented at the IV International Congress on Cosmetic Dermatology "Progress in Cosmetic Dermatology: Science and Safety" Roma (Italy) October 31 - November 2, 1991.*

Key Words: *Infant Cosmetics; Directing Cosmetic Sales; Cosmetic Toxicity.*

Synopsis

The first part of this paper deals with the marketing of cosmetics to infants, children, and young adults in the U.S.A. and selected European markets. An analysis of marketing techniques and the objectives of directing cosmetic sales to certain age groups under certain circumstances are outlined. The size and the potential dollar value of these markets is indicated and the importance to the industry and the degree of effort exercised in promoting these markets will be discussed.
The second part of the paper deals with some of the scientific aspects of the development of cosmetics for various young age groups. These are discussed under the foillowing subject headings:
1. Systemic toxicity issues, reabsorption and ingestion
2. Skin, eye, and genital irritation
3. Preservatives in skin flora issues
4. Allergic sensitization and photosensitization issues
5. Packaging issues

Riassunto

Nella prima parte di questo lavoro viene effettuata un'analisi di marketing dei cosmetici rivolti ai bambini ed ai giovani, in genere sia sul mercato USA che su quello europeo. Vengono poste in evidenza anche le tecniche di vendita utilizzata per i cosmetici rivolti alle diverse fasce di età, valutandone il valore economico e l'importanza finanziaria delle industrie cosmetiche.
Nella seconda parte vengono posti in evidenza gli studi scientifici di controllo necessari per la messa a punto di prodotti cosmetici alle diverse fasce di età:
1. Studi sistemici sulla tossicità dovuta ad assorbimento
2. Controllo della irritazione oculare, cutanea e degli organi genitali
3. Controllo del sistema di preservazione
4. Controllo dell'eventuale effetto sensibilizzante e fotosensibilizzante
5. Studio sul packaging

All consumers oriented insdustries are constantly looking for new customers. This constant search for new sources of business is the job of the marketing branch of the industry. Market managers have proved to be innovative and dynamic in promoting various segments of the population into becoming prospective customers for cosmetics. Considerable success in promoting teenage female use of cosmetics may be contrasted with the general failure to successfully penetrate the adult male market. nevertheless, other potential markets such as senior citizens, teenage males and children are in the process of being developed.

Developing a market for children's cosmetics is a challenge for marketing innovation. Why do children whose skin and hair are so naturally endowed need embellishment with cosmetics? Is this not painting the lily? Also, who is going to pay for these items. These questions have heen adequately addressed by the cosmetic industry.

The children's market can be divided into three groups: Babies, the 3-12 age bracket and the 12-17 age group.

Cosmetic targeted for babies are primarily personal care products such as shampoos, haby bath products, baby lotion, baby oil, fragrance and powder. They are generally advertised as having undergone dermatological testing for skin and eye irritation, toxicity safety and bacteriological control. Also certain lines stress the elimination of allergens or irritants such as talc, paba, color dyes, alchohols, petroleum derivatives and promotion of natural ingredients such as soap-free baby bath, vegetable based baby oil, vegetable jelly that has no petroleum derivatives or mineral oil and corn starch or oatmeal powders. The baby shampoos are advertised as mild and are tear-free, dye-free and hypo-allergic.
In the 3-12 year old bracket there are more than 36 million children in the U.S.A. Parents spend over $60B on products for them. Cosmetics for this segment divide into toys and toiletries. The toy cosmetic market targeted to the younger children stresses the play and educational value of the cosmetics. the advertising for this group soft pedals the pretty or nicer sexually connotative words and stresses the play and educational value of the products helping mom to teach basic hygiene to the kids. The packaging of these products is innovative and can be converted into toy purses or novelty containers indicating the imagination of the marketing people.

The toiletry portion of this market is tbe older children in the 3-12 year bracket and is frequently targeted to the mothers. The health and hygiene of these products as well as the growing up mimicry of the parents appeals to mom. In addition the Saturday a.m. T.V. advertisments bombard the kids with marketing messages which are not forgotten. Even sophisticated upscales such as children's perfumes are promoted. These are fashioned after the popular international children's book characters such as Mickey and Minnie Mouse and Babar the elephant and his wife Celeste, popular in France for example.
Also the natural ingredient pure botanical lines which stress environmental protection and uses pH balanced shampoos that cleanse without detergents and environmental protection cream that purports to protect against environmental elemnts such as wind, pollution and heating and air conditioning systems. In addition endangered species soap in the form of rhinoceroses, green turtles, blue whales and giant pandas bave been introduced to combine cleansing of the skin with information about protection of endangered species.

The older children 13-17 are estimated to spend $ 33B of their own disposable monies. This market addresses products in the adult market with a youtful marketing twist. All toiletries as well as embellishing cosmetics are promoted and used. Cleansing agents, shampoos, con-

ditioners and moisturizers are promoted as slowing down of aging of the skin as well as prevention of skin cancer.
Dermatologists are recommending their use routinely in over 3 year olds and under certain circumstances under 3 years of age. The bronzed look introduced by Coco Chanel in the late 30's is giving way to the alabaster look of the pre-World War I era. The skin cancer foundation has been warning that "by the time many children reach early adulthood, they have already soaked up enough sunlight to grow their first skin cancer".

The sun tanning booths popular in the U.S. the past 10 years are being rightly given bad publicity as potential health hazards and are being brought under control of local authorities and regulating bodies in many states.
In addition all embellishing cosmetics: Hair products, eye make-up, foundation, blush, lipstick, fragrance, moisturizers and toners are highly promoted in this age group by standard and innovative marketing techniques.

The scientific touchstones to the development of children's cosmetics relate to special risks of products sold for children and a basic dictum. The dictum is "primum non nocere" do not do any harm.
The areas of concern are:
I. Systemic toxicity issues re-absorption and ingestion.
II. Skin, eye and genital irritation.
III. Preservatives and skin flora issues.
IV. Allergic sensitization and photosensitization issues.
V. Packing issues.

I. Systemic toxicity issues re-absorption and ingestion.

In my previous paper on percutaneous absorption of chemicals through the intact skin of infants and children it was pointed out that premature infants absorbed potentially toxic materials through the intact skin at a much greater rate than term-birth babies. Also the high body surface to weight ratio of infants and young children wonld promote increased absorption of certain solutes if they used over a large area of skin surface. Also there was a selective absorption of some materials through the intact skin.

These points are of paramount importance since infant deaths have been reported from the absorption of 3% hexachlorophene and phenol: thyroid disease from iodine containing cleansers; Cushings disease from steroids and cyanosis from Castellani's paint (phenol and resorcin) and toxicity from boric acid.

It goes without saying that potentially toxic substances should be eliminated from cosmetic formulations for infant and children's skin. All substances used in cosmetics for infants should be screened by both in vitro aud if possible in vivo studies to delineate absorption into the system.

II. Skin, eye and genital irritation.

Genital irritation and cystitis from bubble bath products in young females was an FDA issue in 1978. The chief culprit was sodium lauryl sulphate and other surface tension lowering agents which also irritate the eyes if contained in shampoos.

Other shampoos containing lye can cause serious irritation around the eyes. Artificial straightening of children's hair requires strong chemicals which are potentially irritating to both skin and mucous membranes of the eye.

Cosmetically induced acne is a potential hazard in pre-teens aud teens. Chronic use of materials such as isopropyl myristate, octyl palmitate, decyl oleate, butyl stearate and lanolin deriva-

tives - found in cosmetic cream vehicles - which are all comedogenic by virtue of blocking normal exfoliation of epithelial cells in the sebaceous duct have been indicted in this respect after long-term use.

III. Preservatives and skin flora issues.

The normal skin of infants and children is resistant to most bacteria by virtue of its protective desquamating process of the stratum corneum. Previously it was theorized that the low pH of the skin provided an "acid mantle" which together with fatty acids protected the skin from bacteria. Today it is felt that the relative dryness of the skin coupled with the constant shedding of the stratum corneum including the bacteria thereon is the major protection of the skin from infection. bacteria thrive in the skin normally and are actually helpful to normal physiology. These are the so-called resident flora. There are also transient bacteria which may cause infection in broken or diseased skin.

Cleansing preparation for children: soaps, liquid lotions, do not routinely require antiseptic or antibacterial ingredients. Antimicrobial soaps should require a warning label for use in infants because of the potential for percutaneous absorption of toxic substances such as hexachlorophene.

Cosmetic preparations should be formulated so as not to promote bacterial growth. This is accomplished with preservatives which prevent bacterial growth. Generally speaking preservatives do not irritate or sensitize normal non-disrupted skin. Agents such as parabens are excellent preservatives and are not highly sensitizing to normal skin but are quite sensitizing to irritate or eczematous skin. Other agents such as imidazole urea and triclosan are frequently found in cosmetics and have a low allergenizing potential.

IV. Allergic sensitizing and photosensitizing issues.

The chronic use of cosmetics may promote allergic sensitization and photosensitization. While the skin of infants and young children to the age of 8 are not easily sensitized, older children do not differ from adults in that regard. Therefore if they use potentially allergenic substances early in life and continue to do so the potential for sensitization is enhances theoretically. Before the introduction of cosmetics into the children's market most allergic dermatitis in children came from inadvertent contact with mothers cosmetics - primarily their fragrance. This observation has held true for children's cosmetics as well in which perfumes and balsam of Peru a cross reactor are identified as causing allergic reactions.

Photosensitization is caused by a toxic or allergic reaction from materials applied to the skin and exposed to ultraviolet A or B. Typical cosmetic reactions come from photosensitization to sunscreens or fragrances. An uncommon hut striking photosensitization reaction is from foucomarins such as lime juice and celery. Red-purple streaking in areas of application of the material - face, neck, hands, forearms - and sun exposure is classical in making this diagnosis.

In general the identification of the sensitizing culprit and their elimination is all that is necessary.

V. Packaging issues.

The packaging of cosmetics potentially hazardous to children if ingested should be done in child-proof containers. While there is not a high incidence if this type of poisoning there are some agents such as bromate home permanents, sculptured nail acetonitrile glue remover and talcum powder in liquid look-alike nursing bottles which might cause aspiration of talcum powder if improperly used.

For the most part cosmetics designed for children's use do not contain potentially toxic chemicals if ingested.

The cosmetic industry like all consumer industries must evaluate the risks versus benefit of all its products released to the public for general use. We live in a litigious society in the USA where burden of proof of product liability is not as important as the deep pockets of any agency involved in the manufacture, packaging or selling of any given product. The "caveat emptor" of the last century has been changed to "caveat vendor" today.

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J. Appl. Cosmetol. 11, 29-40 (January - March 1993)

THE ROLE OF VITAMINS IN AGED SKIN

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Receveid: *October 30, 1991. Presented at the IV International Congress on Cosmetic Dermatology "Progress in Cosmetic Dermatology: Science and Safety" Roma (Italy) October 31 - November 2, 1991.*

Key words: *Vitamin E Acetate; Vitamin E Linoleate; Vitamin A; Vitamin C; Panthenol; Vitomin D;*

Synopsis

Skin is the body's largest and most complex organ. It is also the most dependable, maintaining its primary function of protection throughout one's life. Nevertheless, as skin ages, it becomes subject to problems ... cosmetically annoying as dryness, wrinkles, age spots or life threatening, such as malignant lesions. The skin aging process itself takes two distinctive pathways: chronologic, marked by histologic and physiologic changes and photoaging - changes that occur in habitually sun-exposed skin. Although mankind has been searching for the "Fountain of Youth" throughout history, only in recent years has science provided us with ways of slowing down the aging process of the skin by protecting it, or reversing the photoaging effects. Studies conducted in recent years have provided strong evidence that certain vitamins, when applied topically, can play an important and beneficial role in tbe aged skin. Some act to protect the body cells and tissues from damage caused by natural body processes, certain lifestyle choices and environmental stresses, while others can provide the proper environment for the correction of damage caused to the skin. Of particular interest are vitamins A, E, C Panthenol (Pro-vitamin B5) and their derivatives.

VITAMIN E ACETATE - THE PROTECTOR

The central role of vitamin E Acetate is that of an in vivo antioxidant. It helps protect against cell damage caused by UV and pollution-induced free radicals and, as such, might play a role against skin aging. In addition, vitamin E helps maintain the connective tissues' firmness and texture.

VITAMIN E LINOLEATE - THE MOISTURIZER

Vitamin E Linoleate is a superior moisturizer. It accumulates in the stratum corneum and repairs the Intercellular Moisture Barrier of the skin.

VITAMIN A - THE NORMALIZER

Regulates the growth and activity of epithelial cells. It increases the skin elasticity and helps in thickening the dermis and epidermis.

VITAMIN C - THE CORRECTOR

Vitamin C, when applied topically from the proper vehicle, can quench oxygen free radicals and prevent UV damage. Recent studies indicate possible stimulation of collagen synthesis in the skin.

PANTHENOL - THE BEAUTIFIER

Panthenol (provitamin B5) stimulates the proliferation of fibroblast cells and aids in tissue repair. Furthermore, it can promote the wound healing process which slows down as skin ages.

Riassunto

L'organo cutaneo è il più esteso ed il più complesso tra gli organi e svolge la sua principale funzione

che è quella di proteggere tutto l'organismo umano.
Con l'invecchiamento sorgono alcuni problemi quali la formazione delle rughe, l'aumento della secchezza cutanea, di "macchie di vecchiaia" fino a formazioni tumorali. Per quanto riguarda l'invecchiamento cutaneo è ormai chiaro che si può parlare di due tipi di invecchiamento: quello cronologico e quindi già predeterminato dai geni, e quello provocato dalla luce, il cosiddetto fotoinvecchiamento.
Con i cosmetici si può intervenire soltanto su quest'ultimo e le sostanze notoriamente attive in tal senso, sono senza dubbio le vitamine A, E, C, il pantenolo (o provitamina B5) ed altri derivati.
VITAMINA E ACETATO - PROTETTRICE
Il ruolo centrale della Vitamina E Acetato è di agire "in vivo" quale ossidante. Protegge la cellula dai danni provocati dagli UV e dagli inquinanti ambientali, attraverso la formazione dei radicali liberi. Combatte, quindi, l'invecchiamento cutaneo ed aiuta il tessuto a mantenersi compatto.
VITAMINA E LINOLEATO - L'IDRATANTE
E' un'idratante importante. Si accumula a livello dello strato corneo agendo come riparatore della barriera cutanea.
VITAMINA A - NORMALIZZANTE
Regola la crescita e l'attività delle cellule epiteliali. Incrementa l'elasticità della pelle modulando il turnover cellulare.
VITAMINA C - CORRETTRICE
La vitamina C, se applicata topicamente con un veicolo adatto può legare l'ossigeno dei radicali liberi, prevenendo il danno da UV. Recenti studi la indicano come possibile stimolante della sintesi del collagene.
PANTENOLO - PER LA BELLEZZA
Il pantenolo (Provitamina B5) stimola la produzione dei fibroblasti e facilita la riparazione cellulare. Accelera, inoltre, i processi riparativi della cute, processi che rallentano con l'invecchiamento.

Introduction

Skin is the body's largest and most complex organ. It is also the most dependable, maintaining its primary function of protection throughout one's life. Nevertheless, as skin ages, it becomes subject to problems ... cosmetically annoying as dryness, wrinkles, age spots or life threatening, such as malignant lesions.

The skin aging process itself takes two distinctive pathways: chronologic, marked by histologic and physiologic changes and, photoaging - changes that occur in habitually sun-exposed skin. The structural changes that take place in the skin with aging cause reduction in its principal functions by as much as 50-60%. The physiological changes associated with these reductions include impairment of the barrier function, decreased turnover of epidermal cells, residual number of melanocytes, keratinocytes, fibroblasts and decrease in vitamin D synthesis, sebum production, hair and nail growth. The synthesis and diversity of Langerhans cells, and T cells which are part of the immune system are also reduced. All of the above result in fribrosis, atrophy and thus skin aging.

Although mankind has been searching for the "Fountain of Youth" throughout history, only in recent years has science provided us with ways of slowing down the aging process of the skin by protecting it, or reversing the photoaging effects.
Recent studies indicate that vitamins and their derivatives can play a very important role in the war against aging.

The association between vitamins and good health has long been established. Unfortunately, vitamins were not widely used in cosmetics or dermatology because of tbe belief that vitamins could not penetrate skin, and mostly because the metabolism of skin was not fully known. In addition, the emphasis in cosmetics was more on decorative products, which could cover-up imperfections and the signs of advancing age, rather than prevention or correction of damage to skin, hair and nails.

Studies conducted in the late '80s and especially in the last (3) years, have provided ns with growing evidence that certain vitamins, can protect the body cells and tissues from damage caused by natural body processes, certain lifestyle choices and environmental stresses, while others can provide the proper environment for the correction of damage caused to the skin because of chronologic aging and photoaging.

Vitamins - General benefits

- Vitamins are naturally occurring ingredients required for normal growth and maintenance of the body functions.
- Vitamins catalyze reactions as part of the enzyme system within the organisms.
- Certain vitamins, such as vitamins C, E and Beta Carotene can protect skin cells and tissues.
- In cosmetic dermatology, vitamins can provide a beneficial environment for protection, correction and renewal processes of skin, hair and nails, which slow down considerably with aging.

Of particular interest are vitamins A, B5, C, D, E and their derivatives.

Vitamin E Acetate - The protector

Natural body processes, certain lifestyle choices, environmental pollution and UV radiation can cause the formation of free radicals which are very reactive molecules and as such, may cause damage to cells and tissues and accelerate the aging process.

There is growing evidence that antioxidants

function as in vivo free radical quenchers, thus inhibiting the damage caused by peroxidative reactions. Throughout the years, vitamin E has been mainly used by the cosmetic and toiletries industry as a 'Natural Moisturizer', to relieve dry skin. However, studies conducted in recent years have provided information on its benefits beyond moisturization.
There is significant evidence that vitamin E, when topically applied, plays a crucial role in - protecting - the skin from free radicals damage. However, because of the poor stability to oxygen of Tocopherol (free vitamin E), its use is impractical as an in vivo antioxidant (although it will help in extending the shelf-life of cosmetic products) and therefore, vitamin E acetate is used.

Vitamin E acetate, (an esterified form of Tocopherol) is a very stable ingredient, but is not an antioxidant per se. However, its addition to skincare and suncare products at the proper levels has demonstrated that upon penetration into the skin, it can provide in vivo antioxidant activity in tbe same way as free vitamin E.

A recent study (1) (February, 1990), conducted by Dr. Edward P. Norkus, of the New York Medical College has confirmed the bioconversion into free vitamin E.

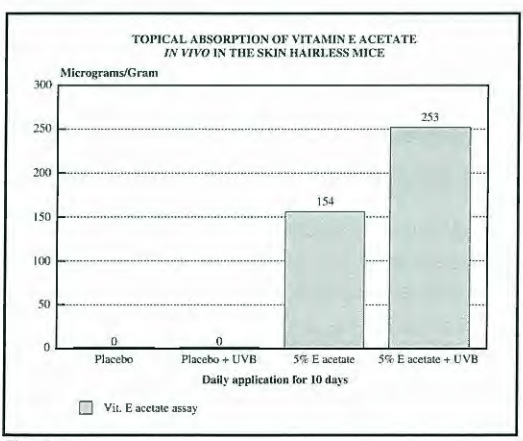

Fig. 1 -

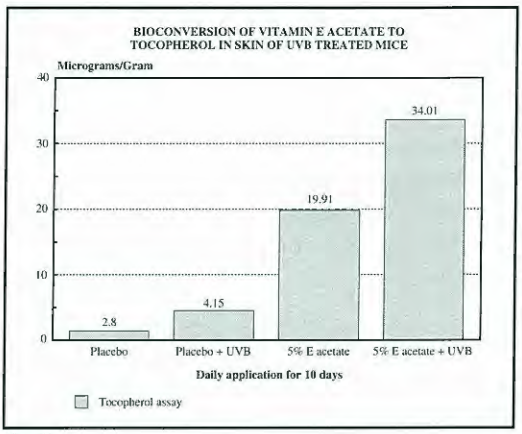

Fig. 2 -

A study conducted by Dr. Madhu Pathak, of Harvard Medical School (2) with topical application of vitamin E acetate on mammalian skin, has shown that this form of Vitamin E can provide protection to the superoxide dismutase (SOD) enzyme, which is one of the most important free radical scavenging enzymes.

Since the level of SOD in normal epidermis is usually low, in tissues that have been exposed for years to UV radiation and chemical pollution the levels are probably even lower, which may explain the susceptability to photoaging and photocarcinogenicity in aged skin and thus lead to the need for increased use of free radical scavengers such as vitamin E acetate in these conditions.

Another study (3) conducted in 1990 on human volunteers, has confirmed that vitamin E acetate when applied topically over a period of ten (10) days from a 2.5% gel, has lessened skin damage from UV radiation as measured by reduced erythema. (Single application did not have any effect).
Application of a commercial sun blocking product of SPF 2 on top of tbe vitamin E application site, lowered the erythema considerably. Since the number of melanocytes in the skin of

the elderly is sharply reduced, vitamin E acetate can provide natural protection against excessive sun damage.

The effect of vitamin E deficiency on the levels of lipid peroxides and solubility of collagen was investigated by A. Igaraski and M. Uzuka of Shiseido Laboratories 4 in rats fed a vitamin E deficient diet for three (3) and six (6) months. The lipid peroxide content in the skin was markedly increased in the vitamin E deficient group as compared with that of controlled rats on a normal diet.
The amount of insoluble collagen in the dermis of rats on vitamin E deficient diet was substantially higher than in those fed on a normal diet. On the other hand, the level of soluble collagen, which is abundant in young skin, was higher in the rats fed a normal diet, as compared to those maintained on vitamin E deficient diet.

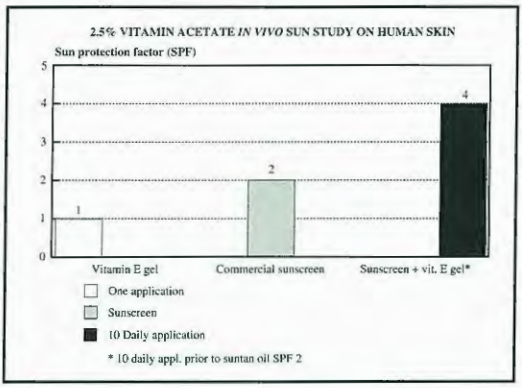

Fig. 3 -

The results of this study suggest that high levels of vitamin E in the skin reduce the amount of insoluble collagen by inhibiting formation of peroxides. The changes in the skin produced by lack of vitamin E resemble those in aging and vitamin E may have a role in slowing down aging.

Table I

IN VIVO PHOTOPREVENTIVE EFFECTS OF VITAMIN E ACETATE ON SOD ACTIVITY

in vivo reaction systems	units of sod in 50Uug epidermal proteins	% decrease of sod activity	% protection of sod by quencher
Skin homogenate (control)	0.96	0	100
Skin + UVA	0.61	36.5	63.5
Skin + topical sod + UVA	0.89	7.3	92.7
Skin + aTCA + UVA	0.89	7.3	92.7
Skin +3cp + UVA	0.32	66.7	33.3
Skin + 3cp + aTCA + UVA	0.75	22.0	78.0
Skin + UVB	0.63	34.4	65.6
Skin + aTCA + UVB	0.83	13.6	86.4

3CP = 3-Carbethoxypsoralen. (M.A. Pathak, 1988)

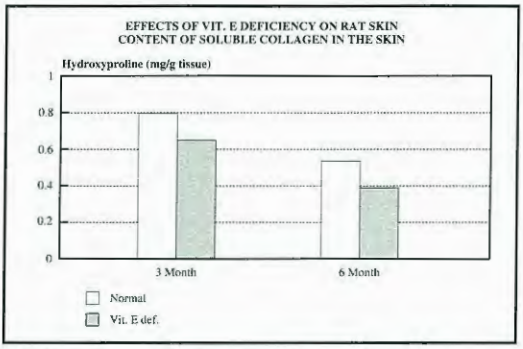

Fig. 4 - (A. Igarashi, M. Uzuka and K. Nakajima)

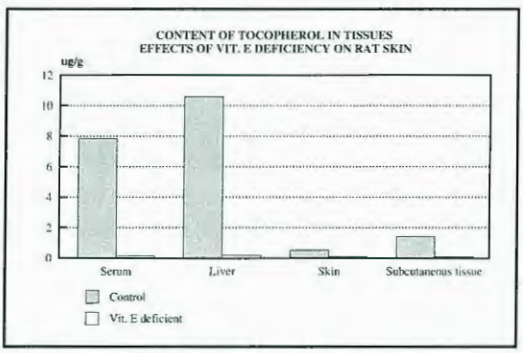

Fig. 5 - (A. Igarashi, M. Uzuka and K. Nakajima)

Vitamin E Linoleate - The moisturizer

One of the major signs of aged skin is the impaired Intercellular Moisture Barrier of the stratum corneum, which manifests itself in excessive dryness and scaliness.

Studies conducted in the last (10) ten years have revealed that although water plays an important role in keeping the skin moist and supple, the ability of the stratum corneum to resist moisture loss, depends on the presence of long chain polyunsaturated lipids known as Essential Fatty Acids (EFA).

These lipids, which consist of linoleic, linolenic and arachidonic acids cannot be synthesized by the body, although when topically applied can be metabolized in the skin and be incorporated into the structural lipids of the epidermis (ceramides) - the building blocks of the Intercellular Moisture Barrier of the skin.

In the elderly, due to deficient diets, or poor transport to the skin because of poor absorption (improper functioning of metabolic systems, or drug interference), the levels of the necessary EFAs could be much lower than in young skin, thus important role in repairing the moisture barrier.

Vitamin E Linoleate, which is characterized by excellent stability and non-irritancy can play a very important role in repairing the moisture barrier.

Studies conducted with radio-labeled vitamin E Linoleate (5) have shown that this derivative accumulates mostly in the stratum corneum and is incorporated into the ceramide lipids, making it an ideal building block of the Intercellular Moisture Barrier of the skin.

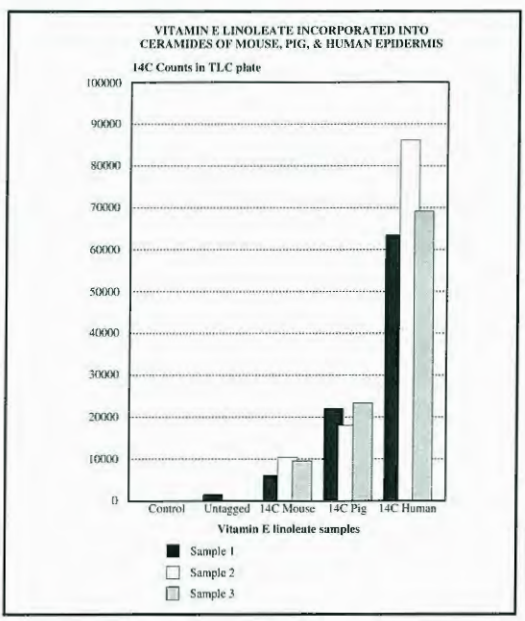

Fig. 6

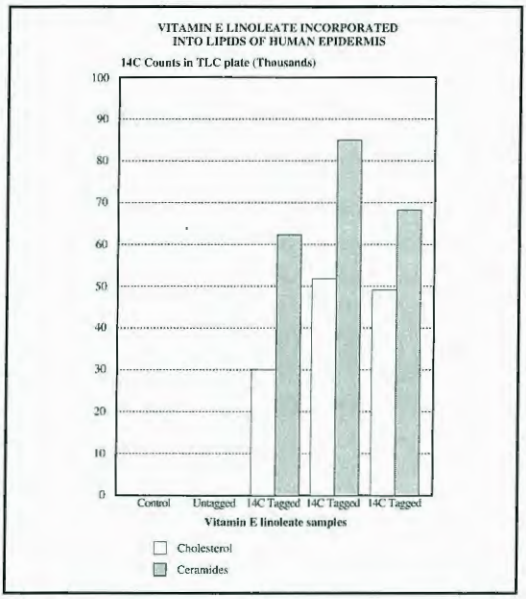

Fig. 7

Transepidermal water loss has been used as a parameter for measuring the barrier function of the skin.
It has been demonstrated by many prominent researchers that skin deficient in essential fatty acids exhibits high TEWLs, manifesting itself in high keratinization and subsequent dryness and scaliness.

In a study conducted by Dr. Peter Elias of the University of California in San Francisco (6), the effect of 1.5% vitamin E linoleate was tested against a placebo base, for its Transepidermal Water Loss Reduction on the skin of hairless mice (maintained on an essential fatty acids deficient diet).

The results of this study showed a significant reduction in TEWL with the gel containing 1.5% vitamin E linoleate vs. the placebo base (65% vs. 10%); reaching a peak after the fourth (4th) day of application. These data provide strong evidence that vitamin E linoleate can restore the Intercellular Moisture Barrier in the aged skin.

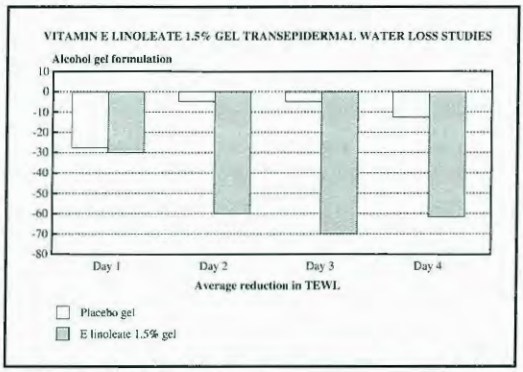

Fig. 8 - (Peter M. Elias. M.D. VSCF. Sept./Nov. 1989)

Vitamin C - The corrective protector

Ascorbic Acid (vitamin C) has been found to be an essential co-factor in the hydroxylation of proline and lysine to form hydroxyproline and hydroxylysine amino acids which are necessary for the formation and function of collagen (7). Studies conducted with cultured human skin fibroblasts demonstrated that ascorbic acid stimulated collagen synthesis preferentially without affecting non-collagen synthesis.

Although the body reservoir of ascorbic acid is about 1500 mg. and normal daily intake can maintain a saturated level; there are many factors that potentially contribute to low ascorbic acid levels. These include age, smoking, infection, and drug intake.

Skin is especially sensitive when vitamin C levels are low, which could result in diminished collagen synthesis even without overt manifestation of ascorbate deficiency. A study conducted with the guinea pigs maintained on sub-chronic vitamin C levels (8) confirmed that when the capacity for collagen synthesis was measured in several tissues, skin appeared to be preferentially depleted compared to other tissues.

These findings support the need to deliver as-

corbic acid directly to the dermis in order to alter local deficiencies and preferentially stimulate collagen synthesis and thus potentially reverse the thinning of the epidermis.
Unfortunately, ascorbic acid, although readily soluble in water, is rapidly oxidized on exposure to air. In addition, because of its polar nature, its penetration into the skin is limited.

Studies conducted by Dr. Sheldon R. Pinnel at Duke University Medical Center (9) have shown that vitamin C can be stabilized and upon penetration into the skin (12,4% after 72 hours) there was three fold increase in the collagen content.

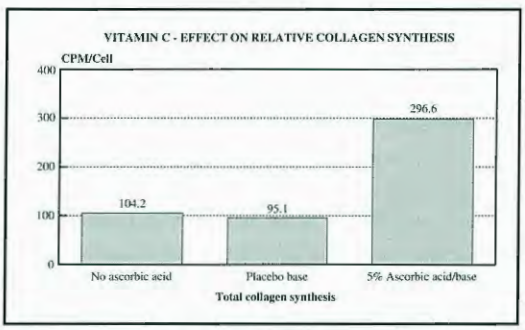

Fig. 9 - (Kaplan et al. J. Cut. Aging & Cos. Derm. 1989)

In addition to the role of ascorbic acid in collagen biosynthesis, Dr. Sheldon Pinnel has shown that topical application of a 10% solution of stabilized ascorbic acid provided significant protection against UV damage when compared with areas of the skin (10) treated with vehicle alone. By using laser Doppler Velocimetry to measure erythema and counting the number of "sunburn cells" in the pigs treated for 1 week prior to UVB radiation exposure. Both parameters were reduced by 50% when compared to the placebo. In addition, the animal studies indicate that the "reservoir effect" persists several days after application.

All of the above points to interesting opportunities in using vitamin C (in the stable form) in slowing down the aging process of the skin, and reversing the signs of aging in mature skin.

Vitamin A - The normalizer

Vitamin A is often referred to as the normalizing vitamin because it is essential not only for normal differentiation of the epidermal cells, but also for the growth and maintenance of bones, teeth, glands, nails and hair. As most other retinoids, it exerts dose-dependent effects, suggesting qualitative differences in the effects caused by high and low doses.

Over the last five (5) years, the vitamin A group has received additional publicity because of the clinical studies conducted with one of its analogs, retinoic acid, which has demonstrated reversal of photoaging.

Vitamin A Palmitate, on the other hand, which also belongs to the Vitamin A group, has not been used extensively because of the belief that it cannot penetrate the skin.

Recent studies have shown that if formulated properly and at the right levels it not only can penetrate skin, but its benefits are similar to those of retinoic acid but without the side effects.

A study conducted in 1988 by David F. Counts of Eli Lilly (11) has demonstrated that topical administration of increasing levels of Vitamin A Palmitate for fourteen (14) consecutive days in a suitable cosmetic vehicle, caused significant dose-related changes in the composition and morphometry of hairless mice skin.

There was a 128% increase of collagen per unit of skin surface area in response to Vitamin A Palmitate administration when compared to the control vehicle. In addition, there was an increase of DNA content and significant thickening of the epidermis and the dermis in the areas where Vitamin A Palmitate was applied.

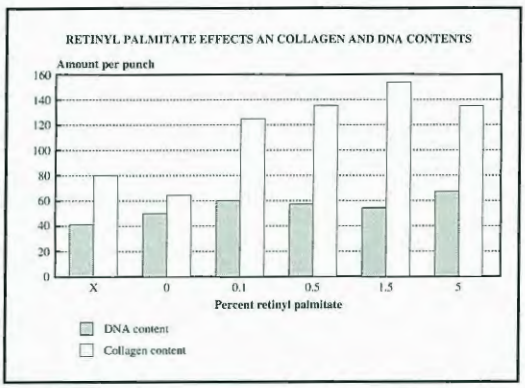

Fig. 10 - (J. Soc. Cosmet. Chem. July/Aug. 1988)

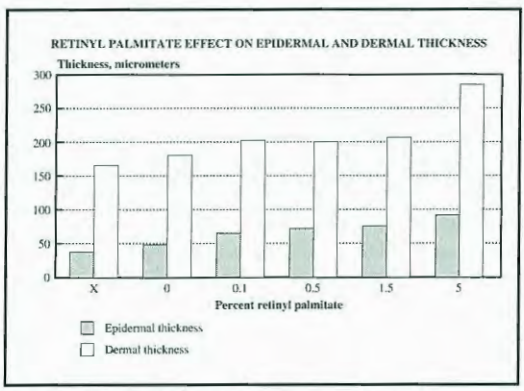

Fig. 11 - (J. Soc. Cosmet. Chem. July/Aug. 1988)

In another study (12) conducted at the Hoffmann-LaRoche Laboratories in Basle, Switzerland, the improvement in the skin elasticity was measured.

This test, which was conducted with Vitamin A Palmitate at levels of 5.000 IU/g and 10,000 IU/g for a period of 15 days, has shown that although the modulus of elasticity was hardly influenced at 5,000 IU/g (less than 3%), it was altered significantly at 10,000 IU/g (14%).

These studies are a good indication that Vitamin A Palmitate can be useful tool in reversing the atrophying of skin with age, and even correcting photodamage, which is associated with collagen cross-linking and thinning off the epidermis and dermis.

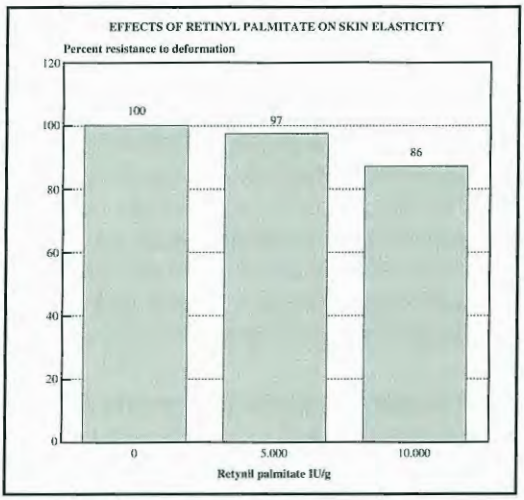

Fig. 12 - (Hoffman - La Roche Inc.)

Vitamin D

Vitamin D is essential for the development and maintenance of the healthy skeletal structure in humans. It can be obtained either by photosynthesis from 7-dehydrocholesterol (provitamin D3) or through nutrition.

With progressing age, the level of 7-dehydrocholesterol is significantly reduced, as demonstrated by Dr. Michael Holik of Harvard Medical School (13) in his study with tissues obtained from various age groups (8-81 years).

Since the epidermis in both the young and older subjects is the major site for the formation of Provitamin D3, accounting for 80% of the total levels, it is imperative that the proper levels are maintained. poor nutrition and extensive use of drugs can cause severe deficiency in the elderly. Furthermore, with the heavy use of high SPF suncare products, this problem is even more acute.

In addition to its function as a regulator of bone metabolism, vitamin D was found to play an important role in preventing damaged melanocytes

from becoming cancerous. The study conducted by Dr. Frank Garland of the University of California in San Diego (14) has shown that because of the use of high SPF suncare products, and the subsequent reduction in D3, the partially damaged melanocytes could turn into cancerous ones.

Although Vitamin D3 is banned for use in cosmetics by some European countries, its emerging importance requires a second look into its usefulness in geriatric cosmetics.

Panthenol (Pro-Vitamin B5) - The beautifier

Panthenol (pro-vitamin B5) was synthesized by Hoffmann-LaRoche in the mid 1940' as a stable analog of pantothenic acid (Vitamin B5).

Pantothenic acid which is part of the B-complex group is present in all living cells and is a constituent of co-enzyme A. The key function of this co-enzyme is to act as a carrier in acetylation reactions (Krebs cycle). The activated acetate formed with pantothenic is essential in the synthesis of lipids, proteins and the linkage between lipids/proteins/carbohydrates.

Deficiency of vitamin B5 can result in many dermatological disorders. There is considerable clinical data about its use in such skin disorders. A large amount of the clinical references deals with the effect of panthenol in wound healing including healing of burns. This activity is related to the effect of Pantothenic Acid on cell proliferation.

Since in wounds and inflammatory disorders the vitamin B5 requirements are increased, the topical application can readily provide this need, especially because of its quick penetration into the skin.

Studies conducted at Hoffmann-La Roche in 1987 by Dr. H. Weiser (15) on hairless mice, indicate considerable reduction in the wound healing time as compared to the vehicle without panthenol. The blister technique was used with the course of healing measured in 24 hours intervals.

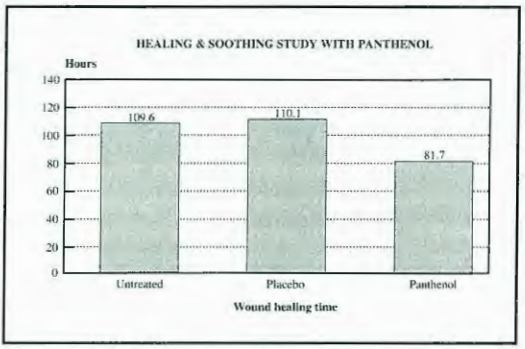

Fig. 13 - (Dr. H. Weiser, January 1988)

The healing effect was confirmed in a study conducted by B. Lacroix (16) in 1988. In this study, human skin fibroblast cell cultures were treated with Pantotenic Acid at levels of 40-80 mcg/ml. The cell proliferation was measured by cell count and determination of H3 thymidine incorporation. The protein synthesis and secretion were determined by the total quantity in the cells and culture medium. the test indicates that addition of pantothenic acid (vitamin B5) induces a strong cellular stimulatory effect. This effect was at a maximum during days 2 and 3. In addition, pantothenic acid stimulated intracellular protein synthesis but did not induce release of protein into the culture medium.

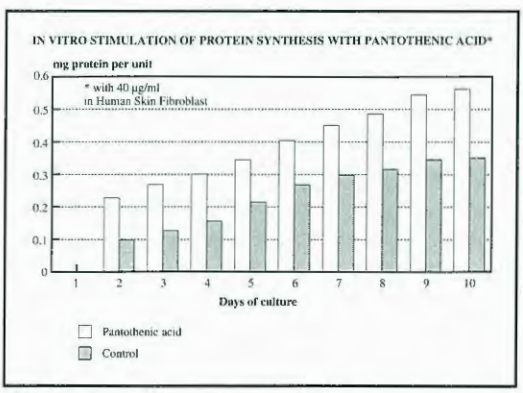

Fig. 14 - (B. Lacroix et al.)

Both studies are indicative of the role panthenol (pro-vitamin B5) can play in aging skin which suffers from slow healing due to many factors, and in particular, reduction in cell proliferation.

Summary

Although the association between vitamins and good health had been established long ago, vitamins were not widely used in skincare products, because of the belief that vitamins could not penetrate the skin.

Studies conducted in recent years have provided growing evidence that certain vitamins do penetrate and can play an important role in skincare products.

Some act to protect cells and tissues from damage caused by natural body processes and environmental stresses (chemical pollution, smoke, UV), while others correct and beautify. Their role is even more important in treatment of aged skin, which is affected by physiological changes associated with decreased turnover of epidermal cells, residual number of melanocytes, keratinocytes, fibroblasts, Langerhans cells and decrease in vitamin D production.

Vitamins, which catalyze many reactions as part of the enzyme system within the organism can provide the skin with the proper environment for protection (especially the antioxidant vitamins C, E and Beta Carotene), correction and renewal (Vitamin A,C), accelerated wound healing (Panthenol) and also good moisturizing properties.

On going studies conducted at Hoffmann-LaRoche and major scientific institutes around the world continue to unravel the importance of vitamins in the war against aging.

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J. Appl. Cosmetol. 11, 41-46 (January - March 1993)

THE EFFECTS OF NEW GENERATION COSMETICS ON EPIDERMAL BARRIER PERMEABILITY.

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Receveid: *September 24-26, 1992. Presented at the 24th Dermatological Congress Goansk, September 24-26, 1992.*

Key Words: *Stratum Corneum; Corneocytes; Photoaging; Alpha-hydroxy Acids; Liposomes; 3C System Technology.*

Synopsis

Synopsis skin with a surface area of 1.8 square meters and an average weight of approximately 4 kilograms is the largest and heaviest organ of human body. The outernost intergumentary tissue, the epidermis, maintains a reserve of germinal cell layers whose proliferation, stratification and differentiation result in production of stratum. Organized into a two compartment system, the stratum corneum consists of protein enriched corneocytes embedded in a lipid-enriched, intercellular lamellae.
The two compartment arrangement explains both the ability of cells in the other stratum corneum to take up water as well as the differences in rate of percutaeous absorption of topically applied lipophilic versus hydrophilic cosmetic agents.
Age and the environment bring about a reduction in the metabolic activity of the skin and a consequent reduction in the speed of extracellular renewal. Ultraviolet and infrared rays accelerate the process of skin aging by developing free radicals which interact at the cellular level with proteins lipids and DNA.
Appropriate cosmetic products can intervene at different level to slow down, limit and reverse damage deriving from photoaging.
They if correctly used, may be very helpful to the dermatologist by resolving medical-aesthetic problems without their patients taking oral drug too much.

Riassunto

La pelle umana con il suo peso di 8 kg e con la sua superficie di circa 1,8 metri quadrati rappresenta l'organo più esteso e pesante di tutto il corpo umano.
Il rivestimento esterno della pelle, l'epidermide, mantiene una riserva di cellule attive la cui proliferazione, stratificazione e differenzazione si estrinseca con la produzione dello strato corneo.
Lo strato corneo organizzato in un sistema a due compartimenti è formato da corneociti proteici immersi in lamelle intercellulari ricche di lipidi.

L'organizzazione in due compartimenti spiega l'abilità esercitata dalle cellule dello strato corneo di assorbire o di respingere sia i composti idro che liposolubuili.
L'età e l'ambiente provocano un rallentamento dell'attività metabolica della pelle e quindi del suo continuo rinnovarsi. I raggi ultravioletti ed infrarossi accelerano il processo dell'invecchiamento cutaneo mediante la formazione dei radicali liberi che interreagiscono con le proteine ed i lipidi del DNA danneggiandoli. L'uso corretto dei cosmetici può spesso ridurre o evitare questi danni aiutando il dermatologo a risolvere molti problemi estetici dei suoi pazienti, evitando l'uso dei farmaci.

The stratum corneum: a two compartment system.

Organized into a two compartment system, the stratum corneum consists of protein enriched corneocytes embedded in a lipid-enriched intercellular medium. Some enzyme activity also takes place in this layer. The two compartment arrangement explains both the ability of cells in the outer stratum corneum to take up water as well as the differences in rate of percutaneous absorption of topically applied lipophilic versus hydrophilic cosmetic agents.

Blank's, observations provided the basis for most products now generally known as moisturizers, the principal ingredient of which is water. Other ingredients include substances which is attract, retain or bind water within the stratum corneum. Another category of cosmetic compounds known to influence the qualitative character of the stratum corneum are the alpha-hydroxy acids. A number of these occur naturally in food.

The alpha-hydroxy acids

Whereas moisturizers affect the stratum corneum already formed, alpha-hydroxy acids determine the quality of the stratum corneum at its formation, promoting normal cohesion among the newly formed cells.

For absorption of most compounds, the stratum corneum acts as the rate-controlling membrane. For lipophilic, water-insoluble compounds, diffusion through the epidermis constitutes the limiting step. For cosmetic purposes, total percutaneous absorption is typically undesiderable, with a sustained local effect at or near the surface of the skin being preferable. Many products require minimal absorption. Absorption followed by long-term accumulation is also undesiderable for frequently used products.

Biopolymers and liposomes

Common cosmetic ingredients have always included biopolymers extracted from plant and animal materials for emollient and protective treatments.

However, these macromolecules work only to protect skin on the surface and are too large to be absorbed through the skin. New delivery systems are enhancing uptake of these molecules and thereby significantly contributing to the overall effectiveness of cosmetic products. In addition, the quality of today's natural materials is much improved due to more sophisticated harvesting, purification, processing, and quality control methods.

Most recently, true cosmeceutical ingredients have been developed. They include: liposomes and niosomes (non -ionic versicles) that can deliver antioxidants; free radical scavengers, and other active ingredients to the dermis; cell extracts and cell energizing complexes that purportedly speed up the rate of epidermal cell renewal; and cell recovery nutrients that enhance the rate o DNA repair following sun exposure.

Photoaging and free radicals

Significant differences exist between photoaging and the natural aging process. Photoburning enhances and accelerates these effects and promotes DNA damage.

Photoaging results from an uncontrolled level of lipid peroxidation caused by the generation of free radicals when UV photons hit the molecular components of skin. These highly reactive free radicals induce degeneration of the skin's key components. To counteract their destructive effects, skin cells possess enzymatic and non-enzymatic free radical scavengers that control the activity and level of free radicals.

Free radical damage worsens with age, due to increases in free radical production and declines in the ability of the antioxidant system to reduce levels of peroxidation. Appropriate cosmetic products can intervene at different levels to slow down, limit, and reverse damage deri-

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Lorenzo il Magnifico in Salute e in Malattia

Emiliano Panconesi, Lorenzo Marri Malacrida
Editore: Ed. Alberto Bruschi, Firenze, 1992. Vol. pag. 65, Figg. 7, Bibliografia, £ 20.000.

The background is that fascinating, genial, frenetic scenery of the Italian Renaissance or, in other words, its heart, Florence. Yet, while the Italians dominated Literature and Art in the whole of Europe, the political mind was practically absent, thus making it possible for foreign invaders to raid the peninsular. In this exciting, historical period dominated the figure of Lorenzo dei Medici, called the Magnificent who, besides wishing to increase the prestige of phylosophy, literature and poetry in Florence and medicine in Pisà, managed to keep an intelligent peace policy with the nearby states, showing himself to be courageous, patient and an able weaver of alliances and political balance. A good poet himself, he was the inspirer and protector of scholars and genial artists.
Focusing their attention on the cultural, artistic and political environment of the second half of the IV century, Emiliano Panconesi, refined scholar of medical science (dermatology), literature and art, and Lorenzo Marri Malacrida have published Lorenzo il Magnifico in salute e in malattia, with an introduction by Eugenio Garin on the Florentine Renaissance.
Lorenzo the Magnificent died at the age of 43 in 1492 when, with the discovery of the New World by Christopher Columbus, The Modern Era was born. In Italy, The Florentine "Signoria survived for just two years after the death of the "master of city" and then followed the fall of Florence and Italy. Ugly to look at but strong, audacious and valorous, Lorenzo was fond of beauty in all its expressions He was born under the sign of Capricorn and was in the Saturnine circle, that is to say he had the "poetio melancholy" that was considered positive even if linked to negative influences (over - indulgence typical of that ambiguous and many-sided sign of the zodiac. The death of his beloved brother, Giuliano, in the "Congiura dei Pazzi (Madmen Plot) on April 26, 1478 when he had also been wounded in the neck, left its mark on Lorenzo. It seems that he suffered from constitutional eczema while we are sure that he was plagued by gout and that he visited various spas with some results. The illness and suffering worsened considerably and he was treated according to the zodiacal and magic astrology of the time. He was given a potion of powdered emeralds and pearls, a treatment reserved in extreme moments for kings and popes.
Lorenzo's complex personality has been the reason for the interest in calculating the weight of his brain, I,548 gr. in relation to his body weight The co-efficient is very high, 3.045. (Dante Alighieri's was calculated to be 3.268). However, even mediocre subjects and idiots have been known to have a brain of more than average weight.
The death of Lorenzo dei Medici was accompanied by prodigious, premonitory signs. A thunderbolt fell on the lantern of the dome of Santa Maria del Fiore one of the golden balls fell off the Medici coat of arms; ribbons of fire crossed the sky from Fiesole to the top of the church of San Lorenzo; two lions at the Lorenzo villa went wild and fought to death; and finally, the head doctor, Pierleoni di Spoleto, accused of having ".. given the wrong treatment" to Lorenzo "who needed cool things and had been given hot things .." was found dead in a well, giving rise to the mystery as to whether he had been thrown in or had committed suicide.
The book, written without the division of chapters, involves the reader in the events which are scientifically documented and linked by a delicate feeling of estime for Lorenzo dei Medici who really was Magnificent.

Salvatore Damiano Randazzo

Chiuso in tipografia: 12 July 1993

Journal of Applied Cosmetology published quarterly by INTERNATIONAL EDIEMME, Via Innocenzo XI, 41 00165 Roma Italy. Direttore responsabile P. Morganti. Direzione, Redazione ed Amministrazione Via Innocenzo XI, 41 - 00165 Roma Italy. Stampa Grafica Flaminia Roma. Progetto grafico ed impaginazione STYLOgrafica Roma. Spedizione in abbonamento postale gruppo IV/70. Aut. del Trib. di Roma n. 3173/83 del 8-7-83

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