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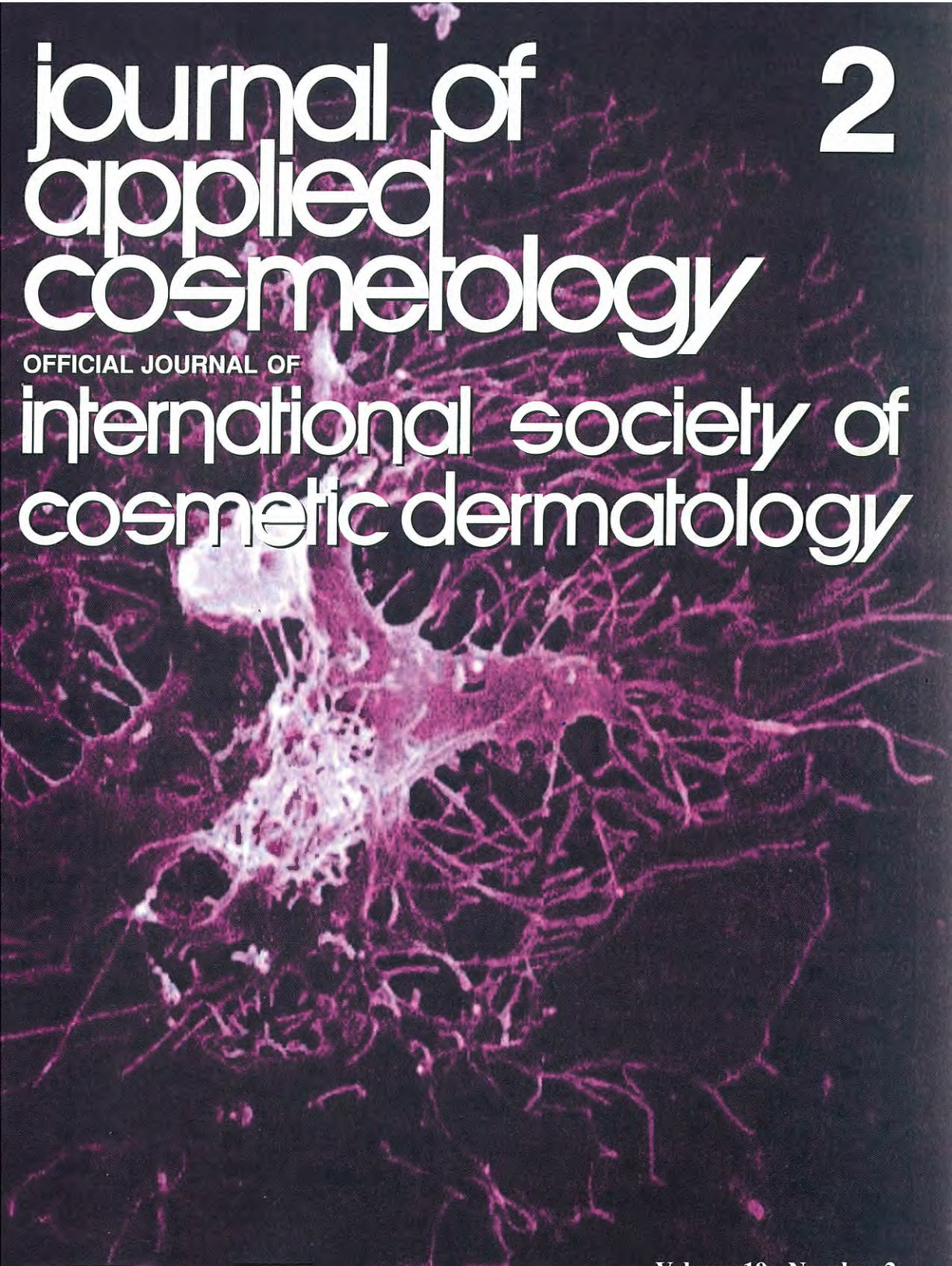

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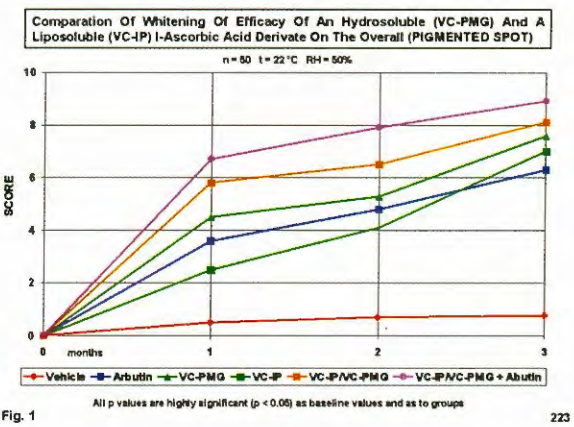

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Contents

SHORT-TERM IMPACT OF LOW CONCENTRATION SALICYLIC ACID ON THE CLEANSING CARE OF NORMAL HEALTHY SKIN

S. Quinta, P. Contreiras Pinto, L. Monteiro Rodrigues
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Received: *April 2001.*

Key words: *Salicylic Acid; Healthy Skin; Cleansing; Biological Impact; Skin Bioengineering*

Summary

Salicylic acid has been used for treating mild to moderate acne for more than 100 years. Being a well tolerated agent which is often employed for the basic skin care, recent interest suggested that low concentrations of Salicylic acid could be particularly useful to ensure skin cleansing when mildness is absolutely necessary. Thus, the present study aimed to assess the acute short-term biological effects resulting from the use of 0.5%, 1.5% and 2% salicylic acid concentration. Using non-invasive technology, the study also aimed to contribute to a better understanding of the skin cleansing impact on the healthy human skin physiology. Under the present experimental conditions only discrete biological effects could be detected. Good tolerability and biological impact expressed in terms of epidermal water content, cleansing capacity (sebum) and biomechanical behaviour, helps to confirm the general mildness of this active which may be particularly suitable for some specific cutaneous dysfunction.

Riassunto

L'acido salicilico viene utilizzato da più di cento anni per trattare l'acne di leggera e moderata intensità, data la sua alta tollerabilità riscontrata negli anni.
Con questo studio si sono voluti controllare, con una metodica non invasiva, gli effetti biologici, nel breve periodo, di una soluzione di acido salicilico allo 0,5% – 1,5 e 2% inserito in soluzioni con effetto detergente.
Con questo studio avvenuto con metodologia non invasa, si è voluto comprendere meglio l' "impatto" che il prodotto utilizzato per la setersione ha sulla fisiologia di una cute sana. Nelle condizioni sperimentali utilizzate è stato possibile valutare solamente un discreto effetto biologico.La buona tollerabilità riscontrata da questi detergenti assieme all'impatto biologico positivo rilevati sulle proprietà biomeccaniche della cute, ne confermano la sicurezza e la tranquillità d'uso per persone che abbiano specifiche disfunzioni cutanee.

INTRODUCTION

Salicylic acid has been one of the most useful actives for clinical dermatology. In fact, and mostly as a consequence of the well known keratolytic effect (1-4, 15-17) various application are found among the dermatological practice, mostly depending on the product's concentration and also on the product's galenic format. Partially soluble in water, alcohol and other organic solvents (5) the keratolytic effect is obtained for concentration over 5% making it specially suitable, when topically applied, in the treatment of hiperkeratotic and scaling skin conditions (6,7). Many uncertainties still impair full knowledge about the implied mechanisms of action where a certain amount of protein digestion, specially at the most superficial epidermis, seems to play a role (1,3). Salicylic acid is also known for its antimicrobial action affecting skin microflora (8) which justifies its usefulness alone or in association (e.g. benzoic acid) as a topical fungicidal agent (1-4, 8). More recently, some evidence of anti-UV activity was found after detecting some interference with the efficacy of phototherapy in psoriatic patients (9).
The reported good tolerability justifies some of the formulators preference regarding this active, specially when directed to some specific skin conditions such as acne (pharmaceutics and/or OTC's preparations) where it is very important to improve symptoms while preventing irritant dermatitis (10,11,14). No matter established its pharmacokinetical profile (15-17) it was also shown that the clinical efficacy of salicylic acid depends on the skin persistence which, in turn, is related with the concentration applied (18).
This introduces a new recent interest about the eventual benefit resulting from the use of low concentrations of salicylic acid. In particular for those skin conditions requiring topical therapy such as mild to moderate forms of acne (11) some of the concentration related problems seems to be avoided while promoting a good tolerability and biological efficacy (4, 11-13, 19).
In order to contribute to establish the clinical relevance of this strategy, the present study approaches the biological impact of a short-term application of low concentration of salicylic acid on healthy skin.

MATERIALS AND METHODS

Experimental data was obtained from healthy human volunteers (n=10), both sexes, age between 19 and 26 (mean : 21,6 ± 1,96) years old, after informed written consent. These were previously selected upon several inclusion / non-inclusion criteria. The confirmed absence of any previous history of dermatological disease or any form of cutaneous sensitivity was absolutely required.
The galenic form chosen to minimise the undesirable additional impact of the preparation's basis on skin's physiology was a gel, formulated upon the following ingredients :

- Sodium couceth sulphate and PEG40 Glycerol cocoate (20%)
- Cocoamide propilbetaine (5%)
- Ethanol 96% (10% v/v)
- Deionised water (e.t. 100ml)

The sole active included was the salicylic acid at different concentrations (0.5%, 1.0% and 2.0%). All preparation were previously coded and a double blind methodology chosen. Under this conditions, preparation

A corresponded to the gel basis with 0% concentration of Salicylic Acid
B corresponded to the gel basis with 0.5 % concentration of Salicylic Acid
C corresponded to the gel basis with 1.0 % concentration of Salicylic Acid
D corresponded to the gel basis with 2.0 % concentration of Salicylic Acid

The biological impact of these preparation was assessed trough non-invasive techniques which involved no significant distress (for the patient) while allowing to obtain the skin variables as

near as possible from the normal physiological condition. These involved :

- the epidermal hydration expressed in arbitrary units (AUs) through epidermal "capacitance" obtained by Corneometer CM825 (Corneometer CM 825 " from Courage + Khazaka Electronics GmbH – Germany) and, (20)
- the assessment of the trans-epidermal water loss, expressed in g. cm2/h by means of the "evaporimetry" (Tewameter TM 210 " from Courage + Khazaka Electronics GmbH - Germany), (21,22)
- the assessment of the epidermal skin lipids expressed in mg/cm2 through a reference colorimetric method (Sebumeter SM 810 " from Courage + Khazaka Electronics GmbH - Germany) (23)
- the biomechanical behaviour obtained trough a reference suction method (Cutometer SEM 474, from Courage + Khazaka Electronics GmbH - Germany), expressed in mm (24, 25)

All measurements were conducted in laboratory, involving the permanent control of room temperature and humidity, according with the usual recommendations regarding the application of this type of technologies (20 - 25). Prior to all measurements volunteers were left in the room in order to allow the skin adaptation to room's (temperature and humidity) condition.

The anatomical region chosen for the formulation's impact evaluation was the upper portion of the back (between C3 and D2) where 4 sites of approximately 2cm^2 each were marked, symmetrically, two by two, equally apart from the mean line. This sites were carefully marked in order to avoid any eventual contamination.

After previous randomisation (Latin square), the application-removal routine was standardised according with results published before (14, 26). The critical aspects considered were:

product doses : equal quantities of product were applied at each site,

product distribution : the product was applied always in the same way in order to ensure an equal distribution for all applications, at all sites

product removal : removal was also standardised involving always the same procedure elements

Basal values were determined before products application and compared with those values obtained following the "application – removal" routine. The acute (short-term) effects resulting from these formulation were registered during the first 30 minutes after removal. This option was taken following previous methodological proposals to assess the biological efficacy of this type of products which usually concentrate the (biological) impact studies on the first 15 to 30 minutes after product removal (14, 26, 27).

Statistical analysis included descriptive statistics, non-parametric analysis (Man-Whitney and Wilcoxon sign rank test) and variance analysis, whenever suitable (Kruskal-Wallis). A 95% confidence level was adopted.

RESULTS AND DISCUSSION

Cutaneous topical formulations with low concentration salicylic acid (1 to 2%) have been recently recommended for several dermatological conditions specially related with mild to moderate forms of acne (4, 10, 11) and other cutaneous dysfunction requiring topical therapy as well. No matter existing several substances such as benzoil peroxide, retinoic acid and some antibiotics which can be topically used to control some complicant aspects of these dysfunction, it is also known that undesirable side effects, from irritant dermatitis to increasing resistance are often present (4, 10, 18). Thus, and specially regarding this specific conditions, topical efficacy should be improved by promoting a beneficial impact on skin functions while assuring the general mildness of the chosen "actives".

Salicylic acid is a long known "active" in dermatology but, no matter the many different pa-

pers published about its activity, specially in clinical terms, only a few papers approached the identification of the biological effects resulting from its use (4, 7, 28) . Therefore, the present work approaches this perspective, aiming to identify the acute (short-term) effects resulting from the use of low concentration salicylic acid formulations on skin variables obtained by non-invasive methodologies, on in vivo healthy skin.

One of the most important aspects to ensure a mildness cleansing capacity when some cutaneous conditions, specially those involving inflammatory components, are concerned, is to avoid any irritancy risk and therefore, to prevent cumulative exposure of skin and "barrier" impairment. Regarding cleansing care, this should imply a mild detergency capacity involving controlled effects over the epidermal "barrier" if possible involving minor changes at the epidermal water balance, while assuring an adequate surface lipids removal, specially when hyper-seborrheia is an obvious complicant.

After applying the above mentioned standardised procedure, and considering the present rationale, several results were obtained as follows. Regarding the skin water balance changes, results are illustrated at Figure 1 and Table I.

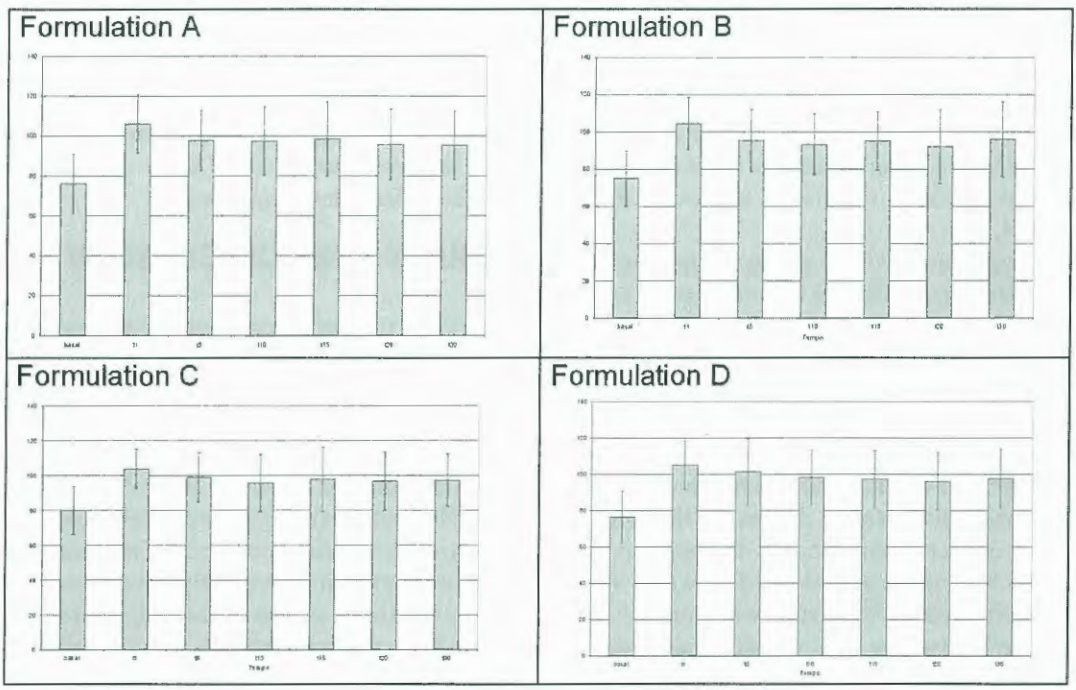

Figure 1. Epidermal "capacitance" changes recorded for each formulation according with the standardised application-removal routine. Results, as shown in Table I, are expressed in arbitraty units (AU's).

TABLE I.

Descriptive statistics for the epidermal "capacitance" results obtained under the present experimental conditions as illustrated at Figure 1.

Formulation A	Basal	T1	T5	T10	T15	T20	T30
Mean	76,13333	106,1667	97,9	97,5	98,53333	95,76667	95,4
St. deviation	14,86831	14,67109	14,89556	17,12355	18,59523	17,71102	17,04663
Mín	50	66,66667	63	55,33333	53,66667	55,33333	55,33333
Máx	98,66667	117,6667	115,6667	116,3333	117	113,6667	112,3333
Formulation B							
	Basal	T1	T5	T10	T15	T20	T30
Mean	75,13333	104,5667	95,46667	93,3	95,23333	92,13333	96,16667
St. deviation	14,82507	13,98769	16,74883	16,39666	15,79346	19,94325	20,14959
Mín	48,33333	70,66667	62,66667	64	64,66667	57	49,33333
Máx	94	118,6667	115	111,3333	117	117,3333	118,3333
Formulation C							
	Basal	T1	T5	T10	T15	T20	T30
Mean	79,9	103,9	99,03333	95,63333	97,76667	96,76667	97,23333
St. deviation	13,80289	11,19198	14,06374	16,34992	18,46254	16,79951	15,03662
Mín	50	82,33333	66,66667	58	58,33333	59,66667	67,33333
Máx	98,66667	115,3333	114,6667	117	118,3333	117	118,6667
Formulation D							
	Basal	T1	T5	T10	T15	T20	T30
Mean	76,5	105,2333	101,4667	98,26667	97,4	96	97,6
St. deviation	14,131	13,32504	18,17623	15,08887	15,64482	15,7723	16,09294
Mín	51,33333	71,33333	59	64	62	60,33333	59,66667
Máx	96,66667	117	118,6667	114,3333	114	112,3333	113,3333

All formulations, but specially those containing the higher salicylic acid concentration (C and D) were able to induce significant changes on epidermal "capacitance" during the experimental procedure (Table II) when compared with basal values. These results may only express a direct consequence of the overall formulation's impact over the skin surface since variance analysis (Kruskall-Wallis) could not demonstrate any significant differences ($p>0.05$) among formulations for the periods of time considered.

Table II.

Comparative statistics (Wilcoxon sign test) for the epidermal "capacitance" data obtained. The significant level adopted was $p< 0.05$.

	Basal-T1	Basal-T5	Basal-T10	Basal-T15	Basal-T20	Basal-T30
Formulation A						
Z	-2,803	-2,701	-2,703	-2,803	-2,666	-2,803
Asymp.Sig (2-tailed) «» p	0,005	0,007	0,007	0,005	0,008	0,005
Formulation B						
Z	-2,803	-2,497	-2,499	-2,803	-2,295	-2,803
Asymp.Sig (2-tailed) «» p	0,005	0,013	0,012	0,005	0,022	0,005
Formulation C						
Z	-2,803	-2,803	-2,803	-2,803	-2,803	-2,803
Asymp.Sig (2-tailed) «» p	0,005	0,005	0,005	0,005	0,005	0,005
Formulation D						
Z	-2,803	-2,805	-2,803	-2,803	-2,701	-2,701
Asymp.Sig (2-tailed) «» p	0,005	0,005	0,005	0,005	0,007	0,007

Regarding the transepidermal water loss assessment, results seems to express those changes which would normally be expected when a topical formulation interacts with skin components (29, 30). In fact, as shown in Figure 2 and Table III, the peak TEWL values obtained after the application-removal routine are a direct consequence of the gel's aqueous components and the normal skin constituents interaction. This evokes some degree of solubilization which is evaporating (after removal) until the end of the essay. However, although discrete, some differences can be found at the curve profiles obtained for different formulations. The highest values after removal and more pronounced decays are obtained for the A formulation, while more slower profiles are obtained for the rest of the formulations (Table III).

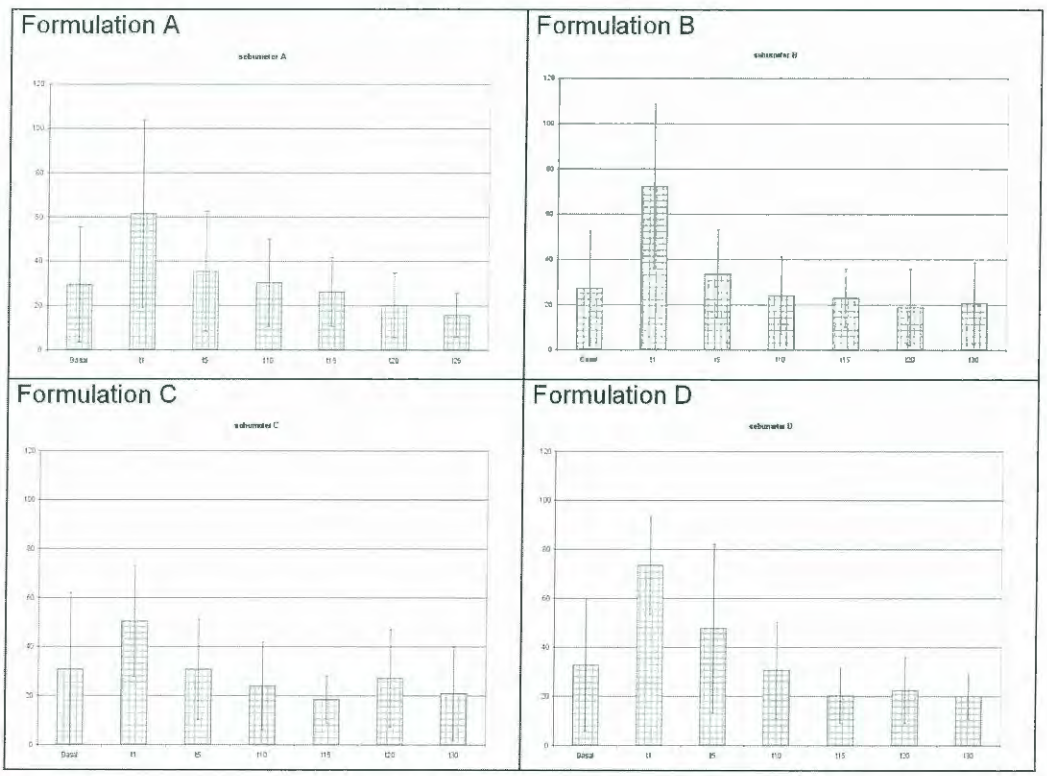

Figure 2. Transepidermal water loss (TEWL) changes recorded for each formulation according with the standardised application-removal routine. Results, as shown in Table III, are expressed in g/h.m².

Comparative testing allowed to confirm that significant changes on TEWL were found for all formulations for the T1. For the following periods, only formulation A exhibited a significant difference, regarding basal values, at T5 (Table IV). Eventually, these more discrete profiles may result from the different salicylic acid concentration which may determine a mild effect regarding the solubilization of some epidermal components. However, probably due to the reduced population involved, variance analysis (Kruskall-Wallis) could not demonstrate any significant differences ($p>0.05$) among formulations

Table III.

Descriptive statistics for the TEWL results (g/h.m²) obtained under the present experimental conditions as illustrated at Figure 2.

Formulation A							
	Basal	T1	T5	T10	T15	T20	T30
Mean	11,73	22,05	14,38	13,32	13,36	12,27	11,77
St. deviation	2,224135	13,25454	4,006328	3,220697	3,382701	2,710084	2,591032
Mín	6,8	11,7	8,5	8,7	8,6	7,6	8,3
Máx	14,3	55	19,2	19,1	20,3	16,7	16,5
Formulation B							
	Basal	T1	T5	T10	T15	T20	T30
Mean	12,34	19,67	14,37	13,75	13,2	13,19	12,33
St. deviation	1,91729	8,255106	4,453975	2,547003	3,456716	2,666854	2,667937
Mín	9	11,9	8,3	10,1	8,6	10	8,7
Máx	14,4	36,6	23	17,5	19,6	17,3	16,1
Formulation C							
	Basal	T1	T5	T10	T15	T20	T30
Mean	11,56	18,03	13,34	12,72	13	13,11	13,72
St. deviation	3,240439	8,657951	2,2594	2,783204	3,941517	3,827517	3,816863
Mín	6,5	10,4	10,9	8,3	8,3	9	8,1
Máx	16,3	39,7	18,3	17,3	21,2	22,1	19,7
Formulation D							
	Basal	T1	T5	T10	T15	T20	T30
Mean	11,85	19,28	12,82	12,56	11,76	12,44	12,9
St. deviation	1,869789	10,70989	3,724633	3,18336	3,224972	2,886828	3,401307
Mín	9,5	10,1	9	8,1	8,4	8,3	8,5
Máx	15,5	47,7	20,3	17,3	18,9	18	18,3

Table IV.

Comparative statistics (Wilcoxon sign test) for the TEWL data obtained. The significant level adopted was p< 0.05

	Basal-T1	Basal-T5	Basal-T10	Basal-T15	Basal-T20	Basal-T30
Formulation A						
Z	-2,803	-2,142	-1,580	-1,785	-0,866	-0,153
Asymp.Sig (2-tailed) «» p	0,005	0,032	0,114	0,074	0,386	0,878
Formulation B						
Z	-2,293	-1,478	-1,479	-0,663	-1,020	-0,153
Asymp.Sig (2-tailed) «» p	0,022	0,139	0,139	0,507	0,308	0,878
Formulation C						
Z	-2,701	-1,734	-1,428	-1,122	-1,008	-1,326
Asymp.Sig (2-tailed) «» p	0,007	0,083	0,153	0,262	0,314	0,185
Formulation D						
Z	-2,395	-0,255	-0,969	-0,306	-0,663	-1,376
Asymp.Sig (2-tailed) «» p	0,017	0,799	0,333	0,759	0,507	0,169

The relative cleansing capacity was tested considering the surface lipids as the main indicator of this property. As shown in Figure 3, all formulations exhibited a similar pattern .when this curve profiles are compared. No significant differences were found between time periods (except between Basal and T1 for formulation B and C) or among formulations. However, in absolute terms (Table V) the formulation A promoted a more pronounced removal of the surface lipids.

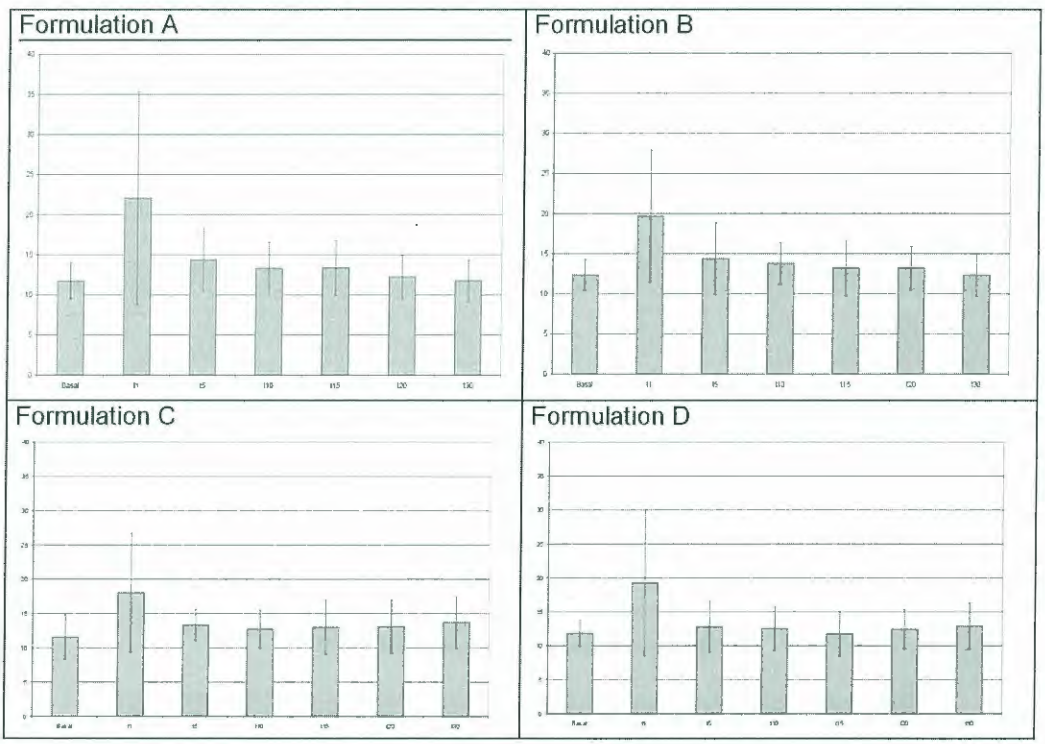

Figure 3. Epidermal lipids assessed by "sebumetry" obtained for each formulation according with the standardised application-removal routine. Results, as shown in Table V, are expressed in mg.cm2.

Considering also that the application-removal process may contribute to the epidermal penetration of some lipid fraction, as published before (12, 31-33), this results suggests that the inclusion of different concentration of salicylic acid on the formulation basis may contribute to the mild behaviour so far observed with other functional variables.

Table V.

Descriptive statistics for the "sebumetry" results (mg/cm²) obtained under the present experimental conditions as illustrated at Figure 3.

Formulation A							
	Basal	T1	T5	T10	T15	T20	T30
Mean	29,6	61,5	35,5	30,3	26,3	20,2	15,8
St. deviation	26,05635	42,46109	27,16718	19,69236	15,51379	14,65757	9,81835
Mín	3	24	10	3	5	5	3
Máx	78	169	101	56	60	51	35
Formulation B							
	Basal	T1	T5	T10	T15	T20	T30
Mean	27,3	72,3	33,6	24,1	23	18,8	20,7
St. deviation	25,3686	36,26155	19,57436	17,01927	12,96148	16,73851	17,95086
Mín	3	3	10	5	4	5	4
Máx	83	141	69	56	42	57	66
Formulation C							
	Basal	T1	T5	T10	T15	T20	T30
Mean	30,9	50,4	30,8	24	18,5	27,2	21
St. deviation	31,0893	22,66274	20,55778	17,88233	9,629238	19,90422	19,14854
Mín	4	13	11	8	7	9	5
Máx	98	74	76	69	34	72	69
Formulation D							
	Basal	T1	T5	T10	T15	T20	T30
Mean	32,7	73,6	47,8	30,7	20,3	22,5	20,1
St. deviation	26,7583	19,96219	34,37312	19,60754	11,23536	13,4433	9,314863
Mín	1	48	10	6	5	4	5
Máx	83	101	127	67	43	45	35

Finally, the biological analysis also included the study over the biomechanical changes eventually implied with the acute use of these formulations. The assessment technology , a "perpendicular applied negative pressure" - method so called "cutometry", allows to obtain a "creep" curve from which several biomechanical descriptors can be directly calculated (24, 25). For the specific purpose of the study the chosen descriptors were Total extensibility (Uf) and the Total recovery after deformation (Ua) .

Results are shown in Figure 4 and Tables VI and VII.

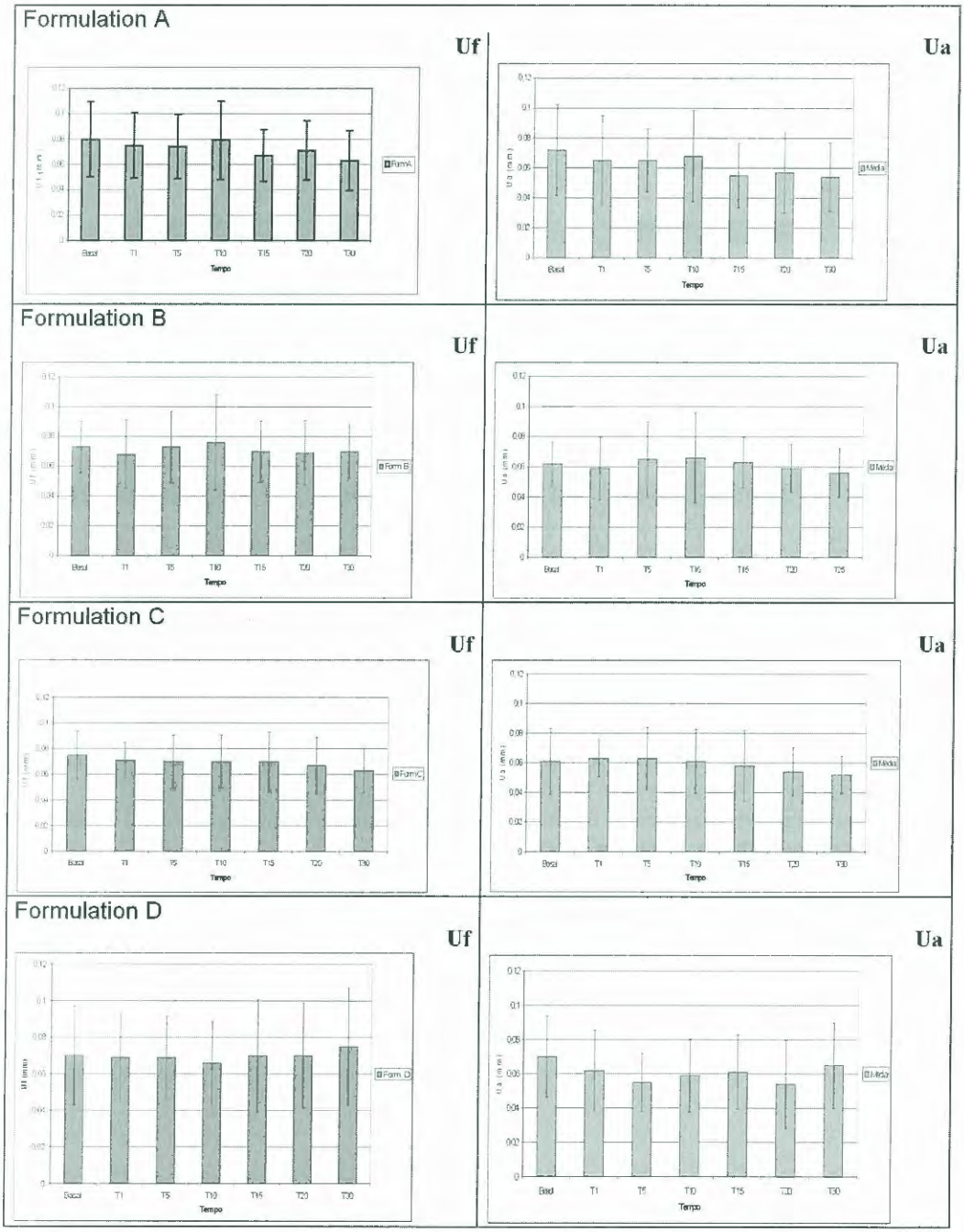

Figure 4. Biomechanical changes detected by the biomechanical descriptors Uf and Ua obtained through "cutometry" for each formulation according with the standardised application-removal routine. Results are expressed in mm

Table VI.

Descriptive statistics for the Total Extensibility (Uf) biomechanical descriptor (mm) obtained under the present experimental conditions as illustrated at Figure 4.

Formulation A							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,08	0,075	0,074	0,079	0,067	0,071	0,063
St. deviation	0,03127	0,02718	0,02675	0,03247	0,02163	0,0247	0,02497
Mín	0,04	0,03	0,03	0,04	0,03	0,03	0,02
Máx	0,14	0,13	0,13	0,13	0,09	0,11	0,11
Formulation B							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,073	0,068	0,073	0,076	0,07	0,069	0,07
St. deviation	0,01829	0,0244	0,02497	0,03373	0,0216	0,02283	0,01886
Mín	0,04	0,02	0,05	0,03	0,03	0,03	0,04
Máx	0,11	0,1	0,11	0,14	0,09	0,11	0,1
Formulation C							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,075	0,071	0,07	0,07	0,07	0,067	0,063
St. deviation	0,01958	0,01449	0,0216	0,0216	0,02404	0,02312	0,01829
Mín	0,05	0,05	0,04	0,03	0,03	0,03	0,04
Máx	0,11	0,09	0,1	0,11	0,1	0,1	0,09
Formulation D							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,073	0,069	0,069	0,066	0,070	0,070	0,075
St. deviation	0,02846	0,02558	0,02378	0,02366	0,0324	0,03028	0,03375
Mín	0,04	0,03	0,04	0,03	0,05	0,03	0,04
Máx	0,12	0,11	0,12	0,1	0,15	0,13	0,14

Table VII.

Descriptive statistics for the Total Recovery after deformation (Ua) biomechanical descriptor (mm) obtained under the present experimental conditions as illustrated at Figure 4.

Formulation A							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,07201	0,065	0,065	0,06799	0,055	0,057	0,054
St. deviation	0,03191	0,03171	0,02223	0,03224	0,02273	0,0283	0,02412
Mín	0,03	0,02001	0,02001	0,02	0,02001	0,02001	0,02
Máx	0,13006	0,13	0,09997	0,11999	0,09	0,1	0,09
Formulation B							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,06199	0,059	0,06499	0,066	0,063	0,059	0,056
St. deviation	0,01549	0,02183	0,02593	0,03134	0,01768	0,01663	0,01713
Mín	0,03	0,02	0,04	0,02001	0,03	0,03	0,03
Máx	0,08998	0,08001	0,1	0,11998	0,08001	0,08998	0,08001
Formulation C							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,061	0,063	0,063	0,061	0,058	0,054	0,052
St. deviation	0,02332	0,01338	0,02214	0,02282	0,0253	0,01713	0,01317
Mín	0,03997	0,04	0,04	0,02001	0,02001	0,03	0,04
Máx	0,11	0,08001	0,1	0,09999	0,1	0,08	0,08001
Formulation D							
	Basal	T1	T5	T10	T15	T20	T30
Mean	0,07	0,062	0,055	0,059	0,06099	0,054	0,065
St. deviation	0,02495	0,02486	0,01779	0,02234	0,02283	0,02716	0,02635
Mín	0,04	0,03	0,04	0,03	0,04002	0,03	0,03
Máx	0,11004	0,11	0,09	0,09	0,12	0,10998	0,11004

This evaluation did not allowed to demonstrate any significant differences, regarding the in vivo biomechanical variables, following the experimental procedure adopted. Other acute intervention on in vivo skin, specially regarding the hydration capacity of the most superficial layers has been demonstrated (12, 26, 27) to induced slight but yet significant modifications in the rheological characteristics of the skin. However, under this procedure, the superficial hydration detected by the epidermal "capacitance" changes seems not to be relevant enough to promote any significance modifications of the biomechanical behaviour of the skin. The variance analysis performed could not find any significant changes among the tested formulation

CONCLUSION

Under the present experimental circumstances a complete definition and characterisation of the acute (short-term) biological effects of low salicylic acid concentration was achieved.
Relevant effects in terms of epidermal hydration (or desiccation) and excessive cleansing eventually involving exposure of the most superficial layers of the skin and its biomechanical compromise are discrete. This results, although not significantly different from the reference formulations (A and B) may be directly related with the referred dependence of the salicylic acid efficacy with its skin persistence. Thus, the reduced contact with skin should explain the discrete effects found. But other (biological) expression in the presence of mild to moderate forms of acne or other cutaneous dysfunction involving sebum hyper-secretion may reasonably be expected. In any case, this preliminary results should be further investigated in order to fully establish the global impact of this active on skin's physiology and pathophysiology.

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THE EFFECT OF A NEW SKIN OINTMENT ON SKIN THICKNESS AND ELASTICITY

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Summary

The present open pilot study was carried out in order to investigate a new patented concept for skin treatment. The new concept is intended for use in treatment of ageing skin. The ointment contains conjugated linoleic acid (CLA) and retinyl palmitate (RP). Both ingredients are conjugated with the biopolymer chitosan in order to improve water solnbility, increase skin penetration and inhibit oxidation of the active substances. A number of studies have previously been carried out with conjugated retinyl palmitate, where the conjugation mostly has been done using β - cyclodextrin.
We included 20 females in our study and the treatment period was three months. Objective measurements of skin-thickness and elasticity were carried out initially and after three months. Snbjective observations and scores were performed by the participants themselves using visual analogue scales (VASs) initially and at the end of the study.
The results showed a significant improvement in skin quality both with regard to objective as well as in subjective parameters after treatment with the new ointment. In comparison to our previous studies with ointments containing only conjugated RP the effects on skin thickness and elasticity were more pronounced with the new formulation showing an average improvement in skin thickness of 51% and in skin elasticity of 27%. The self evaluation scores of the participants were also highly favourable and significant, and all of the participants would like to continue with the ointment after the formal study was closed. The tolerability of the treatment was excellent and all subjects concluded the study according to the protocol.

Riassunto

Questo studio pilota è stato condotto per verificare una nuova e brevettata metodologia di trattamento per l'invecchiamento cutaneo.
La crema contiene acido linoleico (LLA) retinil palmitato (RP) complessati tra loro. Entrambi gli ingredienti sono complessati con biopolimeri di chitosano per aumentarne la solubilità in acqua, la penetrazione transcutanea e per impedirne l'ossidazione.
Alcuni studi preliminari sono stati condotti utilizzando il retinil palmitato complessato con ß-ciclodestrina. Nello studio clinico sono state inserite 20 donne per un periodo di tre mesi durante il quale è stato valutato lo spessore e l'elasticità della pelle. Le stesse pazienti hanno espresso il loro parere personale utilizzando una scala analogica.

I risultati ottenuti hanno dimostrato un netto miglioramento della qualità della cute sia con la metodica soggettiva che con quella oggettiva.
La nuova formulazione è risultata migliore della RP utilizzata in precedenza sia per quanto riguarda lo spessore (+51%) che l'elasticità (+27%).
Il prodotto è risultato ben tollerato con soddisfazione piena di tutto il gruppo.

INTRODUCTION

We have for a number of years been interested in investigating the efficacy of different topical treatments on the skin structure, especially skin thickness and elasticity, in humans.

We have published a number of studies on water soluble retinyl palmitate showing that by conjugating this Vitamin A ester with β cyclodextrin a significant better effect on these two skin parameter is obtained than after using the unconjugated ester. In fact, the effect after using the unconjugated ester is not significantly different from using the ointment vehicle (placebo) (1-3). However, still a number of ointments containing the unconjugated Vitamin A esters are available in the market.

We have also made a double - blind comparison of Retinoic acid (RA) and the conjugated ester (RP). The strength was 0,025% for RA and 0,2% for ester. In these concentrations the two preparations were equipotent and the effect was good for both preparations. However, the tolerability was significant improved by using the RP ointment (3).

Others have confirmed our results that by using a «tween» together with the ester is essential for having a good skin penetration (4,5)

A new ointment has been developed by Jan Wadstein MD; Ph.D., who previously has been involved in the development of the conjugated RA ointments we have tested. The new ointment contains two new agents, chitosan and CLA (conjugated linoleic acid) in addition to retinyl palmitate.

CLA is a polyunsaturated fatty acid with unique properties. The effects of CLA on body composition have been studied in animals and humans. CLA is a naturally occurring substance also detected in the tissue and body fluids in humans and is a such regarded as non-toxic. We were interested in investigating the effect of CLA on the skin. However, CLA is easily oxidised and for oral use it is enclosed in amber capsules to prevent oxidation. The application of CLA to many food systems as an ingredient has a limitation due to its limited solubility in water and oxidation by O_2. To solve this problems inclusion complexes with β - cyclodextrin (CD) have been studied. Oxidation of CLA complexed with CD was greatly reduced as compared to uncomplexed CLA (6) Conjugation is a proper method for inhibiting oxidation and has been used with success in inhibiting retinyl palmitate and other sensitive substances from being oxidised. We decided therefore to try to use chitosan as a conjugation agent instead of the more conventional b cyclodextrin. From a structural point of view these two substances have similarities both being complex polysaccharides. In this way we felt that it should be possible to combine the potential effect CLA and the documented and positive effect chitosan has on the skin.

Chitosan is well documented as a cosmetic ingredient through improvement of skin compatibility and the capacity to release bioactive cosmetic ingredients (7).

The decision was taken to test the new ointment after the same method we have used in our previous studies. As this was a pilot study the decision was taken to run it open before doing a formal randomised double - blind placebo controlled study.

MATERIAL AND METHODS

The study was carried out as an open study in 20 females who applied the ointment on the right volar (protected part) of the right forearm. The left forearm was used as a control and was not treated. The total treatment period was 3 months and administration was bid (in the morning and in the evening) during the study period. The study was carried out in accordance with the revised Helsinki declaration. All subjects received information about the aim of the study before inclusion and participate voluntarily in the study and signed an informed con-

sent before being included.

THE INVESTIGATIONAL FORMULATION

The formulation used in this study was made according to a formula developed by one of the authors (JW). A patent application has been filed for this formulation. Norvegian application No. 20005718 the conjugation is made as follows: 100 g of CLA (Tonalin, 80, Natural ASA Norway) is heated to 70°C under pressure with 30 g Chitosan (Chitoclear, 400 Primex AS Norway). When conjugation has taken place (milky appearance of the solution) it is cooled down to 50°C and the other ingredients are added. Retinyl palmitate is conjugated with chitosan in the same way as for CLA. The cream base is of a standard type comprising of soybean oil and peanut oil in a suitable concentrations to achieve an acceptable cosmetic formulation. Other ingredients are Vitamin E as stabilisator and preservatives. The pH is adjusted to 6,5 using lactic acid. To our knowledge this is the first ointment containing these two active ingredients Chitosan and CLA conjugated.

MEASUREMENTS OF SKIN THICKNESS AND SKIN ELASTICITY

The measurements of skin thickness and skin elasticity were performed by ultrasound using Dermascan and Dermaflex instruments, respectively (Cortex Inc. Aarhus, Denmark). Measurements were carried out at baseline, after 1 months and after 3 months, by the same person (ET) on both occasions and measurements were performed at the mid - region of the volar part of the forearm. All measurements were in triplicate and average values used for statistical evaluation.

SELF-EVALUATION BY THE PARTICIPANTS

At the same time as the objective measurements were carried out , participants made a self-evaluation of skin quality using visual analogue scales of 10 cm with end -points of «no change» and « very pronounced change ». Subjects were asked to score the global change in skin quality by placing a mark on the line between the end-points. The distance from the end-point (0 cm) to the mark was used as the score for the subject.

STATISTICAL METHODS

A significance level of 5% was used in the tests and two-tailed tests were applied. The one-sample test was used analysing change over time within groups. Two -sample t-test were used to compare arms with regard to continuos variables.

RESULTS

20 females aged between 40 and 60 years (mean49,2 yrs) were included in the study and all participants were compliant with the protocol.

EFFICACY PARAMETERS, SKIN THICKNESS AND ELASTICITY

Tbe results from the skin thickness measurements are shown in Table 1. As can be seen from the table the ointment gave an increase in skin thickness of 51% as compared to no change for the untreated arm. This change is highly significant ($p<0.01$).

Table I

Change in skin thickness (mm) after administration of the ointment and no treatment for 3 months in 20 females.

		Initially	After 1 month	After 3 months
Ointment	Mean (SD)	0.89(0.13)	1.10(0.20)	1.35 (0.19)
No treatment	Mean (SD)	0.90 (0.10)	0.91(0.11)	0.89 (0.12)

The viscoelastic properties of the skin is shown in table 2.

Table II

Change in skin elasticity (%) after administration of the ointment for 3 months in 20 females

		Initially	After 1 month	After 3 months
Ointment	Mean (SD)	59.0 (8.0)	70.0 (7.9)	75.2 (8.5)
No treatment	Mean (SD)	61.0 (7.5)	60.0 (8.0)	61.5 (8.1)

The results show that the elasticity is improved by 27% on the ointment treated arm while no change is observed on the control arm.

EFFICACY PARAMETERS, SELF-EVALUATION BY USE OF VAS.

The self - evaluation shows impressing results. The average score was 7.9 cm for the ointment treated arm. This is highly significant ($p<0.001$) as compared to the control arm where »no change« was reported. The participants felt that they got a smoother and more elastic skin. They also expressed that they were highly satisfied with the cosmetic properties of the ointment. The rapid penetration of the ointment into the skin was highly appreciated by the participants.

TOLERABILITY

No tolerability problems were reported during the study. The tolerability was excellent. All participants would like to continue with the ointment.

DISCUSSION

The results from this study shows very good effects in improving skin thickness and elasticity. As compared to our previous studies with conjugated Vitamin A esters the results are better showing an average improvement in skin thickness of 51% and in elasticity of 27%. This should be compared with around 32% and 19 % with the conjugated creams we have tested previously using the same measuring devices. The average global score on the satisfaction of the cream is also impressive with an average final

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TO PROTECT AND REGENERATE THE SKIN AFTER LASER TREATMENTS

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Key words: *Skin Inflammation; Laser Resurfacing; Chemical Peeling; Chitosan, Sucrabolol®; Skin Hydration; Xerosis.*

Summary

As it is known laser treatments can cause a partial or total destruction of the epitelia and sometime part of the dermis. The cutaneous regeneration is not always fast, and often a not pleasant scarring can appear.

The aim of this study was to evaluate the property of a new "green" cosmetic product containing both an innovative chitosan derivative known as glyco-chitosan and a sugar derivative named Bisabolol®, to increase hydration and elasticity, to restore surface skin lipids and to decrease inflammation alleviating symptoms of dry skin during a 8 weeks treatment course.

Tbe two-months trial was a randomized double-blind-placebo-controlled study carried out on 30 dry skinned female volunteers aged 22-35 with a moderate xerosis of grade 5 according to Dahl, and witb some grade of inflammed skin after laser and/or peeling treatment.

Surface lipids, skin hydration and TEWL were detected by the 3C System (Dermotech, Italy); erythema was detected by a Chromameter® C200 before and after laser treatment. Skin elasticity and softness were evaluated by the Dermaflex A (Cortex Technology, Denmark).

The treatment with this "green" cosmetic induced a significant and progressive improvement in skin hydration (+58%, $p<0.005$), surface lipids (+65%, $p<0.005$), skin elasticity (+17%, $p<0.05$) and a contemporary decrease of TEWL (-41%, $p<0.005$) and inflammation (-62%, $p<0.005$) compared to vehicle and to non treated areas. No side effects were observed during the study period.

The antinflammatory improvement, comparable to corticosteroid compounds and that starts to be evident from the first week of treatment, shows how these cosmetic products could be considered as useful means to improve skin hydration and elasticity and to reduce side effects of laser treatments.

Riassunto

Come è noto, i trattamenti laser possono causare una parziale o totale distruzione dell'epitelio cutaneo assieme a parte del derma.

La rigenerazione del tessuto non sempre è rapida e spesso può verificarsi una cicatrizzazione non esteticamente gradevole.
Scopo di questo studio è stata la valutazione di un nuovo cosmetico eco e biocompatibile basato su un derivato del chitosano contenente coune attivo un nuovo principio attivo derivato dallo zucchero (sucrabolol®) che ha dimostrato, con studi precedenti, di possedere una intensa attività antinfiammatoria reidratante contribuendo anche a migliorare l'assetto lipidico della barriera e l'elasticità cutanea.
E' stato condotto per due mesi uno studio a doppio ceco su 30 donne volontarie di età compresa tra i 22 ed i 35 anni, che presentavano una moderata xerosi di grado 5 secondo Dahl, unitamente ad una cute infiammata a causa di trattamenti laser e/o di peeling chimici.
L'idratazione cutanea, i lipidi di superficie e la TEWL sono stati controllati con il 3C System, il grado di eritema è stato valutato mediante l'uso del Chromameter C200®, mentre l'elasticità cutanea è stata verificata con il Dermaflex®.
Il trattamento con questo nuovo cosmetico "verde" ha incrementato l'idratazione cutanea del 58% (p.<0,005), i lipidi di superficie del 65% (p.<0,005), l'elasticità del +17% (p<0.005), riducendo la TEWL del 41% (p. <0,005) e il processo infiammatorio del 62% (p. <0,005) in confronto al veicolo ed alle aree non trattate.
Quel che è interessante sottolineare è che l'azione antinfiammatoria è risultata simile al corticosteroide utilizzato come confronto.

INTRODUCTION

Laser or peeling treatments, purposed to improving or removing skin surface defects, cause a facial burn that results in the partial destruction of the epidermis and dermis, followed by replacement with rejuvenated epidermal and dermal tissues. There is no peeling or laser treatment that will produce ideal results in all individuals, and therefore no treatments that will not produce complications (1-21).
For these reasons a right post-operative skin care regimen may eliminate or mitigate complications by the use of an appropriate cosmetic treatment (22-27).

AIM

The aim of this study was to evaluate the property of a new "green" cosmetic product (28) containing both an innovative chitosan derivative known as glyco-chitosan, and a sugar compound named Bisabolol® to increase hydration, elasticity and antioxidant potential of the skin, to restore surface skin lipids, to decrease inflammation and to accelerate the cutaneous regeneration during a 8 week treatment course.

MATERIAL AND METHODS

For this study was used a glyco-chitosan gel as base, and a patented sugar derivative (Sucrabolol®) as active anti-inflammatory compound. The two-months trial was a randomized double-blind-placebo-controlled study carried out on 30 dry skinned female volunteers aged 22-35 with a moderate xerosis of grade 5 according to Dahl, and with some grade of inflammed skin after a laser and/or peeling treatment.
Surface lipids, skin hydration and TEWL were detected by the 3C System (Dermotech, Italy) (29-30); erythema was detected by a Chromameter® C200 before and after laser treatment evaluating also the intensity of skin redness by pyrexal erythema test (31). Skin elasticity and softness were evaluated by the Dermaflex A (Cortex Technology, Denmark) (32).

EXPERIMENTAL DESIGN

PRE – TEST

Before starting the experiment, the *erythema test* was done in a dermatological office in order to check if the gel would perform also an eventual anti-inflammatory activity. This experimentation was tested on the volunteers' back of 15 patients only, a week before starting the study, according to the methods reported.

SCREENING PHASE

During the screening phase, baseline values of transepidermal water loss (TEWL) (fig.1) and of skin color (parameter a*) (fig.2) were obtained by Chromameter" from a skin area (2 cm2) treated by laser or by chemical peeling. The same area was controlled after a 30 and 60 days of treatment by the carrier B and/or the active cream A.

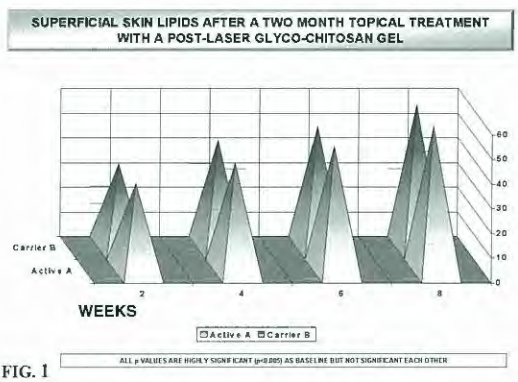

FIG. 1

TEST PROCEDURE

The study was a 8-week, randomized double-blind vehicle-controlled study. Each patient, pretreated by CO_2 laser or by chemical peeling, supplied with two identical tubes containing the testing creams (A and B) was instructed to apply them on their cleansed face twice a day for

all the study period, and was not allowed to use any other skin care product. Each subject was used as her own control the testing creams (A and B), being applied on a randomized basis, on the right or left area of the face.
Moreover they were instructed to apply the same cream always to the designed site after washing first in the morning and just before retiring in the evening. Subjects were also instructed that only the cleansing cream supplied (Alfa 4 Micospuma) at the beginning of the study should have been used to cleanse the test area.
Other instructions included not to apply the testing creams the day of evaluation and to wash their face at least 4 hours before the control. All patients were strongly encouraged to use also the sunscreen (MAVISAN Total) supplied.

BIOPHYSICAL NON-INVASIVE MEASUREMENTS

Measurements were performed, on the 1st day (baseline), after 2, 4, 6, and 8 weeks, (end of the treatment), by means of the computerized 3C System (Dermotech, Rome, Italy) (29,30). This instrument measures the snrface skin lipids having absorbed them by a special frosted plastic foil.
The determinations were always carried out on four sites of right or left areas (forehead, cheek, chin and nose) before evaluating the patients for the calculation of inflammatory lesions.
To achieve a higher degree of assurance, all evaluations were performed after a 30 minutes acclimatization period in a room at 21°C to 22°C and 45% to 50% humidity, even if the 3C System automatically adjnsts environmental conditions to 22°C and 50% relative humidity.

MEASUREMENT EQUIPMENT

Skin surface lipids

Determination is based on photometric measurement of light transmission through a skin surface imprint obtained applying to the designed skin area a frosted plastic foil. It allows adherence of skin lipids in a 1 cm^2 area.
The obtained mean readings are automatically converted into mg/cm2 and are reported on Fig. 1.

Skin Hydration

The hydration of the horny layer was assessed by measuring electrical capacitance of the skin surface.
When the probe was applied to the skin (recording time 0.5 s), the capacitance is displayed digitally in arbitrary 3C units. The results reported on Fig. 2 are expressed as mean values of the measnrements performed on fonr different right or left sites (cheek, forehead, chin and nose).

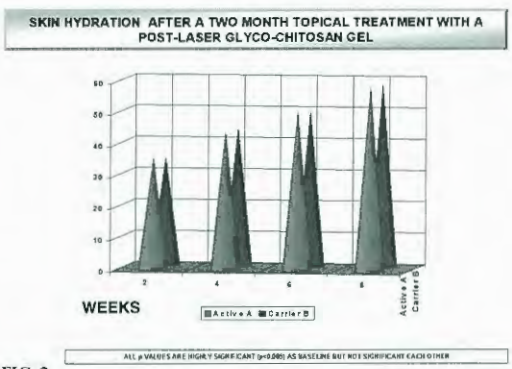

FIG. 2

Transepidermal Water Loss (TEWL)

All evaluations were performed after a 30-minute acclimatization period in a room at 22±2°C and 50% humidity.
Water evaporating from the skin surface was measured quantitatively with the 3C System® methodology.
The 3C System® probe consists of a cylindrical open chamber measuring system, (diameter 14 mm, height 10 mm) and two sensor units, containing thin capacitative film transducer, placed at 3 and 7 mm distance from the skin surface area of 0,95 cm^2. TEWL is calculated digitally

in g/m² h.
The obtained results are shown in Fig. 3.

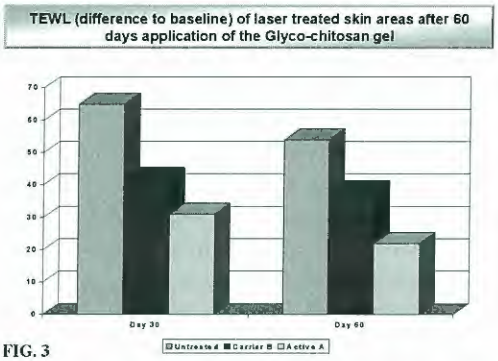

FIG. 3

All p values are highly significant (p<0,005) as control and as to groups

SKIN ELASTICITY

Skin elevation (elasticity) (32) was evaluated electronically (according to G. Gniadeck and Serup) by measuring electric capacitance between skin surface and the electrode placed on the top of the suction chamber on the left or right forearms of the treated volunteers (suction 300 mbar, suction period 20 s, number of cycles 5).
Measurements were performed on 1st day (baseline) and at 10th ,2,4, 6 and 8 weeks (end of treatment) always in the morning between 8 and 11 a.m.
The obtained results are reported on Fig. 4.

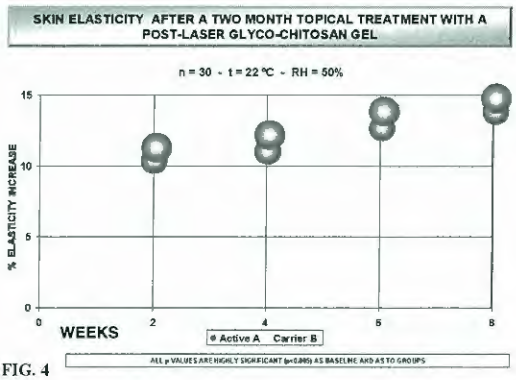

FIG. 4

ERYTHEMA TEST

This inflammation is obtained injecting intracutaneously 0.1 ml. Pyrexal (lipo-polysaccharide from salmonella abortus equii) into dorsal skin of the volunteer subjects, according to Heilmeyer and Hiemejer (31)
These bacterial pyrogens induce an inflammation. The morphologic signs take the form of a sharply defined erythema whose surface area is measured over time. Simultaneous application of an anti-inflammatory cream inhibits its spread. By this injection 8 vials were induced in each subject. These were then topically treated in randomized succession with 0.2 ml. of the 6 different preparations and covered with transparent film.
One of these areas remained untreated to serve as a control and another was treated by 0.2 ml. of betamethasone valerate 0.1% and covered also with transparent film.
In this way the erythema is visible at all times and can be measured through the film. The extent of the erythema was determined 6,8,10 and 12 hours after application, the maximum (a) and minimum (b) diameter being measured and the surface area calculated by the elliptic formula:

$$F = \frac{a \times b \times \pi}{4}$$

The efficacy was classified by determining the sum of the erythema surface areas from the 4th to the 12th hour. A small area means that the preparation is highly effective. The intensity of hydration was assessed also by Chromameter® measurements.
The comparative evaluation was performed with the aid of bifactorial analysis of variance.
The obtained results are reported on Fig. 5 and 6.

STATISTICAL ANALYSIS

Student's test was used in evaluation of all the data before and after the treatment period. All

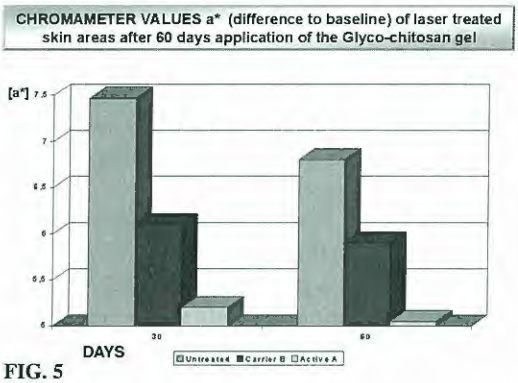

FIG. 5

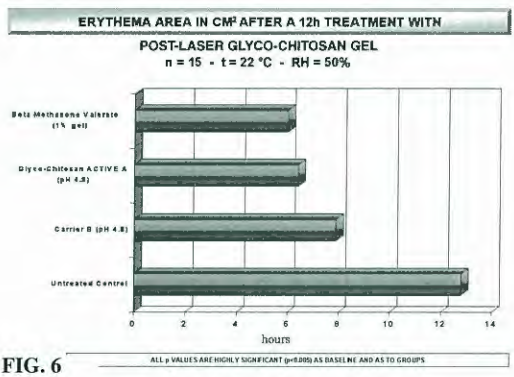

FIG. 6

the analyses were produced using the SAS statistical package, version 5.18 (SAS Institute Inc., Cary, N.C.).
Probabilities less than 0.05 were considered significant.

RESULTS

As clearly shown on figures 3,5 and 6 the gel used proved to have an interesting anti-inflammatory activity.
As a matter of fact, it can be observed a TEWL reduction of 41% ($p<0.005$) by the sole vehicle, and a TEWL reduction of 55,9% ($p<0.005$) by the active cream.
As it is known, the erythema provoked by the laser treatment, or by any other destructive treatment, causes the alteration of the skin barrier and a consequent augmentation of the TEWL (Fig.3).
Also the color value "a" shows a similar decrease of 17% ($p<0.005$) on the areas treated by the sole vehicle, and a decrease of 29,7% if the same areas are treated by the active cream.
If these data are compared with the ones obtained by Erythema Test methodology, it is clear how active is the cream. It should be underlined also that it seems to perform an activity comparable to corticosteroid compounds, even if the active compound used, Sucrabolol®, is a sugar derivative so that it is not classified as drug (Fig.6).
The glycochitosan carrier used, as previously demonstrated by our equipe (28), showed to have an anti-inflammatory activity strengthened by the sucrabolol used as active compound.
As clearly showed in Fig. 1, 2 and 4, this innovative gel is able to rehydrate remarkably (+58%, $p<0.005$) the skin treated (Fig.2), improving also the surface lipids (+65%, $p<0.005$) (Fig.1) and the skin elasticity (+17%, $p<0.005$) (Fig.4).

CONCLUSION

We deem interesting to underline that, stated the remarkable anti-inflammatory activity that is able to rebalance the dry and dehydrated skin, this new gel could be useful both to reduce the side effects of peeling and laser treatments, and to improve the skin of subjects affected by different types of xerosis and erythema.

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ALLERGIC SKIN DISEASE A MULTIDISCIPLINARY APPROACH

By D.Y.M. Leung and M.W. Greaves
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This interesting book provides to the reader an updating on the patho-physiology of allergic skin reactions, as well as their socioeconomic impact and new treatment approaches that take advantage of emerging concepts of skin pathobiology addressing epidemiology mechanisms, occupational effects, environmental triggers, and quality-of-life concerns.
It consists of 28 chapters divided in 3 sections: the General principles of all the allergic skin reactions (section 1: 6 chapters), The specific allergic skin diseases (section 2: 11 chapters) and finally the Management of allergic skin diseases (section 3: 11 chapters).
The first two chapters of section 1, are a precise and complete excursus of the Epidemiological and Socioeconomic impact of all the allergic skin diseases affecting over 20% of the general population world wide at some point during their lifetime.
As matter of fact, the economic impact is really enormous with atopic hand dermatitis representing a major cause of occupation-related disability. To have an idea, the US cost of atopic dermatitis in 16 years has been estimated to be U$ 364 million annually, one third of which was spent on pharmaceutical remedies. From the data available, it seems that in European Communities that cost is further higher.
What is astonishing, is that it was estimated that the Children Dermatology - Life Quality Index (CDLQI) score for atopic dermatitis was 7.7 and was significantly higher than for acne (5.7) and psoriasis (5.4).
Moreover the psychological effect of scratching sleep loss, and visible skin disease may also stress the families in parenting and social functioning; moderate and severe atopic dermatitis have a significantly higher impact on family life than does insulin-dependent diabetes. Finally adverse drug reaction seems to be another daily problem in medical practice and seems to be in the region of 3-5% in the adult population. Therefore it would be useful to improve our life system reducing the pollutant emissions largely produced mainly by factories and cars.
To reduce the severity of these allergic diseases and contain the cost of pharmaceuticals and hospital services, of great help would be using skin protective products as biocompatible cosmetics, educating also patient and family to avoid the use of irritants and stressed way of living.
The other 3 chapters of the General Principles section are focused on the Molecular and Cellular Mechanisms concerning the immune allergic skin responses.
Key cell types, effector molecules, and cytokines, mediators, chemiokines, cells adhesion molecules, and immunogenetic mechanisms that determine the final clinical phenotype of the different allergic skin disorders are well described and delineated.
The mechanisms regulating the development of allergic skin responses are elucidated from the stimulation of initial antigen-nonspecific innate inflammatory responses to the development and accumulation of antigen- specific T cells, targeting also all the new therapeutic strategies involved.

The entire chapter six is also dedicated to the pathophysiology of Pruritus. In fact, itching is the dominant symptom of many skin diseases, and until now there are no specifically antipruritic drugs of proven value.
The patient should be advised to avoid wollen clothing next to the skin, to eschew alcoholic drinks and temperature-hot, spicy-hot foods, drinks and strong soap, bath salts and detergents.
Concerning the emerging therapies, some newer agents including opoid peptide antagonists and capsaicin (0.025-0.075%) seem promising but have yet to achieve the status of antipruritic drug.
In section 2, an outstanding group of allergists, immunologists, and dermatologists, who are acknowledged leaders in their fields, examine the chemical features and phatophysiology of specific allergic diseases, emphasizing the role of immune mechanisms in accounting specific allergic skin diseases, such as Atopic Dermatitis, Physical Urticarias, Urticaria and Angioedema, Chronic Actinic Dermatitis, Immunology of Allergic Contact Dermatitis, Latex Allergic Reactions to stinging and biting insects, Cutaneous Reactions, Mastocytosis and finally pathophysiology and management of "sensitive skin".
This last chapter is very interesting for the cosmetologists and for the dermatologists who prescribe cosmetics in addition to drugs. In fact, especially the specialists became aware that there is a category of response to topical agents that cannot be categorized as either irritancy or allergy in the conventional sense.
This response, purely subjective, neurosensory in nature, and usually described as sting, seems to be due to a compromised barrier function, increased permeability to small molecules and probably to a genetically or environmentally determined alteration in neuropeptide signaling.
The chapters of section 3, underpins the clinical relevance of understanding mechanisms of allergic skin diseases in the context of their differential diagnoses, evaluations, environmental triggers, and concept emerging and established treatments.
Big room is given also to the differential diagnosis of the allergic skin diseases and to their evaluation and management by topical or systemic pharmaco-therapy.
The topical application of potent anti-inflammatory/immunosuppressive drugs that do not have significant systemic absorption represents to day an important approach that has allowed the use of topical steroids in the management of chronic atopic dermatitis and allergic contact dermatitis. As matter of fact the use of high-potency topical or systemic glucocorticoids for prolonged periods places the patients at great risk for severe adverse effects.
Phototherapy continues also to retain an important position in the therapeutic armamentarium for atopic and other allergic skin diseases.
For the future, it is preferably and necessary to develop new safe and effective systemic therapeutic agents and effectively intervene in immunologic cascades that lead to allergic skin diseases. To reach these goals, it will be necessary to understand the immunology of all the allergic skin diseases and use new immunological markers for monitoring disease activity.
With these hopes, ends this interesting volume which represents the today state-of-art for the management of all allergic skin diseases.
For the well detailed description of all the allergic skin diseases as well as of all the new treatments based on the emerging concepts of skin disease pathobiology, this book will provide an useful tool and a valuable resource for dermatologists, allergists, cosmetic chemists, internists, pediatricians, gynecologists, clinical immunologists and for who wants to study the immunological basis and treatment of allergic skin diseases.

P. MORGANTI
Editor-in-Chief

BIOCHEMISTRY AND MOLECULAR BIOLOGY OF VITAMIN B6 AND PQQ-DEPENDENT PROTEINS

By A. Iriarte, HM Kagan and M. Martinez-Carrion
2000. 377 pages. Hardcover
ISBN 3-7643-6145-X
Birkhäuser Verlag
P.O. Box 133 CH-4010
BASEL –SWITZERLAND
Fax. +41.612050799
http://wwwbirkäuser.ch.

This volume undoubtedly represents an interesting up-to-date of all the studies conducted to verify the activity of vitamin B6.
This up-date follows what recently issued by Birkhäuser publishers on vitamins A and D which their key role for the health of skin and its appendages.
The main topic treated in this volume is the cellular and genetic regulation of events involving proteins that require pyridoxal phosphate or quino proteins, especially concerning much cutaneous pathology.
It consists of 13 chapters. The first one is dedicated to the molecular regulation on enzymes controlling levels of vitamin B6, reporting also the genetic and genomic approaches followed in delineating the pathway of piridoxal-5-phosphate (PLP) coenzyme biosynthesis.
As matter of fact, E-coli pathway served as benchmark for, understanding PLP biosynthesis in other organism and the combination of genomics and genetics has helped to elucidate the functions and redundancy of all enzymes involved in PLP biosynthesis. Furthermore the divergence emerged in the biosynthetic pathway of vitamin B6, highlighted its new role as chemical quencher of singlet oxygen.
Therefore, vitamin B6 represents not only an important enzyme co-factor but appears to be also an essential compound into a specialized defensive role.
In fact, PLP is a co-factor required by numerous enzymes that catalyze transamination, decarboxylation and racemization reactions.
But the formation of PLP from pyridoxal and ATP is catalyzed by pyridoxal kinase and this important enzyme is of particular interest because of its intimate relationship to brain disorders such as convulsive seizures and Down syndrome.
Therefore, further progress in the physiological and functional studies depends upon more detailed information on the structure and action mechanism of this enzyme.
Some studies on this particular enzyme are reported in this chapter.
The 2nd chapter is focused on the studies conducted on regulation of gene expression of PLP-dependent proteins, such as transaminase gene expression by hormones and drugs in humans and rodents; while the 3rd chapter deals with the biological aspect and regulation of the pirroquinoline quinone (PQQ), of great interest because of its presence in foods.
In fact, oral supplementation of PQQ in the n-mol/g-diet range has been shown to improve B-and –T-cell responsiveness to mitogens, mitochondrial function and reproductive outcome in mice.

Further studies on PQQ's importance and its biologic mechanism should aid in improving our understanding of the putative health benefits of other polyphenolic substances common in foodstuffs and the diet.

Chapter four is dedicated to lysil oxidase (LOX), the extracellular enzyme controlling cross-linking and consequent maturation of collagen and elastin. LOX, that is a copper-containing amine oxidase with a high cysteine coutent, oxidizes peptidyl lysine to b-aminoadipic-b-semialdehyde of allysine.

This peptidyl aldehyde can then spontaneously condense with neighboring amino groups or other peptidyl aldehydes to form covalent cross-links in several fibrillar collagen types, desmosines and isodesmosines in elastin.

Recent studies shows that several different lysyl oxidases exist that have also other biological functions including developmental regulation, tumor suppression, senescence, cell growth control aud chemotaxis.

Chapter fifth reports different studies on the evolution PLP had during the nature species selection, and its relative biological implications.

As results of natural selection for optimized function, the vast majority of enzymes in the eukariotic cell have a single and uuvarying location irrespective of cell type or species.

A remarkable exception to this general rule is alanine-glyoxylate aminotrasferase (AGP), an intermediary-metabolic PLP-dependent enzyme that has different sub-cellular distributions in different species. Thus, AGP is mitochondrial in carnivores, peroxisomal in herbivores, and both mitochondrial and peroxisomal in omnivores.

The diverse roles played by PLP at level of the enzymes in the different species, allows to understand its biological functions, fundamental for studying new drugs necessary to cure diverse pathologies. For instance, the biotin biosynthetic pathway found, only in plants and microorganisms, making it an attractive target for herbicide and antibiotic development.

As matter of fact, in Escherichia coli the first committed step in the biosynthesis of biotin is catalyzed by the PLP-dependent enzyme gamma-amino-7-oxononanoate synthase (AONS).

Glutamate semialdehyde aminomutase, PLP dependent enzyme is also a recognized target for selective herbicides and autibacterial agents because it provides the aminolevalinate from which tetrapyrroles are synthesized in plants and bacteria but not in animals.

By the way, also D-aminoacids transaminase, containing PLP as co-factor, which convert keto acids in their correspondent D-aminoacids, important components of bacterial cells, are other attractive candidate for the development of anti-bacterial agents.

Many more are the sections in this volume devoted to the mechanisms of folding and to addressing the molecular physiology and pathology of these numerous families of proteins and their participation in enzymatic activity.

Every single chapter should deserve a note because remarkably interesting for the reader, since the latest known information on structures and mechanisms operating in all the known PLP-dependent enzymes are reported.

All the involved enzymes are in fact of great interest for both cosmetic chemists and dermatologists involved in Cosmetic Dermatology.

In fact, to formulate and to prescribe effective cosmetic products, it is necessary to know the eventual activities they should perform on skin and its appendages.

The wide knowledge on raw materials and active principles, give a first approach to evaluate by the careful reading of volumes dedicated to biochemistry and molecular biology, as this book is, in order to detect the le cross-reactions existing between the enzymes of our skin and the compounds

contained in the cosmetic product applied.
This interesting volume reporting all the current news on proteins dependent upon vitamin B6, PQQ or other quinones for function, should be in the private library experts biologists, dermatologists, gynecologists, plastic surgeons, cosmetic chemists, students of medicine and pharmacy, and all the operators involved in Cosmetic Dermatology.

P. MORGANTI
Editor-in-Chief

OXIDANTS AND ANTIOXIDANTS IN CUTANEOUS BIOLOGY

By J. Thiele and P. Elsner
X + 194 p., 36 fig., 5 tab., hard cover, 2001
CHF 216.- / DEM 280.- / USD 188.00
ISBN 3-8055-7132-1
Karger AG
Allschwilerstrasse 10
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Owing to the growing interest of the pharmaceutical and cosmetic industry in therapeutic antioxidant strategies, this book surely will be an interesting editorial success.
It is divided in 5 parts and 15 chapters all particularly detailed with an updated references section.
The first part reports a complete review of the several methods available today to detect free radicals.
The most important known technique is undoubtedly the Electron Paramagnetic Resonance Spectroscopy (EPR). By this technique it has been possible to detect, characterize and quantify many free radicals present in the biological systems.
In fact free radicals are paramagnetic species due to the unpaired electron in the outer orbit and have, therefore, a magnetic moment.
If an external magnetic field is applied to these molecules, their axes are directed either parallel to the external field or in the opposite direction. When electromagnetic waves, which match the energy difference between the parallel and antiparallel electronic moments (microwaves) are applied to this system, a change in the orientation of these molecules will occur. The net absorption of the microwave energy under these resonance conditions is quantitated and the 2nd derivative is recorded as the EPR signal.
Thus EPR spectroscopy is concerned with the resonant absorption of microwave radiation by paramagnetic samples in the presence of an applied magnetic field.
Moreover the spatial distribution of free radicals within a biological sample can also be analyzed by utilizing field gradients in a manner similar to that of NMR imaging. This methodology is EPR imaging (EPRI).
In the last years EPR spectroscopy and EPRI techniques have been considerably developed to give useful biochemical and biophysical information, even if these methodologies need to be improved and several intrinsic technical problems have to be still resolved.
However these new methodologies have significantly contribute to own better understanding of barrier function of the epidermis and free radical processes and redox biochemistry.
Moreover the better understanding of deleterious oxidation events in skin will lead to the development of new technologies such as metal chelators and antioxidant treatments to mitigate free radical events prior to inception of dermatophatological changes.
The first two chapters end with these hopes.
The antioxidant response of Stratum Corneum (SC) to environmental stress is the main topic of the

second part of the book.
SC is frequently and directly exposed to a prooxidative environment, including air pollutants, UV radiations, chemical oxidants such as 03, and microorganisms.
To counteract this oxidative injury, skin is equipped with a network of non-enzymatic, such as vitamin E and C, ubiquinone and glutathione, and enzymatic antioxidants (superoxide dismutase, catalase, glutathione reductase and peroxidase).
By compromising antioxidant defenses, and inducing oxidative damage to lipids and proteins, the prooxidative environment may effect the structural integrity of the SC.
For all these reasons the SC lipid composition and structure play key roles in determining barrier integrity, which is essential for skin moisturiziation, normal desquamation and healthy skin condition.
Vitamin E seems to be the most import lipid-soluble antioxidant of the non-enzymatic network in human tissues. Thus low levels of SC vitamin E are associated with a high degree of SC lipid disorder and vitamin E depletion may account for common side effects such as dry and scaly skin.
For all these reasons topically applied antioxidants, for instance vitamin E, or lipoic acid provide protection against UVB-induced oxidative-damage in SC lipids.
However the mechanism of action of exogenous antioxidants is not clear and, to understand this protective activity it is important to clarify their physiological distribution, and regulation. Also, the generation of ROS by the resident and transient microbial flora and their interaction with cutaneous antioxidants appears to be of relevance for the redox properties of skin.
For the progressive augmentation of pollutants present at ground level, as past of photochemical smog, first of all the ozone 03 that poses a severe urban air quality problem, the development of more lower full pharmaceutical and cosmetic strategies involving antioxidant formulation seem necessary to prevent UV-induced carcinogenesis and photoaging as well as to modulate desquamatory skin disorders.
The fourth and fifth parts of the book are focused respectively on oxidative DNA damage and on UVA/UVB induced signal transduction in skin.
The effects of solar radiation on cellular DNA can be rationalized in terms of direct interactions of UVB radiation with pyrimidine and purine nucleobases on one hand, and photosensitization reactions mediated by UVA and visible light, on the other.
The measurement of DNA photodamage in skin could be used as marker of exposure and for photoprotection studies.
The currently available HPLC-MS/MS method could also be used to monitor the release of dimeric pyrimidine photoproducts in urine as the result of DNA repair through the nucleotide excision pathway.
Moreover, singlet oxygen is an important intermediate in the effects of UVA and Photodinamic Therapy (PDT) on cutaneous processes.
Further understanding of the mechanisms involved in regulating the cellular response to such treatments will help explain the effectiveness of UVA and PDT treatments for cutaneous disorders, and likely lead to the development of improved therapeutic strategies.
It should also provide better understanding of the mechanism of UVA-induced photoaging and photo-carcinogenesis.
Antioxidants can be used therefore in chemio-prevention of skin cancer but there is also a need to initiate clinical trials to select the more useful natural antioxidants present in the common diet for skin cancer chemio-prevention.
This approach appears to have practical implications in reducing the skin cancer risk because, unlike

the carcinogenic environmental factors, individuals can modify their dietary habits, use of skin care products and lifestyle.
In fact, the oral intake and topical use of balanced carotenoids, vitamins C, E and melatonin may act as protective substances in intrinsic or UV-induced extrinsic aging and in carcinogenesis by scavenging free and lipid peroxyl radicals, by binding metal ions or by removing oxidatively damaged biomolecules.
The protective effects of topical use and systemic intake of antioxidants in humans are well described in the last five chapters.
Due also to the large and updated bibliography, this book is an incredible source of new applied ideas for who, industrially and academically, is devoted to the dermatological and cosmetological aspects, and for the medical community operating for the establishment of new chemical strategies in dermatology, pediatrics and gynecology.

P. MORGANTI
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NUTRI-COSME-CEUTICALS: A CHALLENGE FOR THE FUTURE
Rome – 6-7-8 February 2002

This international and multidisciplinary Symposium organized to celebrate the XX anniversary of the scientific activity of the International Society of Cosmetic Dermatology, intends to give a complete picture of the progress had over the last twenty years in skin physio-biological activity and in the manufacturing of innovative cosmetics and dietary supplements useful to improve people's health and appearance, and to prevent possible patho-

logies in the early age, in the middle age and in aged people.
For the first time participants could assist to scientific discussions presented by international experts in Physiology and Biology involved in the basic studies on skin and its appendages; by specialized technicians in Cosmetic Chemistry and Dietetics involved in the setting-up and production of cosmetics and dietary supplements; by Dermatologists, Gynecologists, Pediatrics and Dieticians who daily advice and prescribe to their patients these categories of products.
The Symposium will give proper room also to dietary and cosmetic aspects in Alternative and Complementary Medicine, such as Chinese Medicine and Indian Ayurvedic Medicine.
Aesthetic Medicine using medical-surgical devices, such as "filler", or methodologies, such as ionophoresis, ozone therapy or mesotherapy and natural products based on mineral waters and therapeutic muds of thermal origin, will be widely treated.
These topics will try to highlight all the problems concerning the activity performed by the different active principles and by the relevant carriers used for the setting-up of the finished product. The activity performed by hoth cosmetic and dietary products is, in fact, always in dependence of the chemical physical formulation of the active principles selected, which will be described by the formulators working for the raw materials industries, and, of course, in dependence of the carriers used in the setting-up of the finished product described by the chemists and technicians working for the cosmetics and dietetics industries.
Their real efficacy and the eventual undesirable side effects when coming into contact with the skin areas or the mucous membranes, will be investigated by a huge number of biologists, physiologists and pharmacologists involved in the absorption through the different biologic membranes.
The medical community, comparing their opinions with their colleagues chemists, biologists and physiologists, will discuss why to prescribe and how to use these products.
Because of these considerations, the Symposium will consists of five main sessions:

1. The current knowledge on skin, hair, nail and mucous membranes
2. Percutaneous and mucous absorption: the new control-release carriers
3. Functional food and cosme-ceuticals needs at different age: the-state-of-the-art
4. Botanicals, sea salt and mud in Alternative and Complementary Medicine
5. Innovative medical devices and nutri-cosme-ceuticals in Aesthetic Medicine: present and future market

We have the pleasure to invite you to participate at this happening, as attendee or as a speaker, giving your personal contribute to its success.

CALL FOR PAPERS

Authors who wish to present a paper for poster or oral presentation according to the Symposium topics are requested to forward their one-page abstract to the Symposium Secretariat.
Abstracts should be written in English, typed single space in Times New Roman font, 11-12 point, in an area of 15 x 23 cm (6 x 9 inches) on a single sheet A4 page.

Authors may either send their abstract by e-mail to iscd@libero.it, as a Word attachment or mail the abstracts on a diskette in Word format to reach the Symposium Secretariat together with a 4 copies. Material should be sent by air mail in a padded envelope that should be marked "do not fold".

Please be advised that authors registering as participants of the Symposium may submit more than one abstract.
The Scientific Committee will make final decisions on the acceptance of abstracts and allocate them to oral or poster presentation.
Presenters of abstracts will be informed by a separate letter regarding the status of their abstract whether it was accepted as an oral or poster presentation. Accepted abstracts will be printed in the book of abstracts and distri-

buted at the symposium.

DEADLINE FOR ABSTRACTS SUBMISSION: SEPTEMBER 30, 2001

Please note that all presenting authors must register

EXHIBITION

A trade exhibition will be held in conjunction with the meeting.
Manufacturers and suppliers of cosmetic and pharmaceutical raw material specialties and medical equipment are invited to present their services , products and literature.
For exhibition space, please contact the Organizing Secretariat:

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Via Crati, 1
00199 Roma
fax: +39 06 855 15 44
e-mail: *viaggi.perigeo@fnc.net*

LANGUAGES

The official language of the Symposium will be Italian and English. Lectures, discussions and printed material will be in English.
To facilitate exchange of opinions and discussions simultaneous translation in Italian will be available in the main hall only.

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Rome – 6-7-8 February 2002

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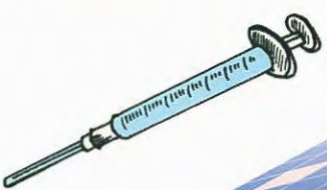

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