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ABOUT CLAIMS SUBSTANTIATION FOR TOPICAL FORMULATIONS: AN OBJECTIVE APPROACH TO SKIN CARE PRODUCT'S BIOLOGICAL EFFICACY

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Synopsis

In the recent past years a fast growing interest in skin care products has justified major investments on their global design development, involving new formulations, new molecules and new concepts regarding their use and efficacy. Among the latter, skin cleansing products are nowadays widely used as an effective and at the same time mild way to assure proper skin detergency. These effects are, sometimes difficult to demonstrate in a scientific basis; however, recent technological developments made possible to approach these claims. Present work pretends to contribute to the definition of the "biological efficacy" concept for this range of products, through the evaluation of the most relevant cutaneous variables changes following the application of several equivalent (commercially available) skin cleansing products, to human healthy volunteers. Results showed to be reproducible in the experimental conditions chosen, leading to the confirmation of the generally accepted "mildness" quality of these products. Results also suggest that transitory epidermal changes may result from the use of formulations with extreme values of pH, and that the dynamic water balance established at skin surface may require the complementary use of other products in order to avoid an eventual desiccation effect.

Riassunto

Il crescente interesse di questi ultimi anni nei confronti dei prodotti della pelle, ha giustificato i maggiori investimenti rivolti allo sviluppo di nuove formulazioni, nuove molecole e nuove metodologie di studio sull'efficacia del loro uso. Tra i prodotti cosmetici di grande uso molte attenzioni vengono rivolte ai detergenti che debbono assicurare una profonda pulizia senza, peraltro, risultare aggressivi per la pelle. Il presente lavoro cerca di dimostrare "l'efficacia biologica" di questa categoria di prodotti attraverso la rilevazione dei cambiamenti indotti sulla pelle dei volontari dopo l'uso di alcuni detergenti in commercio. I risultati ottenuti nelle condizioni sperimentali prescelte dimostrano che è giusto ed accettabile definire i prodotti prescelti come "non aggressivi" per la pelle.
I risultati ottenuti dimostrano, inoltre, le variazioni comunque indotte sia sul pH cutaneo che sulla dinamica dell'acqua, consigliano l'uso successivo di altri prodotti cosmetici necessari per evitare eventuali fenomeni di disidratazione.

Skin care products are a very important component of the R&D effort of both pharmaceutical and chemical industries, reflecting their current remarkably good acceptance not only by consumers but also by clinical dermatology among which the image of "mildness" is generally accepted, specially when confronted with other classical forms (e.g., soaps) used for skin detergency. In fact, most of the studies performed with this class of products are specially concerned with their safety profile (most often related with surfactants), failing however, to demonstrate their biological effects [3, 6-8].

The recent development of objective methodologies to assess skin most representative variables (Skin Bioengineering) allowed the establishment of new perspectives for all the areas related with such important organ. In fact, a detailed analysis on skin dynamic behaviour (physiological and/or pharmacological) objectively characterising skinís response following topical products application, is now possible, thanks to this novel technological tools. Ultimately, is now possible to rationalise and to define the "efficacy concept" for a wide range of topical products, including cosmetics [4] whose claims, from 1997 on, will have to be substantiated [9]. This implies that, concerning this particular class of products, precise rationale for methods and techniques will have to be defined in order to anticipate the relationship between the proposed instrumental measures and the relevance of the study used for claim support. Facing these entirely new perspectives, the authors tried to contribute to the biological effects definition of Skin Cleansing products, proposing an original methodology to evaluate the (acute) consequences of their application on skin surface. This procedure also intends to contribute for the development of other methodologies which will be fundamental (including for official authorities) to evaluate efficacy claims not only for cosmetics but, eventually, also applicable to a wide range of topical products.

Thirty commercially available cleansing products were selected on the basis of their label designation (Skin Cleansing product) and galenic formulation

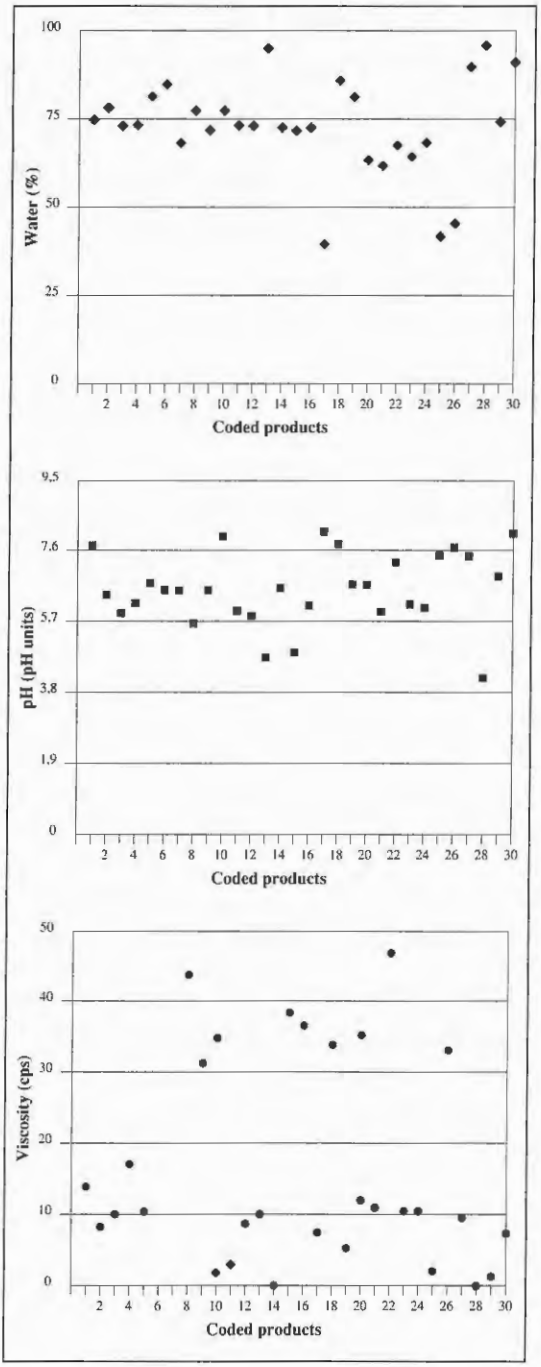

Fig. 1: Physical chemical data obtained from 30 different (coded) skin cleansing products.

(emulsions O/W). Planned as a standard study on their *Biological Efficacy Analysis*, a simple physical and chemical analysis, consisting on the determination of pH (direct potentiometry - *Metron Merisau pH-Meter E516*), Viscosity (*Brookfield LV viscosimeter*), and Water content (IV dissecator - *Moisture Analyser Sartorius MA50*) was, nevertheless, performed in order to establish the formulationís proximity.

Biological (in vivo) *Efficacy Analysis* was carried out on 14 healthy volunteers of either sexes with ages between 19 to 23 years old (mean: 21 ± 2,83), chosen after pre-defined inclusion criteria appreciation. All products were applied on all volunteers.

Evaluation of skin most important variables was performed using non invasive techniques such as: Corneometry (Corneometer CM820®) as a direct measure of skin hydration; Sebumetry (Sebumeter SM810®) to evaluate total epidermal lipid content; Trans Epidermal Water Loss -TEWL (Evaporymetry - Tewameter TM210/TM215®) an indicator of skin barrier function; and Potenciometry (Skin pH-Meter PH900®) for the assessment of skin pH changes. All devices were manufactured by *Courage+Khazaka electronics, Germany*. Room temperature and humidity were fully controlled in order to implement a complete standardisation of product application and removal routines (according with the manufacturer specification) and measurement.

Lipid Removal Capacity (forehead), *Acute Epidermal Water Dynamics* and *Cutaneous pH* changes (volar forearm) were evaluated after 15min following the application and removal of the cleansing products. These results were compared with the corresponding values for each variable obtained immediately before the protocol execution (basal line values). Significance was considered based on the exclusion of the 100% value from 95% confidence intervals around the mean.

In spite of all products exhibited the same general classification on their labels, data from elementary physical-chemical analysis showed clear qualitative and quantitative differences regarding pH, viscosity and water content (**Fig. 1**). This fact, apart from reflecting the lack of the information supplied from the manufacturer, cannot be ignored in terms of the final evaluation of each product efficacy, no matter the claim involved. Thus, fundamental question was, to test the capacity of the proposed methodology, in discriminating different levels of efficacy for each product in terms of the biological

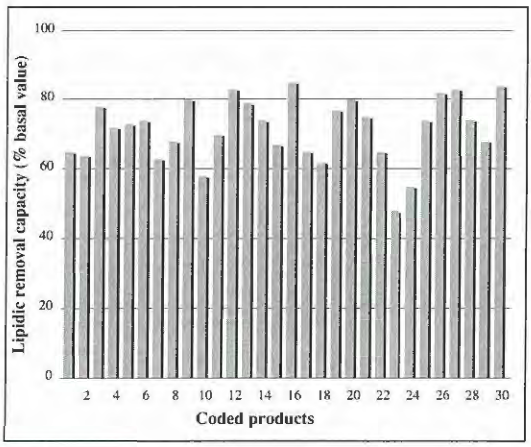

***Fig. 2a**: Graphic representation of Lipidic removal Capacity determined for each cleansing product;*
***Fig. 2b**: Graphic representation of epidermal pH changes following the use of each cleansing product.*
In both cases, values were obtained 15 min (reference time) after removal of each product (standardized routines). Results are expressed as a percentage variation of basal values.

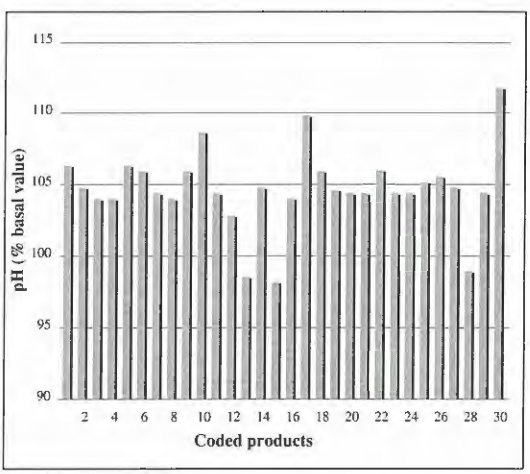

Table 1

	Trans-epidermal Water Loss (TEWL) (%)						Epidermal Hidration (%)					
	1'			15'			1'			15'		
	Mean	SD	Sign.	Mean	SD	Sign.	Mean	SD	Sign.	Mean	SD	Sign.
Cp 1	593,8	191,7	*	160,8	35,2	n.s.	124,2	6,9	*	122,9	7,6	*
Cp 2	681,3	189,6	*	140,0	15,5	*	124,2	9,8	*	108,8	4,0	*
Cp 3	748,8	188,1	*	189,7	15,1	*	125,3	17,0	n.s.	101,3	4,2	n.s.
Cp 4	525,9	99,0	*	173,0	13,9	*	132,9	14,2	*	116,7	5,8	*
Cp 5	740,5	115,2	*	140,4	20,0	*	122,3	11,0	*	103,8	4,6	n.s.
Cp 6	770,0	117,5	*	134,7	15,9	*	117,1	7,4	*	100,8	2,4	n.s.
Cp 7	639,4	163,8	*	121,2	14,9	n.s.	126,9	8,2	*	119,9	6,4	*
Cp 8	702,8	176,2	*	127,6	13,4	*	106,7	4,7	n.s.	101,4	3,1	n.s.
Cp 9	699,5	168,3	*	158,0	21,5	*	119,3	9,2	*	105,1	4,6	n.s.
Cp 10	628,7	146,9	*	150,6	14,3	*	125,5	9,4	*	101,6	1,4	n.s.
Cp 11	603,0	93,9	*	111,4	13,6	n.s.	118,8	10,3	*	113,3	8,8	n.s.
Cp 12	419,1	157,3	*	109,0	6,9	n.s.	106,4	4,5	n.s.	101,0	1,2	n.s.
Cp 13	898,5	116,1	*	254,6	107,4	n.s.	121,2	6,6	*	110,4	4,1	*
Cp 14	541,8	95,6	*	123,6	12,8	*	120,5	10,6	*	113,2	9,6	n.s.
Cp 15	557,8	144,7	*	125,0	18,2	n.s.	115,0	8,8	n.s.	101,4	2,3	n.s.
Cp 16	419,4	76,3	*	113,1	8,7	n.s.	115,1	6,2	*	109,6	8,1	n.s.
Cp 17	328,5	74,5	*	105,8	9,9	n.s.	114,1	5,6	*	110,5	8,6	n.s.
Cp 18	697,0	147,6	*	150,8	16,5	*	128,1	8,1	*	110,4	5,2	*
Cp 19	681,3	1081	*	127,6	13,4	*	112,3	9,0	n.s.	101,7	4,0	n.s.
Cp 20	565,4	142,1	*	118,4	10,1	*	109,9	5,0	*	108,6	2,6	*
Cp 21	524,3	121,9	*	116,7	8,7	*	111,3	4,5	*	105,1	6,0	n.s.
Cp 22	661,7	119,8	*	119,7	11,0	*	115,4	5,2	*	103,7	4,4	n.s.
Cp 23	408,1	52,7	*	112,3	6,7	*	112,8	3,8	*	110,0	4,8	*
Cp 24	425,7	58,2	*	115,1	6,1	*	113,0	3,3	*	111,5	5,4	*
Cp 25	498,0	114,0	*	114,1	8,2	n.s.	118,1	6,7	*	109,8	4,1	*
Cp 26	481,9	88,4	*	112,3	7,1	n.s.	115,8	5,9	*	109,8	4,1	n.s.
Cp 27	598,0	130,8	*	136,4	22,8	n.s.	121,4	6,5	*	105,7	7,3	n.s.
Cp 28	615,0	132,3	*	137,7	23,4	n.s.	124,7	7,7	*	99,4	6,0	n.s.
Cp 29	564,6	78,1	*	127,1	8,8	*	111,3	4,3	*	105,2	4,6	n.s.
Cp 30	564,6	123,7	*	132,1	15,5	*	123,8	6,5	*	101,5	7,2	n.s.

* = significantly n.s. = not significantly different from baseline (æ = 0,05)

***Table 1**: Trans-epidermal water loss (TEWL) and Corneometric (Hidration) Changes obtained after one aplication (and removal) of several cleansing products (Cp 1 to Cp 30). Results (from 14 healty volunteers) were obtained at the 1st and 15th minutes, and expressed as a percent variation from basal values (see text).*

assess chosen. In this view, particular care was put on the experimental development following a variance analysis, specially regarding the application and removal routines (on skin surface) and data collecting. As shown in **Fig. 2** , different Cleansing potencies are detected, in spite of no cleansing product, in the analysis group, has been capable of a total removal of the forehead epidermal lipid component. In our view, these results contribute to reinforce the general mildness characteristics attributed to this class of products, specially if one admits that the process itself (application and removal) may also contribute to the epidermal penetration of some lipid fraction, as it was already descri-

bed in the literature [1,2,5]. Regarding skin surface pH changes induced by the use of this products, the obtained results (**Fig. 2**) allowed to demonstrate that formulations with extreme values of pH may, in fact, alter the basal value for each individual, although this effect is clearly transitory (not significant after 15min) and seeming not to affect other variables. Finally, concerning changes detected on epidermal water balance after the use of cleansing products (**Table 1**) the results suggest the existence of a variable "desiccation effect" on epidermal surface as a primary consequence of the fast evaporation of the aqueous fraction of the disrupted emulsion [1,4]. This results also suggest that, at least where lipids represent a major component of the epidermal hydro-lipidic film, cleansing products exhibiting a strong Lipid Removal Capacity will predictably exert a stronger effect on *Stratum corneum* desiccation and exposure, underlining the need for complementary care (e.g., moisturisers) after cleansing the skin, no matter the cutaneous situation (physiological or pathological) involved.

The proposed methodology showed to be reproducible in the present experimental conditions, allowing a clear definition and characterisation of biological effects for skin cleansing products. This methodology also shows an interesting potential value in further development since it can be used to test different biological capacities for different surfactants or detergent mixtures used in this class of formulations and, eventually, lead to development of "Efficacy Indexes" which may contribute to a better understanding and full characterisation of cosmetics and other topical products efficacy.

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