

STUDIES TOWARDS OBTAINING A PHOTOPROTECTIVE DERMO-COSMETIC COMPLEX PRODUCT WITH NATURAL EXTRACTS OF INORGANIC AND ORGANIC SUBSTANCES

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ABSTRACT. Photoprotective products are considered borderline between cosmetics and pharmaceuticals due to physiological implications they have on skin health considering the environmental changes (radiations, global warming, and the diminished ozone layer) and due to the high demands regarding the balance between the efficacy and the safety of the consumer. The studies we have carried out in this paper consist in the following: selection of the excipients and active ingredients (organic and inorganic filter and/or screen substances, natural products, antioxidants) and the use of a proper technological process for obtaining a dermo-cosmetic product having a good physical and chemical stability, as well as suitable organoleptic and rheological properties in order to ensure the innocuity and pleasant administrating features.

KEYWORDS: *photoprotective dermo-cosmetic product, inorganic ad organic screen photo protective substances, complex photo protective filter*

2000 Mathematics Subject Classification: 92C99

1. INTRODUCTION

Photoprotective products are considered borderline between cosmetics and pharmaceuticals due to physiological implications they have on skin health considering the environmental changes (radiations, global warming, and the diminished ozone layer) and due to the high demands regarding the balance between the efficacy and the safety of the consumer.

If the early 1990's the main purpose was to obtain products with higher photoprotective rates (in some countries the SPF reached 100), with the passing of time there was seen an increased demand concerning the consumer safety. This is the reason for which it was considered necessary to impose a limit regarding the maximum SPF value and it was admitted a limited concentration of filter and screen substances in the formulation of dermo-cosmetic products.

The new trends in research and development of photoprotective products are pursuing the goal of decreasing, down to the elimination if it's possible, of the negative influences on the skin (high allergenic potential, risk of tissue accumulation, hyperpigmentation) throughout the accomplishment of complex formulations. These formulations have the role of obtaining a targeted action of the pharmaceutical form and to incorporate natural bioactive substances which can increase the efficiency of the synthetic photoprotective compounds.

The studies we have carried out in this paper consist in the following: selection of the excipients and active ingredients (organic and inorganic filter and/or screen substances, natural products, antioxidants) and the use of a proper technological process for obtaining a dermo-cosmetic product having a good physical and chemical stability, as well as suitable organoleptic and rheological properties in order to ensure the innocuity and pleasant administering features.

2. RESULTS AND DISCUSSIONS

We have used the following ingredients:

- one organic filtering photo protective substance: ethylhexyl p-metoxycinamate;
- two inorganic screen photo protective substances, insoluble in water and oil: titanium dioxide consisting in particles (having a mean size of 15nm

and a specific surface of $80\text{m}^2/\text{g}$) coated with alumina and silicon (titanium dioxide M170) for improving the stability of the emulsion. We have added in composition zinc oxide which is usually associated with titanium dioxide, who acts on the entire UVA and UVB spectrum (table 1, 2);

- vegetal extracts having a well determined content in active principles: Arnica montana extract, Chelidonium majus extract. Based on the content in bioactive principles and on the therapeutic effects mentioned by the traditional and modern medicine, we have selected two vegetal products having a well defined content in active principles. The extraction of bioactive principles from selected plants was made by cold maceration method to avoid altering the thermosensitive principles;
- one proteic substance: collagen used for the skin elasticity improvement and also known for having an intense skin hydration, firmness and revitalizing effect. Collagen is given much attention today by biologists, chemists, physicists, doctors and pharmacists due to his special qualities in the treatment of burns, in cosmetics, in various activities of restoration and regeneration of old leather. The collagen is found mainly in the dermis, which is subject to aggressive environmental factors (especially temperature and UV radiation) as well as to the substances used in the current activity. The collagen was proved to have a medium antioxidant activity under peroxidase conditions. Adding the vitamins to the system is increasing the protective activity with 5-30%, depending on the type of vitamin used;
- natural antioxidants: vitamin A, E and C and synthetic phenolic antioxidants (butylated hydroxy anisole-BHA);
- natural products having a slight photoprotective effect (inferior to synthetic organic substances) and a hydrating and emollient effect like Hippophae rhamnoides oil (sea buckthorn oil), cacao butter and olive oil;
- viscosity modifying agents which are providing the requested consistency, and by this increasing the stability;
- preservatives which prevent the development of microorganisms during the storage period;

- natural perfumed composition which ensures the desired organoleptic characteristics of the final product. Qualitative and quantitative composition is shown in table(3).

Description of the obtaining process: In the oily phase (wax, cholesterol, olive oil, cacao butter, Hippophae rhamnoides oil) melted on the water bath on a temperature around 60-70°C is dispersed the zinc oxide. The water phase in which we have dispersed the titanium dioxide is separately heated at a slightly higher temperature than the oily phase and then is gradually added under continuous stirring over it. The mixture is prepared in a laboratory emulsifying device equipped with a double mixing system which ensures the supply of necessary energy for a strong mixing and makes it possible to avoid the turbulent flow. Then we added the organic compound previously fine pulverized and dispersed in a small amount of oily phase and vigorously stirred for 15 minutes until homogenisation. The emulsion obtained in the first part of the technological process, has to be cooled down to 30°C to allow the incorporation of collagen, the plant extracts and vitamins. Throughout the preparation, stirring has an important role, which ensures obtaining a stable and homogeneous preparation and an uniform dispersion of insoluble photoprotective components. The physical and chemical methods used to characterize the raw materials and the final products are as following:

- to find out the amount of inorganic substances (with screening role) the samples were incinerated for two hours at 800°C;
- the quantity of organic substance (with the UV filtering role) was determined by an UV-VIS spectrophotometric method;
- vitamins identification was done according to the European Pharmacopoeia VI-th edition;
- the photoprotective ability was tested by applying a standard amount of emulsion on a synthetic skin device ($0,2g/cm^2$);
- to test the microbial stability were applied the European Pharmacopoeia VI-th edition stipulations;
- to estimate the compatibility with the human skin a standard quantity of sample ($0,2g/cm^2$) was laid under an occlusive patch. The test was

Table 1: The characteristics of the titanium dioxide used

Characteristics	Results
Apearance	White powder
Particle size	14 <i>nm</i>
Specific surface	80 m^2/g
TiO2 content	99
Superficial treatment	Alumina+silicon
SPF	25

Table 2: The characteristics of the titanium dioxide used

Characteristics	Results
Apearance	White powder
Particle size	60 <i>nm</i>
Specific surface	17 m^2/g
ZiO content	99
Superficial treatment	Stearic acid
SPF	4,6

made on a $25cm^2$ surface, on healthy volunteers. After 30 minutes the color intensity of the produced erythema was determined;

- the hydrating effect was evaluated through instrumental methods, after applying a sample on a test skin area located on the forearm;
- to determine the consistency were performed viscosity and spreadability determinations;
- for finding out the stability characteristics, a sample was exposed to stable destructive conditions in order to determine if there are significant changes in the physical and chemical characteristics.

3.RESULTS AND DISCUCTIONS

The preliminary tests have allowed us to establish the necessary quantities of substance for obtaining a homogenous product, pleasant after application

Table 3: Qualitative and quantitative composition

Component	Quantity
Ethylhexyl p-metoxycinamate	1g
Titanium dioxide(M170)	3g
Zinc oxide	1g
Arnica montana extract	1g
Chelidonium majus extract	1g
Collagen	0.5g
Vitamin A	300.000 <i>UI</i>
Vitamin E	0.3g
Vitamin C	0.5g
Hippophae rhamnoides oil	3g
Olive oil	15g
Cacao butter	5g
Wax	10g
Cholesterol	1g
Sodium hydrogen carbonate sol. 2%	10 g
Methylcellulosis	0.4g
p-Hydroxymethylbenzoate	0.05g
Vitamin C	0.5g
Buthylhydroxyanisole	0.05g
Perfumed composition	q.s
Distillated water	q.s.ad 100g

Table 4: The physical and chemical characteristics of the product obtained

Characteristics	Results
Appearance	homogenous
Colour	White or slightly yellow
Odor	Pleasant perfumated
pH	6,3
Stability at constant temperature	Stabile, with no segregation of phases
Volatile substances content	65%
Oily phase content	15%
Photoprotective organic substances content	1%
Photoprotective value	15

which can form a uniform film and assure optimal photoprotective characteristics. The physical and chemical characteristics of the final product are shown in table(4).

In order to create an uniform film on the skin surface the forms for dermal application must present the rheological behavior of a liquid. This means that during the contact with the skin the two phases of the emulsion must separate and this separation leads to the decrease of the viscosity down to values that characterize the aqueous solutions. Spreading the emulsion on the skin makes it possible to evaporate the aqueous phase and to obtain a uniform film of photo protective substances. The tixotropic structure of the emulsion ensures an optimal distribution of the photo protective film on the skin's surface. The viscosity returns to high values in a short time after the friction stops (table5 and figures1,2,3).

Microbiological characteristics The total number of aerobic germs and fungi was determined by the decimal dilution method or the multiple tube test. For identifying pathogenic species we have used specific tests (table6).

The evaluation of photodegradation was carried out through the variation of photoprotective factor of the studied product kept 60 minutes under UV radiation at 65°C. The tests revealed the preservation or even a slight increase in the SPF. The use of screen substances in the formulation of photoprotective products results in undesirable sensory characteristics: visible white film on the skin surface, unpleasant sensation, dry or oily skin after application. Therefore we considered necessary to evaluate the cosmetic characteristics after applica-

Table 5: The viscosity of the product

Stage	Alfa	Tensile strength	Dr	Viscosity
1	12	346.8	0.33	105090.91
2	13	375.7	0.6	62616.66
3	14	404.6	1	40460
4	16	462.4	1.8	25688.88
5	18	520.2	3	17340
6	20	578	5.4	10703.70
7	24	693	9	7706.66
8	29	838.3	16.2	5173.45
9	38	982.1	27	3639.25
10	42	1213	48.6	2497.53
11	50	1445	81	1783.95
12	43	1820	145.8	1248.76
11	52	1502	81	1855.30
10	42	1213	48.6	2497.53
9	34	982.1	27	3639.25
8	30	867.2	16.2	5351.85
7	24	693	9	7706.66
6	19	549.5	5.4	10168.51
5	15	433	3	14450
4	13	375.2	1.8	20872.22
3	11	317.6	1	31790
2	10	289	0,6	48166.66
1	10	289	0.33	87575.75

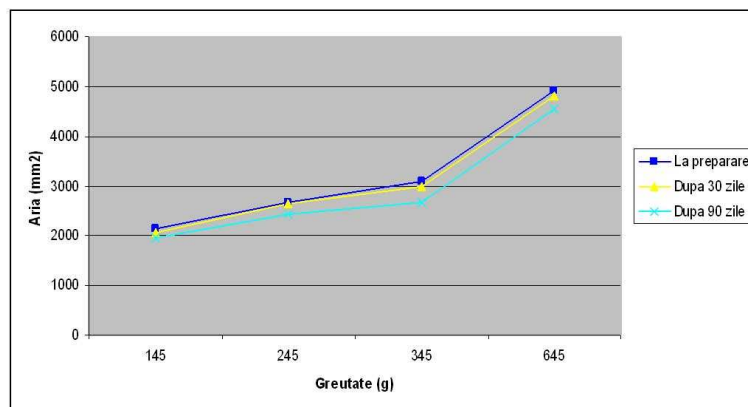


Figure 1: Spreadability (plasticity)

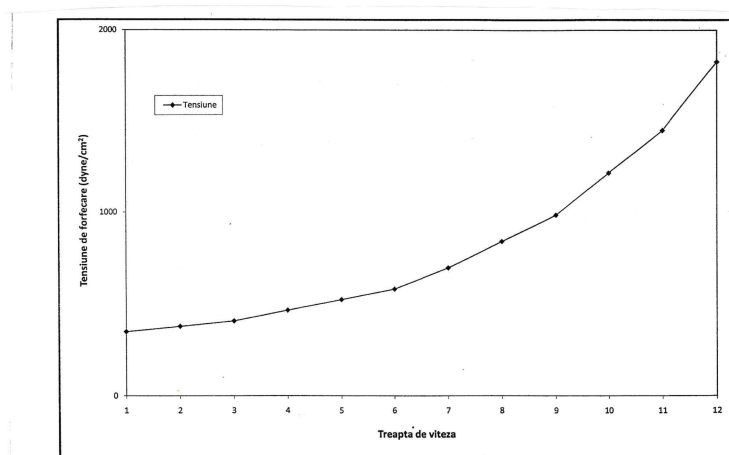


Figure 2: Variation of the shear stress depending on the speed rate

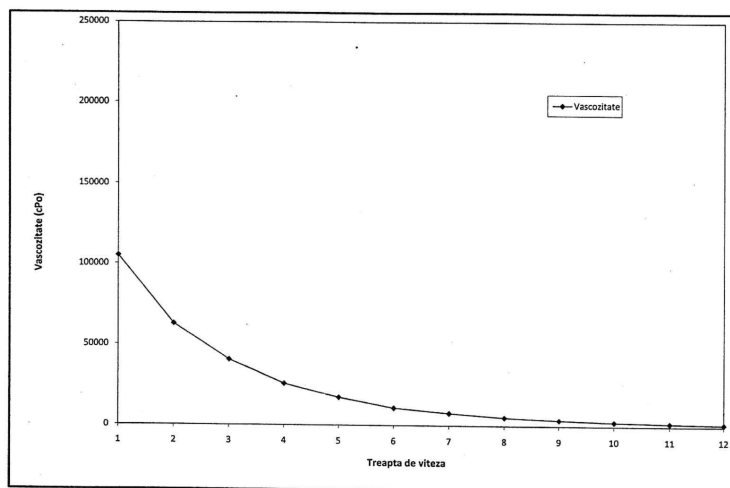


Figure 3: Viscosity variation depending on speed rate

Table 6: Microbiological characteristics of the studied product

Characteristics	Results
Total number of aerobic germs (<i>CFU/g</i>)	Max. 1000
Colour	White or slightly yellow
Odor	Pleasant perfumated
pH	6,3
Stability at constant temperature	Stabile, with no segregation of phases
Volatile substances content	65%
Oily phase content	15%
Photoprotective organic substances content	1%
Photoprotective value	15

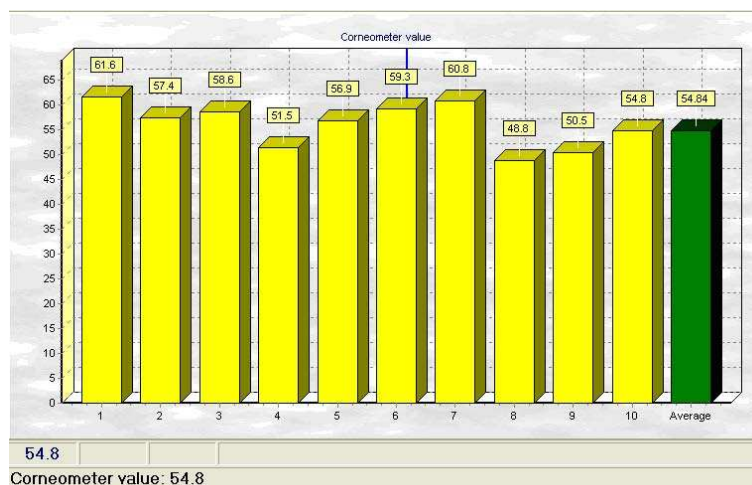


Figure 4: Determination of hydration of the skin before applying the product

tion of the obtained product. The volunteers who applied the product on the skin appreciated the sensory characteristics such as: easiness of use, pleasant texture, easy absorption without oily traces, appearance, odor and pleasant color (figures 4, 5).

The values of the erythema are relatively low, which indicates that the product is compatible with the skin and has no sensitizing potential (figure6).

Having a complex composition of ingredients with varying degrees of unsaturation, with the major organic structure, the product is subjected to destructive processes at the impact of UV radiation and atmospheric oxygen. As a result this organic substances undergo structural changes, embodied in the initial color change, division of chain, forming oxidizing action groups and oxygen free radicals that continue the destructive process. Because of these features, the product was subjected to accelerated tests of thermal and photo destruction. As a result of these tests, the product's characteristics have not changed significantly.

4.CONCLUSIONS

The aim of the study was to obtain a complex photoprotective, dermo-cosmetic pharmaceutical form. The first phase was to sort out the natural products that contain bioactive compounds and to find the best associations

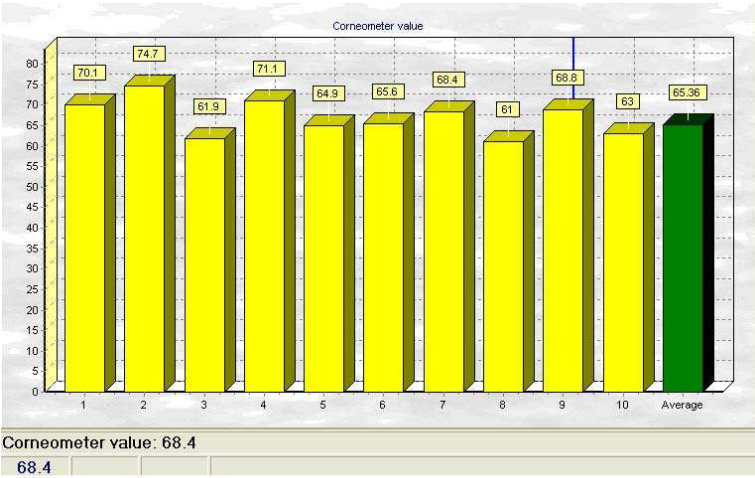


Figure 5: Determination of skin hydration after 30 minutes after application

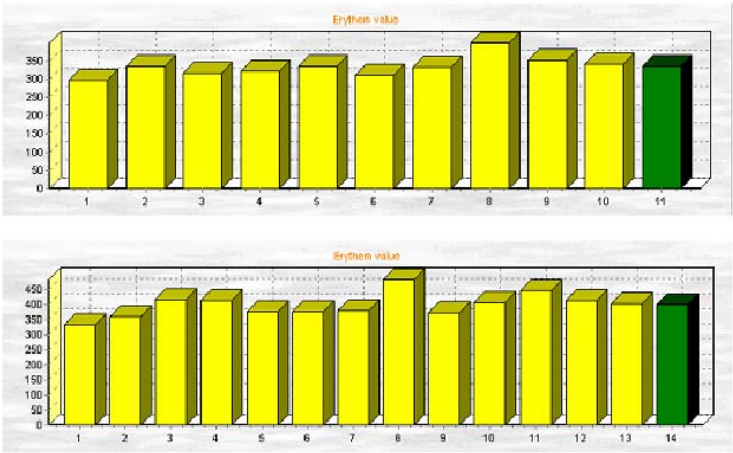


Figure 6: Erythema values before and after 10 minutes from application

with photo protective (filtering and screen) substances. After the formulation stage, we studied the physical, chemical and biological features of the final product, and then its cosmetic efficiency.

References

- [1] Merica, E. - Tehnologia produselor cosmetice, vol I, Substanțe active și aditivi, Ed. Corson, 2000
- [2] Carreras, E., "FH sunscreens - protection against erythema and immunosuppression", Scientific dossier, Barcelona, 2002
- [3] Iftimie N., Giurginca M., Meghea A, Revista de Chimie, 55, 1, 18 - 21, 2004
- [4] Arteel, G. E. A., Sies, H., Environmental Toxicology and Pharmacology, 10, 153 - 158, 2001
- [5] Halliwell B, Nutrition Reviews, 8, 253 - 265, 1994;
- [6] Inchuk, I., Lichtenberg, D., Progress in Lipid Research, 41, 279 - 314, 2002;
- [7] Iftimie, N., Herdan, J. M., Giurginca, M., Meghea, A., Revista de Chimie, 55, 512 - 514, (2004);
- [8] Iordăchescu D., Dumitru, I. F., - Biochimie practică, Ed. A 2 -a, Ed. Universității București, 1988 ;
- [9] Birghilă S., Popescu V., Dobrinaș S., Matei N., Rev. Chim., 54, 3, p. 289, 2003;
- [10] Bungău S., Bâldea I., Copolovici L., Rev. Chim., 54, 3, p. 213, 2003;
- [11] Young, A. R., Walter, S. L., Photodermatol Photoimmunol Photomed, 15, 221 - 225, 1999;
- [12] Boldeman, C., Breitner, H., Jansson, B., Nilsson, B, Ullen, H., Br J. Dermatol 135, 712 - 716, 1996;

- [13] Autier P., Dore F. F., Cattruzz M. S., Et All, , J. Natl. Cancer Inst, 90, 1873 - 1880, 1998;
- [14] Azurdia, R. M., Pagliaro, J. A., Diffey , B. L., Rhodes, L. E., Br. J. Dermatol, 140, 255 - 258, 1999.
- [15] Li GY, Fukunaga S, Takenouchi K, Nakamura F. Comparative study of the physiological properties of collagen, gelatin and collagen hydrolysate as cosmetic materials. Research Group of Animal Product Science, Graduate School of Agriculture, Hokkaido University, Japan. Int J Cosmet Sci. 2005, Apr;27(2):101-6.
- [16] Țăranu, T., Zbranca, A. - "Dermatologie generală și estetică", Ed.Gr.T.Popa, Iași 7-10, 2003
- [17] Elias, J.J. - "Handbook of Cosmetics Science and Tehnology", Marcel Dekker Inc., New York, 19-27, 2001
- [18] Eckert, R.L., Crish, J.F., Banks, E.B., Welter, J.F., J Invest. Dermatol., 109, 501-509, 1997
- [19] Krutman, J., J Dermat.Sci., 23 suppl. 1, S22-S26, 2000
- [20] Riley, P.A. International Journal of Radiation Biology, 65, 27- 33, 1994
- [21] Ciulei, I., Grigorescu, E., Stănescu, U. - "Plante medicinale. Fitochimie și fitoterapie", vol.II, Ed.Medicală, București, 1993
- [22] Knowlton, J. Pearce, S. - "Handbook of Cosmetics Science and Tehnology", Section 2 - "Legislation", 1st Edition, Ed. Elsevier Advanced Technology, Oxford, 52 - 63, 1993
- [23] *** Romanian Pharmacopoeia, Xth Edition, Bucharest, Ed. Medicală, 1993.
- [24] *** European Pharmacopoeia VIth Edition, 2006.

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