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Innovative moisturizing and anti-aging cosmeceutical formulations: development and efficacy and safety assessment

Abstract of the PhD Thesis

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Context

Customization of anti-aging products involves adapting them to consumers' specific requirements and preferences, taking into account factors such as skin type, health concerns and sensory preferences.

The aim of this study is to develop novel cosmeceutical formulations—products designed to serve cosmetic purposes while also demonstrating therapeutic efficacy comparable to medicinal treatments and the *in vitro*, *ex vivo* and *in vivo* tests are a confirmation for the formulator and the consumer both for the efficiency of the preparation.

Main objectives

The first objective of the thesis was to create stable and effective cream bases for the development of some cosmeceutical products. In order to ensure a good spread on the skin and a necessary permeation of the incorporated active principles, it was decided to create emulsion bases, all of which are based on ingredients of organic origin (over 90%) and have their own moisturizing effect. 28 cream bases were developed, each formulated using three distinct methods. The rational selection of the optimal components was supported by comprehensive studies on the characteristics of the products, including the analysis of the macroscopic, physico-chemical, rheological properties, the texture of the products and, last but not least, the evaluation of their stability.

In order to achieve the second objective, focused on the development of anti-aging cosmeceutical products containing N-acetylcysteine and melatonin, four studies were carried out, the antioxidant capacity of the active substances used, the *in vitro* permeation capacity of melatonin through a synthetic membrane from the cosmeceutical products developed, sensory profile of proposed formulas and screening study on human subjects to verify efficiency. The sensory evaluation was performed by 12 selected testers trained according to ISO 8586-1 guidelines. The perception, efficiency and tolerability of cosmeceutical products were demonstrated in a screening study on human subjects conducted in an authorized testing center.

Study 1 Development of emulsifying cream bases

In the first study, 28 formulations were proposed, grouped into seven categories according to the emulsifying system and emulsifiers used, made by means of different preparation technologies, and an effective preservative was selected in the pre-formulation stage. The study of the stability of the cream bases under the shear forces involved in the preparation stage and the evaluation of the organoleptic and physico-chemical characteristics of the resulted products led to the selection of suitable cream bases for further use. Following the evaluation of the organoleptic characteristics of the formulations proposed in the study and the efficacy of antimicrobial preservatives, only 22 formulations were considered optimal.

Study 2 Stability of cream bases under the action of shear forces as a function of preparation method and organoleptic and physico-chemical characteristics for the selected cream bases

Stability analysis is essential to assess the product's ability to preserve the effectiveness of the active ingredients and ensure the user experience, thus preventing possible unwanted changes to the formula. Following the stability test using the dynamic method, it was found that only certain formulations could be kept in the study. The identified formulations are: F1 containing

methyl glucose sesquistearate as emulsifier; F8, using cetearyl glucoside as emulsifier; F14 based on cetareth-20, and the whole group VII (F25-F28) with polyglyceryl-3 methylglucose distearate meet the criteria and can be included in the following studies. In terms of appearance, the preparation by the automated method gives the proposed products a more elegant appearance, which can be considered an advantage over the bases prepared by means of the conventional method.

Study 3 Rheological properties of cream bases correlated with preparation technology

The objective of this study was to assess the rheological properties of various cream bases to determine their flow characteristics. This evaluation aimed to identify formulations that are optimally suited for different skin types or specific application needs, including ease of application and enhanced product longevity on the skin. As a result of the results obtained, the cream bases based on methyl glucose sesquistearate, cetearyl glucoside, cetareth-20 are considered optimal for the production of final cosmeceutical products, and from group VII, formulas that were made with the emulsifier polyglyceryl-3 methylglucose distearate, the only recommended cream base is formula F27 prepared by means of the automated method.

Study 4: Determination of textural characteristics of cream bases

The textural properties of both the traditional and automated prepared formulations were examined using a TA.XT Plus texture analyzer (Stable Micro System, Godalming, UK) by inverse extrusion measurements. All the analyzed texture parameters revealed significant differences between the classical and automated preparation methods, demonstrating considerable changes in the consistency, firmness and adhesiveness of the cream bases depending on the preparation method used. Depending on the emulsifier used and the preparation method applied, these emulsifying cream bases show variable textural parameters, as well as significant differences in the appearance and color of the final product. As a result of the textural characteristics of the cream bases, the formulations F1, F14 and F27, prepared by the automatic method, were selected for the creation of the final cosmeceutical products by incorporating some active ingredients.

Study 5: Determination of the antioxidant capacity of melatonin and N-acetylcysteine

The antioxidant capacity was tested by determining the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical inhibitory capacity using the reference standard, ascorbic acid, the most well-known antioxidant, and by a method using Trolox, a vitamin E analogue, as a control. A comparison of the results obtained for N-acetylcysteine and melatonin shows that N-acetylcysteine exhibits superior antioxidant activity to melatonin. The combination of these two substances may provide an increased antioxidant potential.

Study 6: Preparation of moisturizing and anti-aging cosmeceuticals and *in vitro* permeation study of melatonin through a synthetic membrane

In the three proposed cream bases (F1, F14 and F27) active ingredients were incorporated and the *in vitro* permeation study of melatonin from cosmeceutical products through synthetic membrane was carried out. The study combines two interlinked studies, namely the verification of the analytical performance of a high-performance liquid chromatographic assay (HPLC) method for melatonin and the application of this method in an *in vitro* context, in order to reveal the permeation and diffusion profiles of melatonin in the developed cosmeceuticals. In view of its antioxidant capacities and the results of the melatonin

permeation study, the F1NACM formula is considered a suitable choice for a cosmeceutical product intended for night-time use, while F27NACM is recommended for its anti-wrinkle action during the day.

Study 7: Determination of the sensory profile of cosmeceuticals

The assessment of the sensory profile by experts in the field took place in the authorized cosmetic testing center of the Le Havre University Normandy in France and involved 12 Caucasian female testers aged 21-26 years, selected and trained according to ISO 8586-1 guidelines. This sensory analysis allowed the construction of a radar-type sensory profile to easily observe the differences between the three formulations. The results on the characteristics of the cosmeceutical products coded F1NACM (lipophilic cream) and F27NACM (hydrophilic cream) are the most promising.

Study 8: Testing efficacy of proposed formulas by means of comparative screening

The efficiency of cosmeceutical products was investigated in terms of anti-wrinkle and moisturizing properties by means of a screening study conducted on human subjects in an authorized test center. Both formulas tested demonstrated excellent results in terms of efficiency. Studies have shown that these products can reduce the depth of wrinkles by between 5,7% and 21,3%, reduce the total number of wrinkles by between 71,4% and 74,6%, reduce the surface area of wrinkles by between 50,5% and 74,1% and reduce the length of wrinkles by between 14,4% and 33,3%, all after just 28 days of use. The moisturizing effect was also highlighted.

Conclusions

The research demonstrated the efficiency of two cosmeceutical formulations: a hydrophilic cream, using polyglyceryl-3 methylglucose distearate as an emulsifier, for daily care of wrinkled skin, and a lipophilic cream, formulated with methyl glucose sesquistearate, recommended for night application or as a specific treatment for dry and mature skin. The validity of the theoretical predictions associated with the experimental products was confirmed by assessing the optimal formulations, and the experimental results were consistent with previously established theoretical predictions.

Originality of the PhD thesis

For customized treatments adapted to the needs of consumers, new cosmeceutical products were developed that were made by choosing cream bases with a superior appearance and stability and incorporating in them active principles necessary for the specifics of the skin. It is desired to exploit the cosmetic potential of some substances known for their medicinal effect, as there are currently no anti-wrinkle cosmeceutical preparations containing such active ingredients on the Romanian market. The innovation in this segment involves the selection of active substances with proven effectiveness in the pharmaceutical industry, in order to achieve a superior anti-wrinkle efficiency compared to classic cosmetic products. The latest studies mention that melatonin or N-acetylcysteine can be very effective as innovative antioxidant ingredients and if administered topically, not just internally. Thus, our study used melatonin, N-acetylcysteine, fat-soluble vitamins and arginine in cream bases specific to the skin type, creating new anti-wrinkle and moisturizing cosmeceutical products, with great consumer acceptability and good tolerance. Evaluation of efficiency and tolerability by screening a panel of human subjects selected for the customized use of the cosmetic product adds another dimension of originality to the whole study.