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Short communication

Development and pharmaceutical evaluation of a dermatological cream containing silymarin for topical treatment of melasma

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Introduction

Melasma is a chronic acquired hyperpigmentation disorder characterized by symmetrical brown macules localized predominantly on photoexposed areas of the skin (Rigopoulos et al., 2007). Oxidative stress and ultraviolet-induced reactive oxygen species are considered important contributors to melanogenesis and disease progression (Sarkar et al., 2020). Although conventional depigmenting agents remain effective, their prolonged use is often associated with irritation and safety concerns. Consequently, increasing attention has been directed toward antioxidant-based topical formulations with improved tolerability and supportive anti-melanogenic activity.

Silymarin, a polyphenolic flavonoid complex isolated from *Silybum marianum*, demonstrates significant antioxidant, anti-inflammatory and anti-melanogenic properties (Nofal et al., 2019).

However, its incorporation into topical dermatological formulations is pharmaceutically challenging due to poor aqueous solubility and formulation stability issues.

The aim of this study was to develop and pharmaceutically evaluate a silymarin-containing dermatological cream prepared under pharmacy compounding conditions for potential topical application in melasma management.

Materials and methods

The formulation was prepared using silymarin dry extract standardized to 80% active content, Cleoderm® multifunctional dermatological vehicle (containing *Cleome gynandra* extract, bisabolol, hyaluronic acid, peptides and tocopheryl acetate according to the manufacturer's technical documentation; Fagron Hellas, n.d.) and ethoxydiglycol as co-solvent. The final concentration of active silymarin was 4%. Raw materials were accurately weighed, and the silymarin extract was finely powdered before being dissolved in ethoxydiglycol under continuous stirring.

The obtained solution was gradually incorporated into one-third of the Cleoderm® base, followed by homogenization for 5 min at 500 rpm using a FagronLab Basic homogenizer. The remaining cream base was then added and homogenized for an additional 5 min. Three batches (50 g each) were prepared under pharmacy compounding conditions. Pharmaceutical evaluation included organoleptic assessment, pH measurement, spreadability testing, qualitative identification of silymarin by thin-layer

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chromatography (TLC), and microbiological analysis performed in an accredited laboratory.

Results and discussion

The developed formulation demonstrated acceptable pharmaceutical-technological characteristics during the observation period. Organoleptic evaluation confirmed a uniform appearance, smooth consistency and the absence of visible phase separation or aggregation. The use of ethoxydiglycol enabled successful incorporation and uniform distribution of silymarin within the Cleoderm® vehicle, which provided appropriate consistency and compatibility with the active ingredient. Since Cleoderm® is a multifunctional proprietary vehicle containing several functional skin-conditioning ingredients, the observed pharmaceutical-technological properties cannot be attributed exclusively to silymarin. The measured pH remained within physiologically acceptable limits for topical preparations, while spreadability testing confirmed satisfactory application properties. TLC analysis verified the presence of silymarin in the final formulation, and microbiological testing confirmed compliance with prescribed quality requirements for non-sterile topical preparations.

The selected formulation approach enabled successful incorporation of silymarin into a semisolid dermatological vehicle. No visible instability was observed during the evaluation period, suggesting adequate compatibility between the active ingredient and the vehicle. However, these findings represent preliminary pharmaceutical development results, and further studies, including long-term stability, skin permeation and clinical investigations, are required before therapeutic suitability can be established.

Conclusion

A silymarin-containing dermatological cream was successfully developed under pharmacy compounding conditions using ethoxydiglycol as co-solvent and Cleoderm® as the semisolid vehicle. The formulation demonstrated acceptable physicochemical, microbiological and pharmaceutical-technological characteristics during the observation period, indicating the feasibility of incorporating silymarin into a compounded dermatological formulation.

These findings represent preliminary pharmaceutical development results. Further studies, including long-term stability studies, skin permeation studies, safety assessment and clinical efficacy evaluation, are required before the formulation can be considered suitable for clinical evaluation or therapeutic application in melasma. The present study demonstrates the feasibility of preparing compounded silymarin-containing dermatological formulations using readily available pharmaceutical excipients and standard pharmacy compounding equipment. These preliminary findings provide a basis for future pharmaceutical development and subsequent preclinical and clinical investigations.

References

Fagron Hellas, n.d. Cleoderm™ Skin Rebalancing Cream. Product information. Fagron Hellas, Trikala. https://gr.fagron.com/en-gr/product-innovations/cleodermtm

Nofal, A. et al., 2019. Topical silymarin versus hydroquinone in the treatment of melasma: a comparative study. J. Cosmet. Dermatol. 18, 263–270. https://doi.org/10.1111/jocd.12769

Rigopoulos, D. et al., 2007. Hyperpigmentation and melasma. J. Cosmet. Dermatol. 6, 195–202. https://doi.org/10.1111/j.1473-2165.2007.00321.x

Sarkar, R. et al., 2020. Melatonin and oxidative stress in melasma: an unexplored territory; a prospective study. Int. J. Dermatol. 59, 572–575. https://doi.org/10.1111/ijd.14827