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Short communication

Q3 similarity assessment: a key element in the demonstration of equivalence of semisolid cutaneous products

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Introduction

Demonstration of equivalence between a generic and a reference semisolid cutaneous product is a challenging process due to the complexity of topical formulations. Their performance is governed by the microstructural organization of the formulation, the physicochemical properties of excipients, and their interaction with the skin, which together affect drug release, permeation, and local availability at the site of action.

The regulatory guidelines become open to accept substitute approaches for demonstration of therapeutic equivalence of topical products, in place of clinical endpoint studies. As described in the Guideline on quality and equivalence of locally applied, locally acting cutaneous products (EMA, 2024), pharmaceutical equivalence as part of the stepwise approach for demonstration of therapeutic equivalence, requires demonstration of same pharmaceutical form and method of administration, same qualitative (Q1) composition, similar quantitative (Q2) composition, and same or sufficiently similar physicochemical and structural characteristics (arrangement of the matter, Q3) between the test and the reference product.

The aim of this study is to demonstrate Q3 similarity between test and reference semisolid cutaneous products (1% w/w antifungal cream) through detailed physicochemical, rheological and microstructural evaluation.

Materials and methods

Materials

Three representative batches of the test and reference product, including production-scale batches of the test product and commercially sourced samples of the reference product, were analyzed and compared.

As required by the Guideline on quality and equivalence of locally applied, locally acting cutaneous products (EMA, 2024), statistical comparison of quantitative physicochemical attributes was performed to demonstrate Q3 similarity, using 90% confidence interval for the ratio of means of the test and reference product. For each evaluated parameter (except water activity and drying rate), 12 units per batch were used for demonstration of equivalence.

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pH and relative density

pH value was determined potentiometrically using a pH meter in accordance with Ph. Eur. method 2.2.3, while relative density was measured using an oscillating transducer densitometer according to Ph. Eur. method 2.2.5.

Viscosity and flow behavior

Viscosity and flow behavior were determined using Brookfield rotating viscometer, equipped with appropriately selected RV spindle, under specific test conditions.

Texture characteristics

Texture analyses (hardness and adhesive force) were performed using Spread test fixture (TA-STF) on CT3 Texture Analyser, equipped with a 1 kg load cell, in Compression mode (normal test with a single compression cycle).

Water activity and drying rate

Water activity analysis was performed on instrument LabMaster-aw Novasina, while drying rate was determined by monitoring the mass loss profile of the cream, using thermogravimetric analysis (TGA) under isothermal conditions at 32 °C for 240 min.

Results and discussion

Comparative analysis showed high similarity between the test and the reference product. pH and relative density values were similar. Viscosity measurements showed close alignment between the products, and both exhibited similar non-Newtonian flow behavior characterized by a decrease in viscosity with increasing shear rate. Texture analysis demonstrated comparable hardness and adhesive force, reflecting similar mechanical properties and providing indirect evidence of comparable spreadability between the test and reference product. Water activity and drying rate were comparable between the products, providing indirect evidence of similarity in active substance release and permeation and similarity in microstructural characteristics, respectively.

The calculated 90% confidence interval for the evaluated parameters was within the acceptance criteria of 90.00–111.11%, indicating no statistically significant differences between the test and reference product.

Conclusion

The performed comparative evaluation demonstrated similar physicochemical and microstructural properties between the test and the reference product (1% w/w antifungal cream). The observed results, supported by a statistical evaluation using 90% confidence interval, confirms Q3 (arrangement of the matter) similarity between the test and reference product. The observed Q3 similarity supports the demonstration of pharmaceutical equivalence as part of the stepwise approach for demonstration of therapeutic equivalence. However, it represents only one of the required criteria and must be considered together with other requirements (Q1 and Q2 similarity) to establish pharmaceutical equivalence. Furthermore, in accordance with the stepwise approach, considering the complexity of the formulation, additional evaluations are required to fully support the demonstration of therapeutic equivalence.

References

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