Multiscale engineering of Green Oregano Essential Oil delivery: from interfacial control to deep skin imaging and clinical efficacy

Olga Biganska [1], Franck Clement [1], Catherine Marion [1], Catherine Bredoux [1], Jérémie Rackelboom [1], Carine Tornier [2], Gustavo S. Luengo [3]

[1] L'OREAL Research and Innovation, 94550, Chevilly-Larue, France
[2] L'OREAL Research and Innovation, EPISKIN SA, 69007 Lyon, France
[3] L'OREAL Research and Innovation, 93600, Aulnay-sous-Bois, France

olga.biganska@loreal.com

Green Oregano Essential Oil (GO-EO) is a potent natural anti-inflammatory complex, primarily driven by its main bioactive constituent, carvacrol [1], [2], [3], [4]. While its ability to inhibit PGE2 is well-established, its high volatility and complex delivery through the skin barrier remain significant hurdles. This work presents a holistic approach, combining advanced colloidal formulation, high-resolution mass spectrometry imaging, and clinical validation.

A major challenge identified was the high volatility of GO-EO, with up to 50% of the active lost during the application phase. To overcome this, we optimized a molecular encapsulation strategy using beta-cyclodextrins (beta-CD). By engineering a GO-EO/beta-CD inclusion complex at an optimal 1/9 ratio and incorporating a liquid fatty compound, we reduced evaporation by a factor of 3 to 6 while maintaining carvacrol bioavailability within the dry film formed on the skin.

EO diffusion was assessed using two *in vitro* screens: carvacrol detection via UV spectroscopy after membrane diffusion, and tissue viability (MTT assay) on EpiSkin models to correlate Green Oregano penetration with formulation performance.

The penetration pathways were elucidated using Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) combined with SEM. This high-resolution imaging technique provided unprecedented visualization of carvacrol distribution across human skin cross-sections. Our results demonstrate that carvacrol effectively bypasses the stratum corneum, showing a pronounced accumulation in the deeper parts of the dermis, specifically within triglyceride-containing structures (likely adipocytes and secretory coils of sweat glands). Quantitative analysis (GC-MS) confirmed that approximately 84% of the detected carvacrol reached the dermis, highlighting its strong lipophilic affinity and fast penetration kinetics [5].

The biological relevance of this deep delivery was confirmed through several monocenter, double-blind, randomized clinical studies. Optimized formulations (0.3% to 1% GO-EO) demonstrated significant efficacy in reducing UV-induced erythema and inflammatory skin signs. Furthermore, a 0.5% GO-EO formula significantly improved skin imperfections over 8 weeks, while a 0.3% formula provided superior soothing effects in after-shaving applications.

In conclusion, this study demonstrates how the synergy between fundamental interfacial science, advanced mass spectrometry imaging, and clinical research allows for the successful delivery of volatile essential oils, transforming carvacrol into a high-performance active for deep-skin soothing applications.

Keywords:
Carvacrol; Green Oregano; ToF-SIMS; Skin Imaging; beta-Cyclodextrin; Dermal Delivery; Anti-inflammatory; Clinical Efficacy

References:

[1] K. Hüsnü Can Baser, G. Buchbauer, *Handbook of Essential Oils: Science, Technology and Applications* , CRC Press, 2010.
[2] P. Franchomme, R. Jollois, D. Pénoël, *L'aromathérapie exactement,* Editions Roger Jollois, 2001
[3] P. Landa, L. Kokoska, M. Pribylova, T. Vanek, P. Marsik Arch Pharm Res. *In vitro anti-inflammatory activity of carvacrol: Inhibitory effect on COX-2 catalyzed prostaglandin E(2) biosynthesis* . 32(1):75-8, 2009
doi: 10.1007/s12272-009-1120-6
[4] N. Ade, M. Bretaudeau, A. Staropoli, S. Teluob *Anti-inflammatory efficacy assay / Efficacy report* , Internal Results EPISKIN, Lyon, 2016 (15AIFP01)
[5] P. Sjövall, L. Skedung, S. Gregoire et al. *Imaging the distribution of skin lipids and topically applied compounds in human skin using mass spectrometry* . Sci Rep 8, 16683, 2018.
https://doi.org/10.1038/s41598-018-34286-x