Mechanistic investigation of synergistic mildness in binary surfactant systems: correlating micellar dynamics of anionic/non-ionic mixtures with 3D-RhE and zein endpoints

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Background and Objective
Surfactants are essential components in cosmetic and detergent formulations, yet their potential to cause skin irritation remains a major concern. Although individual surfactants have been extensively characterized, industrial applications increasingly rely on binary and more complex mixtures to optimize both performance and dermatological compatibility. This study investigates the relationship between irritation potential and the physicochemical properties of mixtures of the anionic surfactants polyethoxylated alkyl ether carboxylic acids (EC), and the non-ionic surfactants alkylpolyglucosides (APG). The aim is to identify possible synergistic effects and provide valuable insights for the rational design of safer, more skin-compatible formulations.
Methodology
A multi-methodological approach was employed to evaluate irritation potential, combining a modified version of the zein method described by Gotte and detailed in [1], together with a Reconstructed Human Epidermis (RhE) model (OECD TG 439) using the 3D in vitro skin model SkinEthic™ from Episkin (Lyon, France). Micellar characterization was carried out using Multi-Angle Dynamic Light Scattering (MADLS) with a Zetasizer Ultra (Malvern Panalytical Ltd., Malvern, UK) to determine hydrodynamic size, translational diffusion coefficient (D), and zeta potential.
Results
Findings on individual surfactants indicated that smaller, highly mobile micelles (high D), typical of anionic species like EC, correlate with higher zein numbers and reduced RhE viability, i.e., increased irritation potential. In contrast, non-ionic APGs form larger, less mobile aggregates, which are associated with milder dermatological profiles [2]. The experimental data from the zein protein solubilization assay and the 3D-reconstructed human epidermis (RhE) model confirm a significant synergistic mildness in the binary mixtures. The irritation potential of the EC/APG systems was notably lower than that of the individual surfactants, indicating a clear mitigation of dermal aggressiveness. These results are being correlated with the micellar physicochemistry of the aggregates. Preliminary analysis suggests that the formation of mixed micelles leads to a reduction in the chemical potential of the monomers and a shift in micellar dynamics. Full characterization of the aggregates, including zeta potential and diffusion coefficients (D), provides the mechanistic basis for this synergy by explaining the reduced mobility and penetration capacity of the mixed systems compared to their pure counterparts.
Conclusion
This study demonstrates that combining ether carboxylic acids (EC) with alkylpolyglucosides (APG) is an effective strategy for developing high-performance, low-irritation surfactant systems. The synergy observed through zein and RhE endpoints is fundamentally linked to the micellar architecture of the mixtures. Integration of micellar dynamics data, including size, surface charge, and diffusivity, facilitates an understanding of how intermolecular interactions improve dermatological compatibility. These physicochemical correlations further validate the use of mechanistic in vitro models to predict the behaviour of complex surfactant blends in topical applications.

Keywords:
Skin irritation, non-ionic surfactants, anionic surfactants, zeta potential, 3D reconstructed human epidermis (RhE)

References:

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