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Short communication

Stability profiling of 4% lidocaine hydrochloride emulgels

Maja Djepanova, Biljana Stefanovska, Angela Nastevska, Teodora Tasevska, Lina Livrinska Trpevska, Katerina Goracinova, Nikola Geskovski, Maja Simonoska Crcarevska*

Faculty of Pharmacy, Ss. Cyril & Methodius University in Skopje, Majka Tereza 47, 1000 Skopje, Republic of North Macedonia

Introduction

Emulgels are hybrid systems combining emulsions and gels, offering improved spreadability, prolonged skin contact, controlled drug release, and the ability to incorporate both hydrophilic and lipophilic compounds, making them suitable for dermal delivery. They are particularly useful for lidocaine hydrochloride (LHCl), enabling local action with reduced systemic exposure, although limited studies have investigated LHCl-loaded emulgels and formulation-dependent stability. Their performance is governed by microstructural interactions between emulsifiers, polymers, and lipid components affecting droplet stability, rheology, and drug release (Badruddoza et al., 2024; Kola-Mustapha et al., 2025).

This study evaluated the 6-month stability of 4% LHCl emulgels with varying cetostearyl alcohol (CA) and isopropyl myristate (IPM) concentrations at 4–8 °C, assessing pH, droplet size (DS), PDI, rheology, spreadability, drug content, and in vitro release.

Materials and methods

Materials

LHCl (Moehs, Spain) was kindly donated by Alkaloid AD, Skopje. Other reagents were: Carbopol, Tween 80, Span 80, and CA (Sigma-Aldrich, Merck, Germany), IPM (BASF, Germany); PG (propylene glycol) (Fisher Scientific, Netherlands), MP (methylparaben) and PP (propylparaben) (Fluka Analytical, Japan), TEA (triethanolamine) (Alkaloid AD, N. Macedonia). Purified water (PW) was used throughout the study.

Preparation and characterization of emulgel formulations

Emulgel formulations were prepared using LHCl (4%), Carbopol (0.5%), Tween 80 (1%), Span 80 (0.75%), PG (7.5%), MP (0.2%), PP (0.1%), and TEA (q.s.), with varying concentrations of CA (2%, 3.5%, and 5% in B1, B6, and B7) and IPM (5%, 7.5%, and 10% in B1, B8, and B9, respectively). LHCl was dissolved in water, followed by Carbopol dispersion (40 ± 2 °C, 300 rpm magnetic stirring).

The oil phase (CA, IPM, Tween 80, and Span 80) was heated separately and emulsified into the aqueous phase using high-shear homogenization (40 ± 2 °C, 6000 rpm, 20–25 min, T18 Basic, IKA, Germany). After cooling, TEA was added to induce gel formation (pH 5.0–7.0), followed by PG, MP, and PP. The formulation was then mixed for 15 min and adjusted to a final mass of 100 g.

Formulations were evaluated immediately after preparation (T0) and after 3 (T3) and 6 months (T6) of storage at 4–8 °C as part of the hold-time stability study. pH was determined using a calibrated pH

*msimonoska@ff.ukim.edu.mk

meter (Biobase PHS-3BW, China) at 25 ± 2 °C. DS and PDI were analyzed using a Zetasizer Nano ZS (Malvern Instruments, UK) after sample dispersion in deionized water. Rheological characterization was performed using an Anton Paar MCR 92 rheometer at 25 ± 0.2 °C and 32 ± 0.2 °C. Storage modulus (G′), loss modulus (G″), loss factor (tan δ), torque, and complex viscosity (η*) were determined using an amplitude sweep approach. During each 500 s measurement, 21 data points were recorded. The linear viscoelastic region (LVR) was determined from the relationship between storage modulus and shear strain. Spreadability was evaluated using a parallel-plate method and expressed as percentage diameter increase according to Dt - D0 / D0 × 100 where D0 represents the initial diameter of the sample and Dt corresponds to the diameter measured at a specific time point. Drug content and in vitro release were quantified using a validated HPLC method with UV detection at 210 nm. Release studies were performed using a membrane diffusion method with dialysis membranes (pH 5.5 ± 0.2, 32 ± 0.5 °C, 50 rpm) under horizontal shaking and sink conditions. Similarity factor (f_2), was calculated to compare release profiles.

Results and discussion

All formulations maintained pH values within the acceptable range for topical preparations (5.63 – 7.03), indicating preservation of chemical compatibility during storage. Increased CA concentration generally improved preservation of DS and reduced PDI changes, suggesting enhanced interfacial stabilization and stronger emulsion-network organization. In contrast, higher IPM levels promoted droplet growth and increased heterogeneity, indicating greater lipid-phase mobility and structural rearrangement during storage. Rheological analysis confirmed predominantly viscoelastic and shear-thinning behavior in all formulations, favorable for topical application, which is consistent with recent findings on emulgel systems where rheology, physical stability, and release performance are closely interrelated. Higher CA concentrations promoted structural reinforcement, increased resistance to deformation, and better preservation of viscoelastic parameters over time, likely due to enhanced lamellar organization and intermolecular cohesion. Conversely, higher IPM concentrations increased variability in viscosity-related parameters and promoted a more deformable internal structure. Drug content remained within acceptable limits throughout storage (95.24 – 104.28%), confirming LHCl stability. Formulation composition significantly influenced in vitro release behavior and its evolution during storage. Increased CA concentration resulted in slower and more controlled release, whereas higher IPM levels enhanced release dynamics. f_2 analysis showed changes in release profiles during storage. After 6 months, T0–T6 f_2 values were 71.21 (B1, 2% CA), 57.89 (B6, 3.5% CA), and 36.91 (B7, 5% CA), indicating similarity at lower CA levels (B1 and B6, $f_2 \geq 50$) and dissimilarity at the highest concentration (B7, $f_2 < 50$). For IPM formulations, f_2 values were 71.21 (B1, 5% IPM), 29.57 (B8, 7.5% IPM), and 30.13 (B9, 10% IPM), indicating similarity only for B1, while B8 and B9 showed dissimilar profiles ($f_2 < 50$). Overall, formulations exhibiting greater DS growth and heterogeneity showed higher variability in release behavior, suggesting that structural evolution influenced diffusion consistency.

Conclusion

The stability and performance of LHCl emulgels depended on the CA/IPM balance. Higher CA enhanced structural integrity, droplet stability, and rheological properties, while higher IPM increased lipid-phase mobility and structural rearrangement. Overall, formulation behavior was governed by the interplay between structural rigidity and lipid-phase flexibility, emphasizing the need to optimize the CA/IPM ratio for stability, rheological consistency, and controlled drug release during storage.

References

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