Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 577 - 578 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.278
Short communication

Spectroscopic evaluation of eudragit RL-stearic acid complexes intended for charge-reversal micellar systems

Jovana Angelova[1], Katerina Petrovska[1,2*], Hristina Petrovska[1], Ana Atanasova[2], Packa Antovska[2], Maja Simonoska-Crcarevska[1], Nikola Geskovski[1], Teodora Tasevska[1], Lina Livrinska[1], Katerina Goracinova[1*]

[1]*Institute of Pharmaceutical Technology, Faculty of Pharmacy, University of Ss. Cyril and Methodius in Skopje, 1000, Skopje, N. Macedonia*

[2]*Research & Development, Alkaloid AD-Skopje, Blvd. Aleksandar Makedonski 12, 1000, Skopje, N. Macedonia*

Introduction

Eudragit RL/RS are ammonia methacrylate copolymers with permanently charged quaternary ammonium groups. Literature on Eudragit RS/RL solid dispersions shows that carboxylate/acidic compounds can associate with these groups mainly through electrostatic interaction and/or hydrogen bonding; RL generally has higher binding capacity because it contains more quaternary ammonium sites (Pignatello, 2004). Malkawi et al. (2021) directly used stearic acid-Eudragit RS/RL hydrophobic ionic complexes for zeta-potential-changing micelles. Having in mind the potential of micelles carriers the primary aim of our study is to synthesize and structurally validate a stearic acid-Eudragit RL hydrophobic ionic complex to serve as the functional core for gastrointestinal tract-targeted polymeric micelles.

Materials and methods

Spectra of pure Eudragit RL, stearic acid, the 1:1 physical mixture and the prepared 1:1 equimolar complex (one mole of stearic acid carboxyl groups per one mole of Eudragit RL quaternary ammonium groups) co-evaporates from acetone/ethanol solutions were compared and evaluated using ATR-FTIR, Raman and Vis-NIR/SWIR spectroscopy. FTIR spectroscopy was performed using Diamond ATR-FTIR, Cary 630 (Agilent, Germany) under the following conditions: resolution 4 cm^{-1} , 32 scans per spectrum. Raman spectra were recorded using ATR 3000DH (Optosky, China) instrument. Scans were performed using a fiberoptic probe under the following conditions: laser power 400mW, integration time 60s, resolution 8 cm^{-1}, range 190-2000 cm^{-1}. Vis-NIR/SWIR spectra were recorded using an ASD LabSpec 4 spectroradiometer (Malvern, UK) equipped with a Muglight sample stand. Spectra were acquired in the range of 350–2500 nm and exported at a 1 nm spectral interval. All samples were analyzed under the same instrumental configuration and measurement geometry to enable direct comparison of the spectral profiles.

Results and discussion

The ATR-FTIR carbonyl region provides the most direct vibrational evidence for complex formation. Pure Eudragit RL shows its dominant ester carbonyl band at approximately 1724-1726 cm^{-1}, whereas pure stearic acid shows the neutral/free-acid or dimeric COOH carbonyl contribution near 1698-1701 cm^{-1}. In

*kago@ff.ukim.edu.mk

the 1:1 physical mixture, the low-wavenumber stearic-acid COOH contribution remains clearly visible, indicating the presence of mechanically admixed/free stearic acid. In contrast, the prepared 1:1 complex is dominated by the Eudragit ester carbonyl envelope near approximately 1724 cm^{-1} and shows marked attenuation of the free stearic-acid carbonyl signature around approximately 1700 cm^{-1}. This non-additive carbonyl behavior indicates that stearic acid is no longer present predominantly as a simple crystalline/free-acid phase. Additional support is obtained from redistribution of stearic-acid chain and carboxyl-associated bands in the 1500-1200 cm^{-1} region. These changes are consistent with disruption of the neutral COOH dimer/crystalline stearic-acid environment and formation of an Eudragit RL-stearate ion-pair complex. The Raman spectra provide independent support for the same interpretation. Pure Eudragit RL has a dominant ester carbonyl maximum at approximately 1731.9 cm^{-1}, whereas pure stearic acid gives a weaker Raman acid-carbonyl contribution around approximately 1694.4 cm^{-1}. The 1:1 physical mixture has its carbonyl-region maximum near 1729.7 cm^{-1}, close to Eudragit RL. The prepared 1:1 complex, however, shows stronger shoulder/residual intensity around approximately 1763 and 1700 cm^{-1} after normalization to the 1454 cm^{-1} CH_2/polymer deformation reference envelope. These shoulders are more pronounced in the complex than in the physical mixture and therefore demonstrate non-additive carbonyl/headgroup behavior. In Raman, the bands near approximately 1763 and 1700 cm^{-1} should not be presented as isolated proof peaks for COO^- formation. The carbonyl, carboxylate, ester, CH_2 deformation, and solid-state packing contributions overlap substantially in this region. Therefore, interpretation of the spectral changes point that the prepared complex has a perturbed carbonyl/carboxyl-headgroup environment relative to the corresponding physical mixture. Together with poorer reconstruction of the complex by a simple Eudragit RL + stearic acid linear combination, the Raman spectra support formation of an Eudragit RL-stearate hydrophobic ionic complex rather than a simple mechanical blend. The Vis-NIR/SWIR spectra provide supportive evidence for complex formation. No new UV-Vis chromophore is expected for this system; the relevant information is therefore contained mainly in the broad NIR overtone and combination regions. Compared with the 1:1 physical mixture, the prepared Eudragit RL-stearic acid complex shows non-additive Vis-NIR/SWIR behavior, with structured residuals in the aliphatic CH first-overtone region and in the CH_2/ester combination region. The complex is less well reconstructed as a linear combination of pure Eudragit RL and pure stearic acid than the physical mixture, which indicates that its spectrum is not merely a concentration-weighted sum of the two starting materials. The NIR data also show attenuation and reshaping of free stearic-acid-associated features, particularly around approximately 1730 nm and 2300-2310 nm. These changes support disruption of free/crystalline stearic acid and alteration of the long-chain aliphatic/ester environment in the complex. Because NIR bands are broad and highly overlapped, this evidence should be worded as supportive evidence of non-additivity and altered solid-state organization, rather than as direct standalone proof of a specific COO^- band.

Conclusion

The combined spectra support formation of an Eudragit RL-stearate hydrophobic ionic complex/ion-pair complex rather than a simple mechanical blend. The strongest evidence is attenuation of the free stearic-acid COOH carbonyl, Raman non-additivity in the carbonyl/headgroup region and NIR non-additivity with reduced free stearic-acid-like contribution. The spectra strongly support complex formation but do not alone prove complete stoichiometric conversion of all stearic acid to bound stearate. Zeta-potential, dissociation/release and DSC studies will be further performed in addition to the solid-state spectroscopic evidence.

References

Malkawi, A. et al., 2021. Dual-acting zeta-potential-changing micelles for optimal mucus diffusion and enhanced cellular uptake after oral delivery. Pharmaceutics 13(7), 974. https://doi.org/10.3390/pharmaceutics13070974

Pignatello, R. et al., 2004. Characterization of the mechanism of interaction in ibuprofen-Eudragit RL100 coevaporates. Drug Development and Industrial Pharmacy 30(3), 277–288.