SERS Investigation of pH-Induced Degradation in Ceftazidime

Vinicius Pereira Anjos[1], Amy Colleran[2], Royston Goodacre[2], Denise Maria Zezell[1]

[1]Universidade de São Paulo (*Instituto de Pesquisas Energéticas e Nucleares (IPEN/CNEN)*) ,
[2]University of Liverpool (*Centre for Metabolomics Research, Institute of Systems, Molecular and Integrative Biology*)

e-mail: viniciusanjo1@usp.br

Ceftazidime, a third-generation cephalosporin, plays a critical role in treating severe Gram-negative infections, including Pseudomonas aeruginosa, making its chemical stability essential for effective antimicrobial stewardship amid rising resistance. Substandard antibiotic formulations represent a critical global health risk, particularly in low- and middle-income countries amid rising antimicrobial resistance. Surface-Enhanced Raman Spectroscopy (SERS) offers a non-invasive, rapid, label-free method for pharmaceutical quality control. This study examines pH-induced degradation of ceftazidime using SERS signatures to detect structural changes and spectral discrimination. Hydroxylamine-reduced silver nanoparticles were synthesized and mixed with 10 mM ceftazidime solutions at controlled pH levels (e.g., acidic to neutral). SERS spectra (400–1800 cm^{-1}) were acquired using a 785 nm laser (10 s integration, ~25 spectra/class). Preprocessing involved Savitzky–Golay smoothing, baseline correction, and SNV normalization. Partial Least Squares-Discriminant Analysis (PLS-DA) with stratified train-test split (20%) was applied. PLS-DA achieved robust discrimination of pH conditions, revealing degradation mechanisms in the β-lactam ring. Variable Importance in Projection (VIP) scores highlighted 503 cm^{-1} (thiazine ring deformations, C–S modes) and ~1000 cm^{-1} (C–O–C/aromatic vibrations) as primary markers, indicating pH-sensitive hydrolysis and conformational shifts in ceftazidime's core structure. Strong acid conditions showed rapid degradation, mirroring kinetic profiles with distinct spectral alterations. SERS coupled with PLS-DA provides sensitivity for cephalosporin stability assessment, enabling ultrafast detection of substandard ceftazidime. This approach advances SERS-based antibiotic quality control for clinical and regulatory applications.

Acknowledgements
This work was supported by CNPq (INCT-INTERAS 406761/2022-1; INCT-INFO 409174/2024-6; Sisfoton 440228/2021-2; PQ 314517/2021-9), FAPESP (2020/07065-4; 2025/03135-1), and CAPES: (PDSE 88881.126379/2025-01, finance code 001).

References

J. Cailletaud and C. De Bleye, Journal of Pharmaceutical and Biomedical Analysis 147, 458 (2018).

C. Liu and B. Li, Metabolites, Sensors and Actuators B: Chemical 369, 132383 (2022).

A. Biancolillo and F. Marini, Frontiers in Chemistry 6, 576 (2018).