

Confocal laser scanning microscopy as a novel tool of hyperspectral imaging for the localization and quantification of fluorescent active principles in pharmaceutical solid dosage forms

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Abstract

Confocal laser scanning microscopy (CLSM) supported with multivariate analysis is proposed as hyperspectral imaging technique to identify, locate, and quantify, in a direct way, active pharmaceutical ingredients (APIs) in synthetic tablets, with the aim of establishing a new analysis methodology that collects qualitative and quantitative information from the surface and inner layers of solid dosage forms. This method is proposed as a novel, non-destructive, rapid, and highly sensitive hyperspectral imaging technique, with an excellent spatial resolution at the microscopic level. Two chemical systems comprising pharmaceutical mixtures of acetaminophen–caffeine–excipients and digoxin–excipients were analyzed by multivariate curve resolution-alternating least squares (MCR-ALS) using emission spectra obtained from microscopic images with the pixel sizes of $512 \mu\text{m} \times 512 \mu\text{m}$ to localize the APIs in the tablets. In addition, partial least squares (PLS) regression models were developed and used for calibration to obtain the concentration of the fluorescent active ingredients. The analysis by MCR-ALS delivered excellent results in localizing the fluorescent compounds; meanwhile, PLS achieved good error parameters for prediction of the external validation set for the quantification of caffeine and less successful quantification of digoxin. The performance of CLSM was evaluated by estimation of the analytical figures of merit of the technique to assess the quantification of APIs, including calculations of the uncertainty in the signal, sensitivity, analytical sensitivity, and ranges of detection and quantification limits. Use of CLSM as hyperspectral imaging attempts to increase the application of this technique in direct analysis of solid samples, showing that autofluorescent compounds can be analyzed for qualitative and quantitative purposes in presence of interferents by application of chemometrics. © 2021 Elsevier B.V.

Author keywords

Confocal laser scanning microscopy; Hyperspectral imaging; Multivariate image regression; Solid dosage forms

