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Detecting Trace Levels of Heavy Metals in Pharmaceutical Raw Materials with Wavelength-dispersive X-ray Fluorescence spectroscopy and Curve-fitting Regression

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Abstract

This paper proposes the application of Curve-Fitting Regression (CFR) to wavelength-dispersive X-ray fluorescence as a novel way to quantify traces of heavy metals in pharmaceutical products. This approach compares favorably with traditional (e.g. ordinary least squares regression: OLS) and multivariate (e.g. partial least squares regression: PLS) methodologies. This work compares OLS, PLS and CFR regression using 4 performance indicators (R^2_{cal}, RMSEC, R^2_{val} and RMSEP) for the quantification of heavy metals in 7 pharmaceutical powders, each spiked with 3 heavy metals (nickel, cadmium and lead). Several t-tests were then performed on repeat samplings (obtained by bootstrapping) of these performance indicators to determine how CFR compares to the reference methods (OLS and PLS). CFR was found to outperform both OLS and PLS, as per unilateral t-tests with $\alpha = 0.025$, for the quantification of 86% of the datasets analyzed in this work. The overall absolute error for CFR in validation varies between 3 and 5 ppm depending on the heavy metal analysed.

Keywords

WD-XRF; X-ray fluorescence; Trace element; Heavy metal; Pharmaceutical; Limit of detection; CFR; PLS ; OLS