Prediction of Dissolution Profile of Tablets for tuberculosis using NIR Spectroscopy and Multivariate Calibration

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Introduction:

This work used NIR spectroscopy and multivariate calibration to determine dissolution profiles of four actives principle (isoniazid, rifampicin, ethambutol, pyrazinamide) in tablets for treatment of pulmonary tuberculosis produced by UFRN. The analytical methods used conventionally in quality control (dissolution profile) of drugs by the pharmaceutical industry are mainly high-performance liquid chromatography (HPLC). These methods are slow, destructive and invasive, have a high cost operation and maintenance and generate waste chemicals harmful to the environment.

Materials and Methods:

NIR reflectance spectra (in triplicate) of 38 samples were measured using an FT-NIR Bomem MB 160 spectrophotometer in the 800-2500 nm range. Each measured spectra was the average of 50 scans, obtained with resolution of 8 cm^{-1}. No sample preparation was needed, being the entire tablet analyzed through diffuse reflectance. Spectra and calibration set, full cross-validation tests were treated and correlated with the dissolution profiles results by using the Unscrambler® 9.8 from Camo (Trondheim, Norway). Three tablets from each batch were evaluated for dissolution profile by using an Erweka dissolution apparatus. The dissolution testing was performed in 900 mL chloride acid 0.1 N at 37 ± 0.5°C, and the percentage of drug dissolution from each tablet was measurement at same time interval (45 min), at pH 6.8. For the measurement the isoniazid, rifampicin, ethambutol, pyrazinamide were performed HPLC (Shimadzu - Japan) and an isocratic system LC-20AT, SPD-M20A dual absorbance detector, SIL-20A auto sampler. The influence of various spectral pre-treatment [Savitzky Golay Smoothing, multiplicative scatter correction (MSC), first derivative (D1), second derivative (D2) separately and combined] and regression methods (PLS1 and PLS2) on prediction error are compared.

Results and Discussion:

The squared correlation coefficients for the plots of dissolution from the equipment laboratory (dissolution apparatus and HPLC determination) versus the predicted values (NIR), varied from 0.88 to 0.98. Prediction errors (RMSEP) using PLS2 models, which varied between 9.99% for isoniazid, 8.63 for rifampicin, 8.57 for ethambutol, 9.97 for pyrazinamide.

Conclusion:

Theses results indicating that the NIR diffuse reflectance spectroscopy method is an alternative, nondestructive tool for measurement of drug dissolution from tablets.

Novelty statement:

The dissolution profiles of four actives principle (isoniazid, rifampicin, ethambutol, pyrazinamide) in tablets for tuberculosis using NIR and multivariate calibration methods were studied. The chemometric models developed (PLS2) for this application showed high correlation values and low RMSEP.

Summary:

This work was investigated the potential of NIR technique to determine the dissolution profiles of tablets containing four active ingredients (isoniazid, rifampicin, ethambutol, pyrazinamide) using multivariate models (PLS2) and comparison with the conventional method (HPLC).