140. Title: Quantification of Pharmaceutical Polymorphs and Prediction of Dissolution Rate Using Theophylline Tablet by Terahertz Spectroscopy

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Source: CHEMICAL & PHARMACEUTICAL BULLETIN

Volume:59

Issue:4

Pages: 442-446

Publication year: 2011

Document type:Journal article (JA)

Abstract: Theophylline has an anhydrous form and a monohydrated form, and the dissolution rate of the anhydrous form is higher than that of the monohydrated form. Terahertz (THz) spectra of theophylline tablet containing the theophylline anhydrous form, monohydrated form, microcrystalline cellulose and magnesium stearate exhibited a specific absorption peak at 0.96 THz, where the theophylline anhydrous form demonstrated an absorption peak. Additionally, the intensity of the peak at 0.96 THz gradually decreased as the proportion of the anhydrous form decreased. The multivariate data analysis was performed to correlate the THz spectra of theophylline tablets with the ratio of the theophylline anhydrous form. The calibration model used to predict the mixing ratio of the theophylline anhydrous form from the THz spectra achieved root-mean-squared errors of cross-validation (RMSECV) of 2.89%, a slope of 0.9934 and an R-2 of 0.9927. In addition, there were intentions to develop a prediction model for the dissolution rate of theophylline from the drug product. The dissolution rate of theophylline tablet was gradually delayed as the proportion of the anhydrous form was decreased. The multivariate data analysis was performed to correlate the THz spectra of theophylline tablets with the dissolution rate. The calibration model used to predict the percentage of theophylline dissolved in 45 min from the THz spectra achieved an RMSECV of 3.29%, a slope of 0.9260 and an R-2 of 0.9423. Furthermore, there were no significant differences between the predicted and measured percentages of theophylline dissolved in 45 min in the theophylline tablets that were stored at 84% relative humidity (RH) and 25 degrees C for 12 h or 3d.