

Entacapone Isomer Quantification Using Raman Spectroscopy

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Raman spectroscopy, due to its non-destructive character and speed, has found widespread use in pharmaceutical applications [1]. It is also being used for quantifying various isomer mixtures, best known being the quantification of xylene isomers [2-3]. We here report quantification of isomer mixture of an active pharmaceutical substance.

Entacapone (2-cyano-3-(5-dihydroxyamino-3,4-dioxo-1-cyclohexa-1,5-dienyl)-N,N-diethyl-prop-2-enamide) is an active substance used in treatment of Parkinson's disease. It can be found in two isomeric forms *Z* and *E*. Isomer *Z* appears as a most common impurity in pharmaceutically more active isomer *E*. For this reason the ability to monitor the quantity of isomer *Z*, in isomer *E* is very important. Both isomers come up with a number of polymorphic forms. The most stable forms of the two isomers have distinct Raman spectra (Fig 1). Based on these distinct spectra the quantification of isomer mixture was performed. Physical mixtures of isomer *Z* in isomer *E* were prepared in range from 0% to 10% (w/w). Quantitative model of the mixture was obtained by Partial Least Square (PLS) Regression. The model performance was improved by applying mathematical pretreatment to the spectral data. In the range from 0% to 10% (w/w), the calibration model was linear.

Raman spectroscopy is a fast, non-destructive and reliable technique for quantification of isomer *Z* in the entacapone isomer mixture.

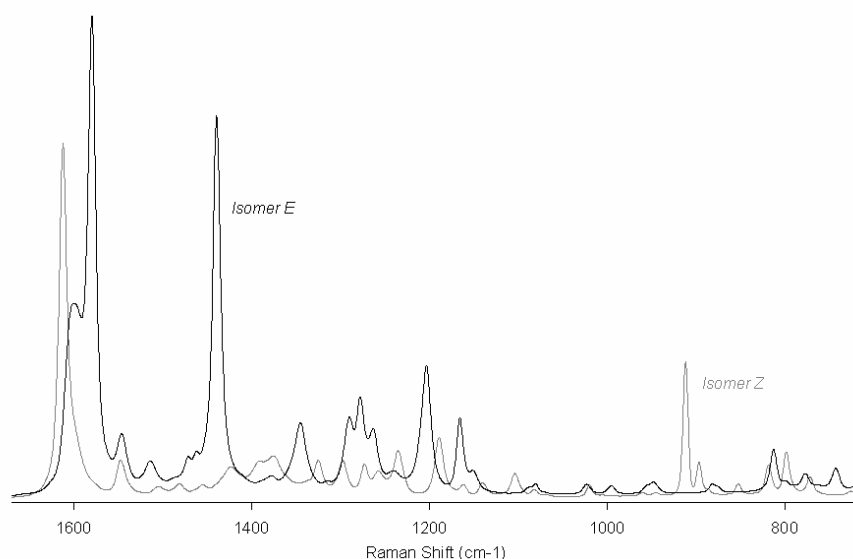


Figure 1: Distinct Raman spectra of entacapone *Z* and *E* isomer.

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