Qualitative Analysis of Polymorphism in Pharmaceutical Preparations by Near Infrared Reflectance Spectroscopy and Chemometric Data Processing

Amir Bagheri Garmarudi*, Mohammadreza Khanmohammadi, Keyvan Ghasemi
Chemistry Department, Faculty of Science, IKIU, Qazvin, Iran
*E-mail: a.bagheri@ikiu.ac.ir

Polymorphism can also result from the existence of different conformers of the same molecule in conformational polymorphism. Polymorphism is important in the development of pharmaceutical ingredients. Paracetamol (4-acetamido phenol) is an analgesic drug which is used world wide in the manufacture of many millions of tablets and other products. Paracetamol I is monoclinic and paracetamol II is orthorhombic can construct to stable polymorph I, the metastable polymorph can be used for direct comparison into tablets and has been reported to be dissolved faster in water. In this research, a novel method has been introduced for qualitative identification of paracetamol polymorphs, based on Fourier Transform Near Infrared Spectroscopy (FT-NIR) and chemometrics techniques e.g. cluster analysis and principal component analysis. A direct comparison was performed between spectroscopic data and those obtained using X-Ray Diffraction (XRD). While no diagnostically useful difference was observed, comparing the NIR spectra with XRD pattern of standard material, some distinct differences were observed between XRD results of paracetamol preparations. These differences are not related to additives and are dependent to polymorphism changes and paracetamol’s purity. Cluster analysis is a popular technique whose basic objective is to discover sample groupings within data. Principal Component Analysis (PCA) is probably the oldest and best known of the techniques used for multivariate analysis. In this study CA chemometric technique was used in total FT-NIR spectra of tablet samples, investigating paracetamol preparations and the dendrogram for 16 spectra of tablets was recorded to classify the paracetamol preparations. Also, PCA analysis by 3 essential factors was applied to the FT-NIR spectra. The 3 dimension score plot of first scores showed that the tablets are classified in separated groups. In the other words, PCA could determine the different classes of tablet samples more accurate than CA.

![Dendogram with complete linkage and absolute correlation coefficient](image1)

**Fig. 1- Dendogram of cluster analysis**

![Scores Plot](image2)

**Fig. 2- score plot of PCA for 3 PCs**