26th Congress of SCTM

Sept. 20-23, 2023, Metropol Lake Resort, Ohrid, N. Macedonia

Multivariate Analysis Approach in API-Excipient Compatibility Testing in the Development of Pharmaceutical Dosage Forms

E. Cvetkovska Bogatinovska,[a,*] V. Stefov,[b] N. Geshkovski[c] and Gj. Petrushevski[a]

[a]*Alkaloid AD, Blvd. Aleksandar Makedonski 12, Skopje, N. Macedonia*

[b]*Institute of Chemistry, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Arhimedova 5, Skopje, N. Macedonia*

[c]*Faculty of Pharmacy, Ss. Cyril and Methodius University, Majka Tereza 47, Skopje, N. Macedonia*

**ecvetkovska1@Alkaloid.com.mk*

Partial least squares–discriminant analysis (PLS-DA)[1] using Simca® 17 software was applied for evaluation of the results obtained from a compatibility study designed for the active pharmaceutical ingredient (API) ibuprofen with selection of twelve excipients used in the formulation of pharmaceutical finished products. Fourier-transform infrared spectroscopy (FTIR) and X-Ray powder diffraction (XRPD) were used as techniques for solid-state characterization of the samples.

The obtained results have shown that the optimal PLS-DA model was obtained for the FTIR spectra, explaining 83.3% of the changes in the FTIR spectra and predicting new datasets quite good (R^2X=0.833, R^2Y=0.991 and Q^2=0.960), as well as the PLS-DA model built based on the XRPD diffractograms (R^2X=0.892, R^2Y=0.986 and Q^2=0.946). Moreover, the main variations in the FTIR and XRPD data were attributed with highest VIP (Variable importance for the projection) scores in the corresponding VIP plots, proving the model capability for predicting incompatibilities. The prediction power of the optimal models for FTIR and XRPD experimental data was further confirmed (Root mean squared error of prediction, RMSEP=0.10% and 0.35%, respectively).

The obtained results demonstrated the potential of multivariate statistical analysis for monitoring of API-excipients solid-state compatibility during the routine analysis in the preformulation development.

Keywords: ibuprofen, compatibility, partial least squares-discriminant analysis

References

1. Bylesjo, M.; Rantalainen, M.; Cloarec, O.; Nicholson, J. K.; Holmes, E.; Trygg, J. OPLS discriminant analysis: combining the strengths of PLS-DA and SIMCA classification. *J. Chemom.* **2007**, 20 (8–10), 341–351. https://doi.org/10.1002/cem.1006