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Short communication

MVA model development for quantification of API in solid state using vibrational spectroscopy

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Introduction

Vibrational spectroscopy is a method for direct measurement of specific chemical bonds of adsorbed atoms and molecules, both between the adsorbate and the surface and the atoms themselves (John et al., 2010). Thus, this technique is defined as powerful toll for fast observation of different molecular arrangements allowing rapid and nondestructive measurements without sample preparation. The combination of the data obtained by vibrational spectroscopy and the multivariate analysis (MVA) tools suitable to explain large and complex data sets, enables development of models for quantitative analysis of the active substances within different samples.

The aim of this study is to elucidate the possibility for application of vibrational spectroscopy methods, such as near infrared and mid-infrared spectroscopy, combined with MVA tool (Partial Least Squares (PLS) regression analysis), for quantification of the active ingredients ibuprofen and ibuprofen sodium. The results would be starting point for the purpose of further development of a PAT tool for monitoring acid-salt solid state transitions that occur during processing.

Materials and methods

Test mixtures for model development were prepared using different ratios of ibuprofen, ibuprofen sodium (BASF, Bishop, US) and disodium carbonate (Dr. Paul Lohmann GmbH, Germany). The composition of the prepared mixtures is presented in Table 1.

After dry mixing of the components in different ratios, a spectrum for each of the mixtures was obtained using a Thermo Scientific™ Antaris™ II FT-NIR spectrometer for NIR analysis, and Varian-660 FTIR spectrometer for MIR analysis. The generated spectra were used for development of a quantification models based on chemometric analysis - Partial Least Squares (PLS) regression using SIMCA® (Umetrics, Sartorius, Sweden) software for MV analysis.

Table 1. Quantitative composition of the standard mixtures

Mixture no.	Component			Mixture no.	Component		
	Ibuprofen	Ibuprofen sodium	Na_2CO_3		Ibuprofen	Ibuprofen sodium	Na_2CO_3
	Concentration (% w/w)				Concentration (% w/w)		
1	100.00	0.00	0.00	**18**	35.09	42.88	22.03
2	100.00	0.00	0.00	**19**	30.57	45.86	23.57
3	98.49	0.99	0.51	**20**	26.24	48.73	25.03
4	97.00	1.98	1.02	**21**	22.06	51.48	26.46
5	95.53	2.95	1.52	**22**	18.05	54.14	27.81
6	94.07	3.92	2.01	**23**	14.17	56.70	29.13
7	92.62	4.87	2.51	**24**	10.44	59.16	30.40
8	89.77	6.76	3.47	**25**	6.84	61.54	31.62
9	88.37	7.68	3.95	**26**	5.43	62.47	32.10
10	85.60	9.51	4.89	**27**	4.74	62.93	32.33
11	78.92	13.93	7.15	**28**	3.36	63.84	32.80
12	72.55	18.14	9.31	**29**	2.68	64.29	33.03
13	66.46	22.15	11.39	**30**	2.00	64.74	33.26
14	60.65	25.99	13.36	**31**	1.33	65.18	33.49
15	55.09	29.67	15.24	**32**	0.66	65.62	33.72
16	49.77	33.18	17.05	**33**	0.00	66.06	33.94
17	44.67	36.55	18.78				

* ▭ mixtures used for MIR method development

Spectral pretreatment was applied for the model development, while the MVA models were evaluated by their regression and prediction coefficients (R2Y, Q2Y)

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and the root median square errors of estimation (RMSEE and RMSEEcv). Further analysis of the Variable Importance for the Projection (VIP) was performed for each model (Eman et al., 2020).

Results and discussion

Analysis of NIR spectral data and development of a quantification method: The NIR spectral analysis of each of the mixtures was performed by repeating the analysis three times, thus generating a total of 99 spectra that are part of the calibration data set used in the development of the PLS model along with the concentration of ibuprofen and ibuprofen sodium within each standard mixture.

Partial least squares regression performed on the NIR spectra indicated that this technique could explain >90% of the sample variability (R2X =0.978; R2Y=0.984) used for model construction, and has high prediction performance (Q2=0.982). The obtained values for RMSEE and RMSEcv of 4.66 and 4.96 respectively, confirm the model's ability to predict the obtained results with ±5% accuracy. The prediction plot is shown in Figure 1.

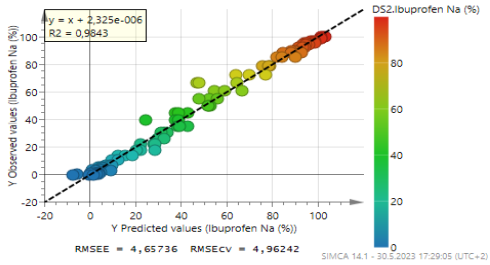

Fig. 1. NIR Regression plot between predicted vs. observed values of ibuprofen sodium

The most significant spectral regions used by the model for the quantification of ibuprofen and ibuprofen sodium are localized in the regions from 6100 to 5600 cm-1 and from 4700 cm^{-1} to 4000 cm^{-1}, which corresponds to the main spectral features of both molecules (Fig.3a).

Analysis of MIR spectral data and development of a quantification method: The MIR spectral analysis of each of the mixtures was performed by repeating the analysis twice, and subsequently, all 42 generated spectra were used as calibration data set for PLS model development.

The PLS model presented high correlation coefficients (R2X=0.902, R2Y=0.983) and adequate predictive ability (Q2=0.958). The obtained values for RMSEE and RMSEcv of 4.13 and 5.89 respectively, confirm the ability of the model to quantitatively determine the content of ibuprofen and ibuprofen sodium with accuracy limits of ±6% of the obtained value. A graphical representation of the generated plot is shown in Figure 2.

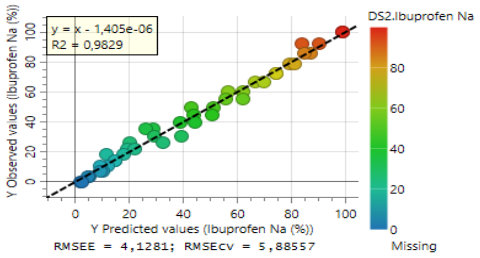

Fig. 2. MIR Regression plot between predicted vs. observed values of ibuprofen sodium

The VIP plot analysis (Fig. 3b), shows that the asymmetrical and symmetric carbonyl carboxyl modes (1722 cm^{-1}, 1545 cm^{-1}) and CH-CO deformation (1420 cm^{-1}) are the most significant used by the model to quantify ibuprofen and ibuprofen sodium. Additionally, the regions 660 to 990 cm^{-1} and 1180 to 1300 cm^{-1} are also found as significant spectral regions.

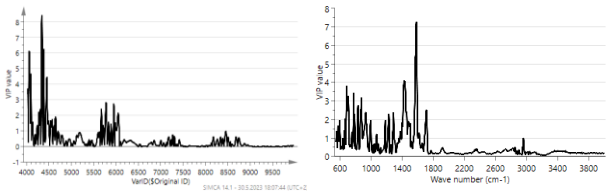

Fig. 3. a) VIP plot NIR model; b) VIP plot MIR model

Conclusion

Multivariate analysis combined with near infrared and mid-infrared spectroscopy can be a useful tool for the quantitative analysis of mixtures containing different concentrations of active components. In this study, statistical models for quantification have been developed using the spectral data generated by NIR and MIR spectroscopic analysis of standard mixtures with different percentages of ibuprofen and ibuprofen sodium in the concentration range from 0% to 100%. Both techniques can be further developed into a PAT tools for monitoring and quantification of ibuprofen transitions during processing of solid dosage forms.

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