The use of NIR to identify KROMASIL modifications and to quantify important quality parameters

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Introduction

Kromasil belongs to the group of chromatographic silica materials that is developed specifically for use in the pharmaceutical industry. Therefore it has to meet high quality standards. KROMASIL is mainly used in preparative liquid chromatography to purify synthesized active substances.

Depending on the chemical affinity and the separation behavior of the active substances, various modified silica materials in addition to the unmodified, bare silica are available. The differences between the KROMASIL types C4, C8, C18, NH_2 and CN are related to the length of the CH_2 chain of the silanes used and the chemical nature of the end groups respectively.

Quality Control of chromatographic materials focuses on numerous quality aspects, such as clear identification of the modification type of each batch before shipping as well as the quantitative determination of chemical and physical parameters of the end product.

The aim of this study was to evaluate the Büchi NIR technology (Fig. 1) to determine the quality parameters of KROMASIL and its use as an quality assurance tool.

Figure 1. BUCHI NIRFlex N-400, 2m reflectance probe, RSS 450

Results

Qualitative Calibration Models

Fig. 2 shows that the chemical differences of the silica types are clearly visible in the NIR range. With the use of a chemometric software (NIRCal) that analyses spectroscopic data a so called

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cluster plot can be generated. There, all silica types are represented as single, individual clusters (Fig. 3) and demonstrate that an identity control is possible by using NIR spectroscopy.

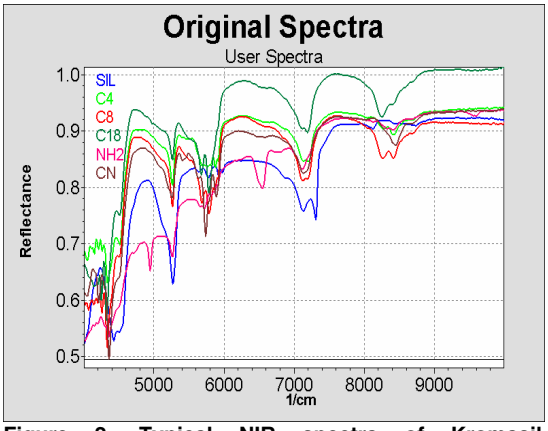

Figure 2. Typical NIR spectra of Kromasil modifications.

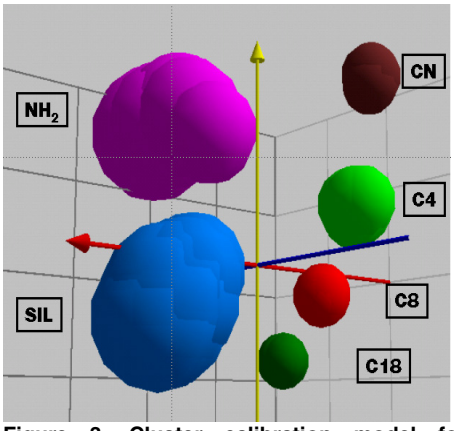

Figure 3. Cluster calibration model for identification of Kromasil modifications.

Not only chemical differences are shown in the spectral information but also physical parameters like particle size that can be used in a cluster model. Fig. 4 shows that product qualities that differ in particle size can be separated and identified clearly.

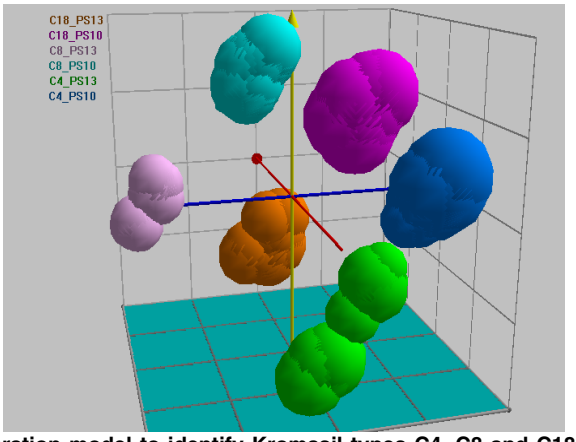

Figure 4. Cluster calibration model to identify Kromasil types C4, C8 and C18 having regard to the differences in particle size.

Quantitative Calibration Models

Quantitative chemical parameters like the water content of unmodified silica (Fig. 5) as well as the carbon content (Fig. 6) of the silane layer of modified silica formed during the derivatisation process, can be determined with reliable accuracy using NIR measurements.

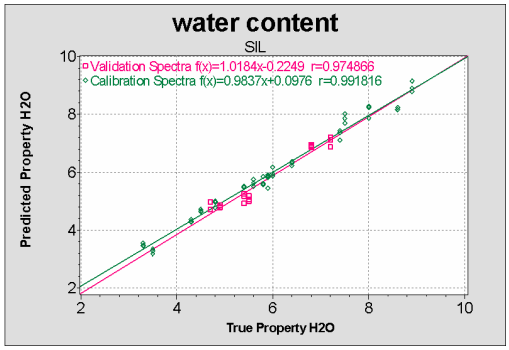

Figure 5. Quantitative calibration result for water content in unmodified silica.

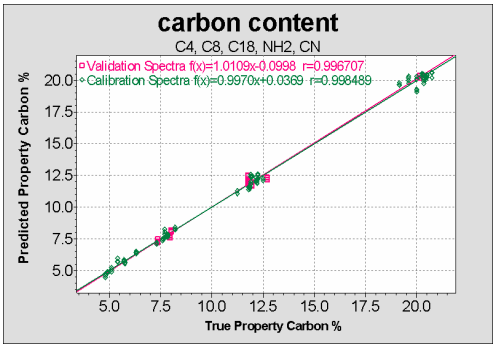

Figure 6. Quantitative calibration result for carbon content in modified silica.

More difficult is the quantitative determination of physical parameters like particle size (Fig. 7), dp90/10 (particle size distribution; Fig. 8), specific surface (BET) area (Fig. 9) or pore volume (Fig. 10). The physical information is hidden behind the dominating chemical information of the samples. Therefore it is neccessary to calibrate the physical parameters with samples of a similar chemical nature. A selection of KROMASIL C18 material with particle size 5 to 16 □m is used in the following experiments.

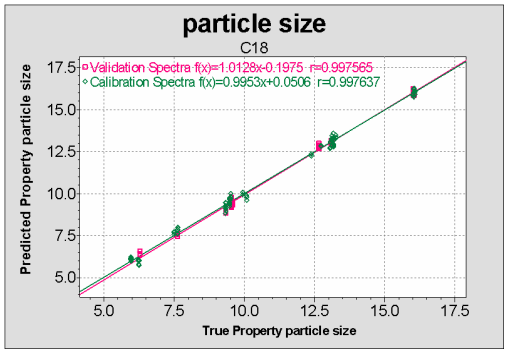

Figure 7. Quantitative calibration result for particle size.

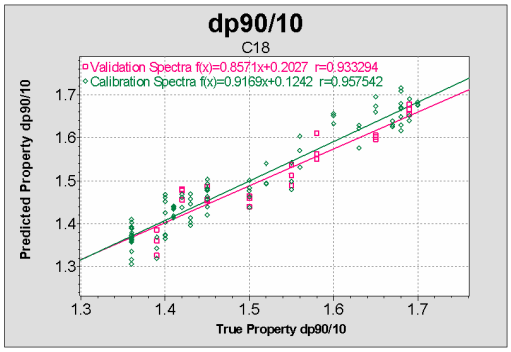

Figure 8. Quantitative calibration result for particle size distribution.

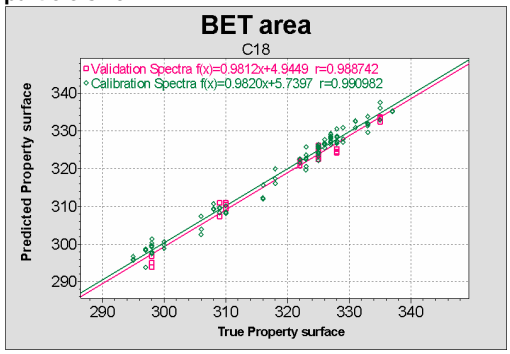

Figure 9. Quantitative calibration result for specific surface.

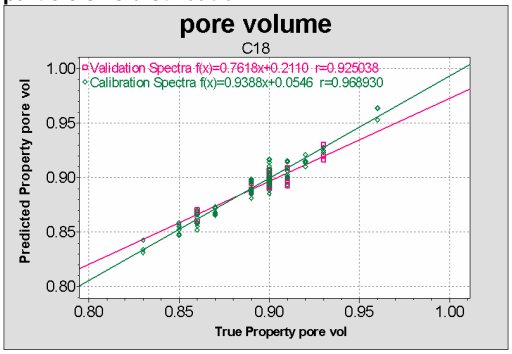

Figure 10. Quantitative calibration result for pore volume.

All shown calibration models used the PLS algorithm. Table 1 gives an overview of the calibration parameters such as number of primary and secondary factors, SEE and SEP, wavenumber range and data pretreatments used in the calibration models. The Q value describes the quality of a calibration model. The closer the value gets to 1 the better is the model.

Table 1. Detailed calibration results.

Calibration Property		Q-Value	SEE	SEP	Factors	Pretreatments
water content SIL	[%]	0.8576	0.21	0.22	1-8/10	db1, ncl
carbon content modified silica	[%]	0.9626	0.31	0.31	1-8/8	ds2
particle size C18	[mm]	0.9749	0.23	0.22	1-3/3	ncl, db1
dp90/10 C18		0.8778	0.034	0.037	1-8/9	sg9, mf, db1
BET area C18	[$m^2 g^{-1}$]	0.9854	1.65	1.74	1-7/8	db1, ncl
pore volume C18	[ml g^{-1}]	0.9523	0.006	0.008	1-8/8	dg1, nle

Conclusion

One NIR measurement can be performed in less than one minute, and can determine all calibrated parameters simultaneously.

Therefore NIR offers a fast and cost-effective alternative to conventional methods in Quality Control. The speed of NIR technology allows complete control of the end products and testing of incoming bulk material in the pharmaceutical industry at low costs.