

# Analytical control of an esterification process by NIR spectroscopy

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## Introduction

Process control in the chemical industry entails determining chemical parameters related to the species involved in the chemical reaction concerned. Such parameters continue to be determined largely by use of wet chemical methods. The esterification of glycerol by medium chain fatty acids to obtain medium chain triglycerides (MCTs) is usually monitored via the acid value (AV) and the hydroxyl value (OHV), which are measures of the amount of free, unreacted fatty acid and glycerol, respectively, remaining in the reaction medium. Both parameters are measured throughout the process and should be minimized when the product to be obtained is the corresponding triglyceride. They are also measures of appropriate reaction development, and used to identify the end-point of the reaction and to connect with the subsequent steps of the manufacturing process (refining). One other parameter to be monitored is the amount of water removed during the reaction in order to displace the equilibrium to the main reaction product.

Determining the above-described parameters entails using labour-intensive analytical (volumetric) methods; consuming some sample; using expensive, toxic reagents and solvents; and generating waste. There is thus a high interest in developing fast, reliable analytical methods circumventing these shortcomings<sup>1</sup>. Such methods should allow one to reduce the product cycle time and avoid the production of out-of-specification batches as a result of problems arising during the reaction step.

Near-infrared spectroscopy (NIRS) constitutes a potential choice for the at-, in- and on-line monitoring of industrial chemical process<sup>2-4</sup>. This is a straightforward, rapid, non-destructive technique that requires no sample pretreatment and is applicable to all types of sample with a view to determining both chemical (water, active principles) and physical parameters (viscosity, density).

Notwithstanding its advantages, NIRS provides spectral data of such complexity that it requires the joint use of some multivariate calibration technique; especially effective in this respect are principal component regression (PCR) and partial least-squares regression (PLSR).

In this work, we developed a NIRS-multivariate calibration method for the simultaneous at-line determination of the AV, OHV and water content in an industrial process for obtaining medium chain triglycerides (MCTs). At-line analysis on the plant site can then be the first step towards continuous process control.

## Experimental

### Apparatus and software

NIR transmittance spectra were recorded on a FOSS NIRSystems 6500 spectrophotometer equipped with a Rapid Content Analyser (RCA) module. The instrument was controlled via the Vision v. 2.51 software package.

The experimental set-up also included a LabMax reactor (Mettler Toledo), and the Metrohm 701 KF Titrino and 716 DMS titrators.

Multivariate calibration models were constructed using the software Unscrambler v. 7.8 from CAMO (Trondheim, Norway).

### Esterification of glycerol by medium chain fatty acids

The process studied was the esterification of glycerol by a mixture of caprylic and capric acids. The process samples used to construct and validate the calibration models were obtained from 8 different manufacturing batches of Uniqema (Mevisa Site, Spain), and 2 batches from the laboratory scale reactor (LabMax). Samplings were done at different reaction times and spanned the ranges 1-150 mg KOH/g for AV, 3-120 mg KOH/g for OHV and 0.01-0.8 % for water content. All samples were subjected to the reference methods endorsed by the Pharmacopoeia Europea<sup>5</sup>, which are summarized in Table 1.

**Table 1. Summary of the reference methods.**

Parameter	Sample	Method	Solvent	Reagent(s)	Time
AV	0.1-20 g	Acid-base titration	25 ml ethanol/xylene	0.1-0.5 M KOH ethanolic solution	5 min
OHV	1-5 g	1) Acetylation	Pyridine	Acetic anhydride	90 min
		2) Acid-base titration	25 ml ethanol	0.5 M KOH ethanolic solution	
Water	1-5 g	Karl-Fischer titration	10 ml Hydranal Solvent	Hydranal composite 5	5 min

NIR spectra were recorded in the transmittance mode at room temperature by using an optical glass cuvette and a gold reflector of 0.5 mm pathlength. Each individual spectrum was the average of 32 scans done at 2 nm intervals over the wavelength range 1100–2500 nm. The amount of sample used was 2-3 g and the reference was made by inserting the gold reflector into the empty cuvette, centred on the sample window with a centring iris. Each sample was used to record two spectra in order to obtain an average value that was used to determine the different parameters studied.

### Data processing

The samples were homogeneous, but its handling could result in the formation of small air bubbles and hence in the scattering of light and alterations in the spectral baseline and slope. These effects could lead to spurious results for the parameters of interest and required the use of a mathematical treatment prior to construction the calibration models. In this work, two different types of treatment were used: the standard normal variate (SNV) and derivatives. Spectrum derivatives were obtained using the Savitzky-Golay algorithm with a second-order polynomial and a window size of 11 points.

The pre-processed data thus obtained were subjected to the PCA and PLS1 algorithms included in Unscrambler. PLS1 models were constructed by cross-validation, using as many segments as samples employed for calibration (leave-one-out procedure). The optimum number of PLS components was determined in order to minimize the sum of the squared differences between the reference and the determined parameter:

$$PRESS = \sum_{i=1}^m (\hat{y}_i - y_i)^2 \quad (1)$$

where  $m$  is the number of samples,  $y_i$  the parameter value provided by the reference method and  $\hat{y}_i$  the value calculated with the PLS1 model.

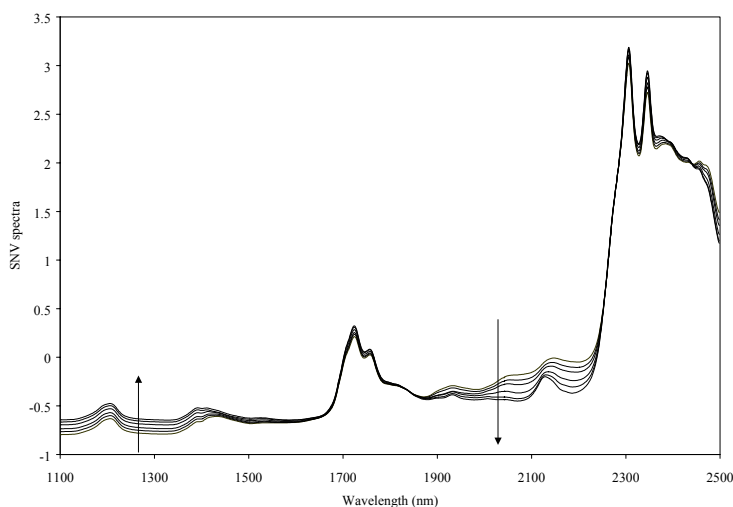
The goodness of the results provided by the different PLS1 models was assessed in terms of relative standard error:

$$RSE(\%) = \sqrt{\frac{\sum_{i=1}^m (\hat{y}_i - y_i)^2}{\sum_{i=1}^m (y_i)^2}} \times 100 \quad (2)$$

and designed as RSEC(%) and RSEP(%) for calibration and prediction, respectively.

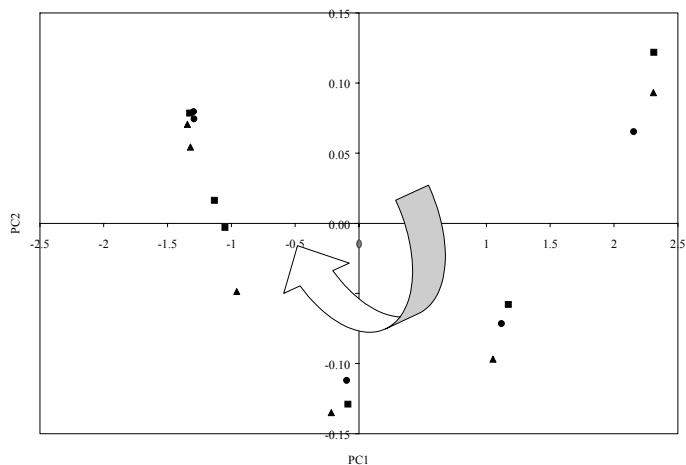
## Results and discussion

Figure 1 shows the variation of the NIR spectra (following SNV pre-treatment) during the reaction step in the industrial manufacturing of an MCT. As can clearly be seen, the spectrum changed markedly in the 1900–2200 nm region, which contains the O–H combination bands for water and those for the hydroxyl groups in glycerol.



**Figure 1.** NIR reaction spectra as recorded in SNV mode. The arrowsheads indicate the temporal evolution of the spectra.

Figure 2 shows the plot of scores of the principal component analysis (PCA) for three industrial processes, which is linked to the chemical composition variation. The arrowhead indicates the evolution of the reaction and its direction coincides with the decrease in the target parameters (AV and OHV). The samples clustered according to the reaction evolution in the first *versus* second PC plot. At the end, samples were all clustered and the point scatter in the scores plot was very low. Based on these results, principal component analysis can be an effective choice for monitoring the reaction and identifying its end-point.



**Figure 2.** Plot of first *versus* second scores obtained in the PCA of three industrial processes.

Calibration models

PLS1 models were constructed by using various wavelength ranges and pre-treatments. Those providing the best results were shown in Table 2.

**Table 2.** Relative standard errors of calibration and prediction for the best PLS1 models for AV, OHV and water.

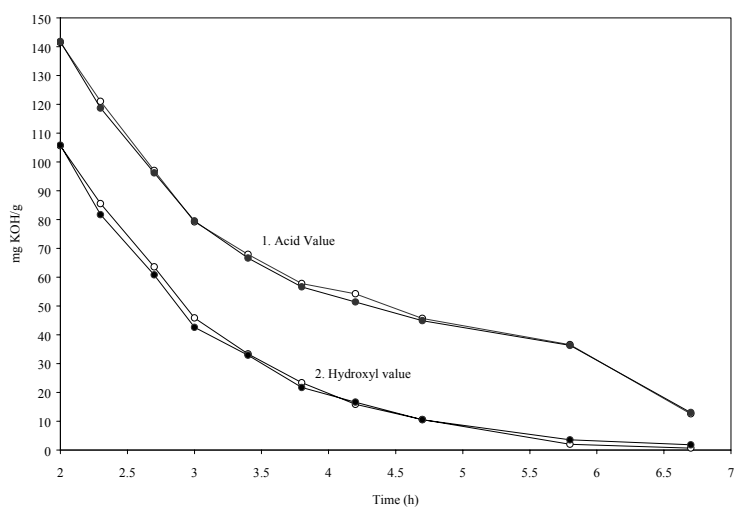
Parameter	Pre-treatment	Wavelength (nm)	Calibration		Prediction	
			Samples	RSEC(%)	Samples	RSEP(%)
AV <sup>a</sup>	SNV	Full spectrum	31	2.2	53	2.5
OHV <sup>b</sup>	SNV	1800-2100	31	5.4	49	6.0
Water <sup>b</sup>	1 <sup>st</sup> D	1800-2100	25	5.3	40	9.5

<sup>a</sup> Number of PLS components used in the model = 2

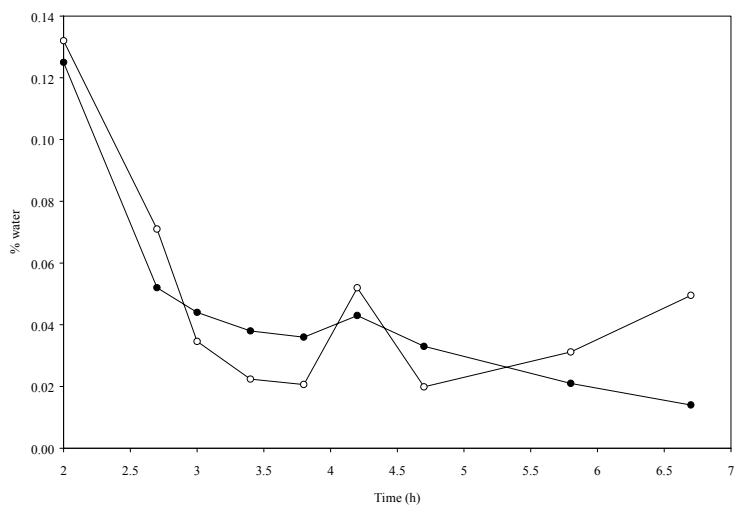
<sup>b</sup> Number of PLS components used in the models = 3

As can be seen, the NIR predicted values obtained with the PLS1 models were quite consistent with the reference values. The figures of merit of the models (Table 3) reveal the absence of systematic errors (slopes and intercepts were not significantly different from unity and zero, respectively).

a)



b)



**Figure 3. a) Reaction profiles for (1) AV and (2) OHV during the esterification reaction. b) Reaction profile for the water content during the esterification reaction. White (○) and black (●) circles correspond to NIR predicted values and reference values, respectively.**

### Process control

Figures 3a and 3b show the predicted profiles for one of the esterification reactions performed in the LabMax reactor. As can be seen, the predicted curves (Fig. 3a) for AV and OHV fitted the results of the volumetric reference methods very closely. On the other hand, the prediction of the water content (Fig. 3b) was not too good. This may have been the result of all the samples in the set having water contents near the lower limit of the calibration curve and hence very close to the limit of quantification of the reference method.

**Table 3. Figures of merit and parameters ranges.**

Parameter	Set	Range	Slope	Intercept	R <sup>2</sup>
AV	Calibration	1-150 mg KOH/g	$0.999 \pm 0.012$	$0.056 \pm 0.895$	0.999
	Prediction	1.5-146 mg KOH/g	$1.009 \pm 0.009$	$-0.016 \pm 0.573$	0.999
OHV	Calibration	2-117 mg KOH/g	$0.995 \pm 0.027$	$0.164 \pm 1.340$	0.995
	Prediction	3-116 mg KOH/g	$1.024 \pm 0.021$	$0.173 \pm 0.809$	0.995
Water	Calibration	0.01- 0.84 %	$0.995 \pm 0.029$	$0.001 \pm 0.008$	0.995
	Prediction	0.02- 0.80 %	$0.990 \pm 0.036$	$0.004 \pm 0.006$	0.990

### Conclusions

A single NIR spectrum, a small amount of sample and PLS1 calibration models allow one to determine AV, OHV and the water content in an industrial manufacturing process. The analysis time is substantially reduced (to less than 5 min), which is very important when the end of the reaction step must be identified (cycle time reduction). Finally, the proposed NIRS method avoids the use of hazardous solvents and reagents, as well as the production of waste.

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