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An infrared spectroscopic tool for process monitoring: Sugar contents during the production of a depilatory formulation

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ABSTRACT

A fast, reliable and economical methodology has been developed to control the production process of sugar-based depilatories. The method is based on the use of attenuated total reflectance—Fourier transform infrared (ATR-FTIR) spectroscopy in combination with multivariate data analysis. A very simple sample preparation process involving the dissolution of samples in water was applied. Employing a multivariate calibration model established from data of 15 well characterized samples, prediction errors equal or below 3.04 mg mL^{-1} for the quantitative determination of fructose, glucose, sucrose, maltose and maltotriose were obtained. Results found in this preliminary study indicate a great potential for the development of at-line ATR-FTIR-PLS methods based on a careful selection of variables from IR spectra, delivering fast and reliable results. As a reference method, a liquid chromatography (LC)–IR method was adapted for sample characterization.

1. Introduction

Process analytical technology (PAT) continues to be an evolving field across several industrial sectors reflected by an ongoing interest in the development and implementation of new analytical tools and methods. Frequently the evaluation of product quality is accomplished by analyzing randomly collected samples obtained from batch processing, employing time-consuming off-line laboratory techniques. This lack of understanding of the process itself hampers effective process control and can result in batch losses. In accordance, the objective of PAT is to enhance understanding and control a manufacturing process following quality-by-design principles, to reduce identified manufacturing risks that are associated with product quality. It should therefore play a crucial role in design, analysis and control of manufacturing processes based on measurements of critical performance attributes [1–3].

Concerning available analytical tools, modern technologies providing multivariate information related to biological and chemical parameters have evolved from those that predominantly take univariate process measurements, such as temperature, pH and pressure. In the last decade, vibrational spectroscopy has been increasingly used for process control and monitoring in many different fields including the monitoring of pharmaceutical [4,5] and bio-processes [6]. The huge number of methods based on different spectroscopic techniques such as mid-infrared (MIR), near infrared (NIR) and Raman spectroscopy can be attributed to their characteristics that make them well-suited for process control and monitoring tasks combining several key-features. In general, spectroscopic methods are able to provide quantitative and qualitative multi-analyte information being at the same time extremely versatile as they allow the measurement of gaseous, liquid and solid samples. Further remarkable aspects that favor the implementation of spectroscopic techniques are that measurements are usually non-destructive and sometimes even non-invasive. The set-ups are robust and economic and ideally allow the implementation of automated data acquisition in real-time measurements. Instrumentation technology for process analytical applications can avoid the deleterious side effects of traditional methods involving an intensive sample preparation and, because of that green analytical procedures have been replacing other PAT [7,8].

Due to the frequent use of vibrational spectroscopic process analyzers and their ability to supply multivariate information, there is a growing need for chemometric methods. Currently, all kinds of multivariate regression and classification models find their application in (bio-)process monitoring [1,8–10] and methods are constantly developed to improve results [11].

Although similar from the viewpoint of an analytical chemist, in contrast to the pharmaceutical sector, PAT still plays a limited

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role in the production of cosmetics. Usually, only final products are analyzed employing standard laboratory techniques to ensure consumer safety according to the EU legislation on cosmetic products [12–14]. On the other hand, IR spectroscopy is known to be a valuable tool for the determination of glucose in complex samples like blood and urine [15]. Furthermore recently a method for the direct determination of fructose, glucose, sucrose and maltose in sugar based depilatories employing ATR (attenuated total reflectance)-FTIR spectra was developed as an alternative to solvent and time-consuming chromatographic methods [16]. Surprisingly, in this study the absence of sucrose in all tested commercial samples was evidenced in spite of the information on components provided by the manufacturers. In fact, sucrose was added during the production process, but due to heating of the primary matter under acidic conditions, a cleavage of sucrose into fructose and glucose was suspected. Moreover maltose was detected in all analyzed samples although apparently no maltose was added during production, which raised the suspicion that glucose syrup instead of crystalline glucose was added.

Based on the foregoing study, in the present study the previously developed liquid chromatography (LC)-IR method was adapted to analyze samples withdrawn at different stages of the production process to gain a deeper insight into changes of raw materials occurring during the production. After sample characterization a direct, green ATR-FTIR method for the simultaneous determination of all sugars present during the batch production process of depilatories was developed as a preliminary study for its implementation as at-line PAT.

2. Material and methods

2.1. Standards and samples

D(−)-fructose, anhydrous D(+)-glucose and maltose-1-hydrate from Panreac (Barcelona, Spain), D(+)-sucrose from Scharlau (Barcelona, Spain) and maltotriose hydrate 95% from Aldrich (Saint Louis, MO, USA) were used as standards. Acetonitrile (HPLC grade) was purchased also from Scharlau and high-purity water, with a resistivity higher than 18.2 MΩ, was obtained from a Milli-Q water-purification system (Bedford, MA, USA). Ten different stages of the batch process were considered, characterized by the addition of sugars and perfume and a temperature program. Aliquots of approximately 3 mL were withdrawn from the batch reactor at each production step and stored until analysis in glass vials in the dark at room temperature.

2.2. LC-IR reference procedure

Recently published LC-IR methods for the determination of sugars were adapted [16,17] for the off-line analysis of samples withdrawn from the production process. For chromatographic separations a Dionex (Sunnyvale, CA, USA) P680 high performance liquid chromatography system, equipped with a Kromasil 100 NH_2 column (250×2 mm, 5 μm) was used running linear acetonitrile:water gradients from 75 to 55% (v/v) of acetonitrile in 15 min, then maintaining the mobile phase constant during 10 min at a flow rate of 0.2 mL min^{-1}. Using a home-made micro flow cell interface with an optical path of 10 μm, consisting of a ZnSe and a CaF_2 window and an aluminium spacer, on-line hyphenation to a Bruker IFS 66/v FTIR spectrometer (Ettlingen, Germany) was achieved. Post-run background correction was carried out employing cubic smoothing splines (CSS) [18] and linear calibration lines were established by measuring the corresponding peak areas obtained from the analysis of standards.

For preparation of sugar standard mixtures, different amounts of pure sugar standards were accurately weighed in 5 mL volumetric flasks and dissolved in 2.5 mL of Milli-Q water. Standard mixtures were sonicated in a JP Selecta ultrasonic water bath (Barcelona, Spain) during 25 min and filled up to volume with acetonitrile. For sample preparation, between 200 and 250 mg of each sample were accurately weighed in a 5 mL volumetric flask following the same procedure as described for standard solutions. Sample solutions were centrifuged at 2500 rpm during 15 min to eliminate un-dissolved particles. Before injection into the chromatographic system, standard and sample solutions were filtered through 0.22 μm nylon syringe filters.

2.3. ATR-FTIR-partial least squares (PLS) procedure

For ATR spectra acquisition, a dry-air purged in-compartment DuraSampleIR accessory from Smiths Detection Inc. (Warrigton, UK) equipped with a nine reflection diamond was installed on a Bruker IFS 66/v FTIR spectrometer. Spectra were recorded in the range between 4000 and 600 cm^{-1}, with a spectral resolution of 4 cm^{-1}, averaging 100 scans per spectrum and using a spectrum of Milli-Q water as a background.

For sample preparation of pure samples, 1.5 mL of Milli-Q water were added to 200 mg of each sample. In addition to the pure samples, 31 mixed samples were prepared as binary mixtures of the pure ones by accurately weighing different amounts of two samples ranging between 150 and 300 mg and adding 1.5 mL of water. The dilution step was necessary because of the high viscosity of samples hindering a proper handling of the aliquots, and enabled at the same time the preparation of homogeneous mixed samples. All samples were sonicated in an ultrasonic water bath during 25 min. Sugar concentrations of pure and mixed samples were calculated employing concentrations determined by the on-line LC-IR reference procedure and the weighed sample masses.

Triplicate spectra were obtained for each sample and sample mixture by depositing an aliquot onto the ATR crystal. The means of the triplicate spectra of each sample and/or sample mixture were calculated and employed to build up a calibration and a validation subset for PLS modeling, containing 15 and 26 spectra, respectively (for details see Table S1 of Suplementary Material). Table 1 describes the main characteristics of the data sets. Prior to PLS model calculation, mean centered row vectors resulting from 9-point cubic Savitzky–Golay first or second derivative spectra were calculated in order to improve PLS calibration. Derivative spectra are commonly used for pre-processing of spectroscopic data in order to remove baseline drifts and offsets. They remove low-frequency features maintaining high-frequency features that contain the signal of interest without affecting the linear relationship with the chemical concentration [19]. Leave-one-out cross validation (CV) was employed for the calculation of internal figures of merit and for the selection of the optimum number of latent variables (LVs). For outlier detection, the Hotelling T^2 statistic and Q residuals were calculated. The Hotelling T^2 statistic is a measure of the variation in each sample within the model defined as the sum of normalized squared scores. The Q residuals are the sum of squares of the error matrix of each sample. The Q residual is a measure of the difference between a sample and its projection into the latent variables space used to build up the PLS model and therefore it indicates how well each sample conforms to the PLS model [19].

A strategy to improve PLS regression model performance is to select one or more spectral ranges containing useful chemical information and to eliminate spectral ranges only contributing noise. A preliminary variable selection was carried out using interval PLS (iPLS), because it has several intrinsic advantages over other variable selection methods: (i) the interpretation of the