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Development and validation of an at-line fast and non-destructive Raman spectroscopic method for the quantification of multiple components in liquid detergent compositions

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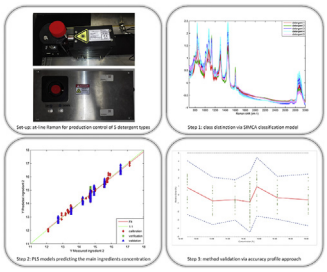
HIGHLIGHTS

- Raman spectroscopy as PAT tool monitoring a liquid detergent production process.
- SIMCA classification model distinguishing between investigated cleaning liquids.
- Quantitative PLS models for determination of the main ingredients concentration.
- Method validation and uncertainty analysis through the accuracy profile approach.
- Developed method demonstrated suitable for routine use at-line.

GRAPHICAL ABSTRACT



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ABSTRACT

Implementation of process analytical technology (PAT) tools in the manufacturing process of liquid detergent compositions should allow fast and non-destructive evaluation of the product quality. The aim of this study was to develop and validate a rapid method for quantifying the chemical compounds of five washing liquid precursors. Raman spectroscopy was applied in combination with a two-step multivariate modeling procedure. In first instance, a SIMCA (Soft Independent Modeling of Class Analogy) model was developed and validated, allowing the distinction between the different laundry detergents. Once the product was correctly identified, it was aimed at predicting the concentration of its individual components using partial least squares (PLS) models. Raman spectra were collected at-line with a total acquisition time of 20 s, using a non-contact fiber-optic probe.

The SIMCA model was perfectly capable of differentiating between the classes of the laundry liquid precursors. Per detergent, the concentration of at least three main ingredients could be predicted with a recovery between 98% and 102% and a standard deviation below 2.5%. Accuracy profiles based on the analysis results of validation samples were then calculated to prove the reliability of the developed regression models. β-expectation tolerance intervals were calculated for each model and for each validated concentration level. The acceptance limits were set at 5% relative bias, indicating that at least 95% of future measurements should not deviate more than 5% from the true value. Furthermore, based on the

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data of the accuracy profiles, the measurement uncertainty was determined. The developed Raman spectroscopic method demonstrated to be able to rapidly and adequately determine the concentration of the components of interest in the liquid detergent compositions at-line.

1. Introduction

The manufacture of liquid detergent compositions requires a careful balance of ingredients and process steps. Their development and production is based on simple mixing of a number of detergent components. The ingredients may be selected from surfactants, builders, chelants, polymers, organic and inorganic solvents, dyes, perfumes, preservatives, antibacterial agents, viscosity modifiers, pH adjustment agents, water or a mixture thereof. Dosing of these cleaning agent constituents should be performed accurately, as the incapacity of meeting the preferred specifications could negatively impact the cleaning or care ability of the composition. Further, it could adversely affect factors such as physical stability, odor profile, safety profile or regulatory compliance.

Since the publication of the process analytical technology (PAT) guidance by the American Food and Drug Administration (FDA) in 2004, it is generally accepted that quality should be built into products rather than be tested afterwards, preventing the process from being an un-comprehended black box system [1], [2]. Thus, advanced manufacturing practices are being implemented in the pharmaceutical, chemical, biotechnological and food industry, enhancing process efficiency and guaranteeing product quality [3–9]. The consumer goods industry, on the contrary, has been slow at adapting this PAT approach. Nowadays, most consumer goods companies still rely on univariate statistical process monitoring methods (based on univariate sensors) to ensure their product quality. These traditional compliance approaches via product checks by employees have limitations with respect to the number of people required and the accuracy of the checks whilst often missing underlying patterns in process data.

Introducing PAT systems in the manufacturing process of liquid detergent compositions would help to achieve assured high levels of quality and productivity. PAT tools should allow real-time measurement of key quality parameters in intermediate raw materials and the finished product.

The aim of this study was to develop and validate a fast and non-destructive analytical method for the determination and quantification of the chemical composition of five washing liquid precursors. These intermediates of the liquid detergent production process are mixtures of liquid detergents based on simple blending of cleaning ingredients, to which perfume, dyes and enzymes are added later to create the final washing liquid product. During manufacturing of these liquid compositions, several chemical reactions take place between the combined constituents, so the term mixture is not employed in its purely chemical definition. Whenever the authors refer to a mixture, the liquid composition formed by assembling detergent ingredients is meant, not implying a lack of chemical interaction during production.

A method based on the combination of Raman spectroscopy with multivariate modeling was developed to predict the composition of the complex liquids non-destructively and within a few seconds. Raman spectroscopy is a molecular vibrational spectroscopic technique allowing rapid and non-destructive measurements without sample preparation. Its ability to record spectra directly through transparent glass or plastic packaging and the possibility to quantify compounds in aqueous formulations makes Raman spectroscopy the preferred analytical technique. The list of Raman applications in the pharmaceutical industry seems endless and the use in other industries (e.g. food, forensics, plastic sorting and recycling …) has been growing extensively in the past few years; but again, the consumer goods field is behind on this [3,4,10–18].

For the multivariate modeling, a two-step approach, consisting of a classification and a quantification phase, was used. During the initial categorization step, a distinction is made between the five types of laundry liquid precursors implemented based on their Raman spectra, thus identifying the sample in front of the probe. Next, the composition of the complex liquids is checked during the quantification step. More concrete, partial least squares (PLS) models regressing Raman spectra versus the chemical composition of the laundry liquids are fitted for each detergent, allowing to predict the concentration of the washing products main ingredients.

To assure that every future measurement that will be performed in routine will be close enough to the unknown true value of the sample, validation of the quantification method is executed by calculating accuracy profiles. This validation procedure, introduced by the Société Française des Sciences et Techniques Pharmaceutiques (SFSTP) [19,20], is widely accepted in the pharmaceutical field as can be derived from the numerous applications in literature [10,21–28]. To our best knowledge, no applications are published from the consumer goods industry, making this a cutting-edge approach in the business.

By calculating accuracy profiles, a reliable representation of the methods performance is created, based on β-expectation tolerance intervals. Within day, between day and operator variability are taken into account to estimate the total error of the procedure, influenced by both bias and standard deviation. The objective is to assess the models predictive power, thus minimizing the risk to accept an inaccurate quantification method or reject a capable one.

2. Materials and methods

2.1. Materials

The examined laundry liquid precursors are mixtures of detergent ingredients consisting of 10–15 components that are blended together into a homogeneous fluid. The five precursors under investigation differ in terms of compounds present and quantity of these composites. As the proprietary confidential formulas cannot be concealed, the laundry detergents are simply numbered 1 to 5 and their components of interest are referred to as ingredient A to E in this publication. The target concentrations of these key compounds in the different laundry liquid precursors are listed in Table 1.

2.2. Sample preparation

Calibration standards were prepared per laundry liquid precursor according to a central composite circumscribed (CCC) experimental design created in MODDE (Umetrics, Sweden). Since it was aimed at predicting the concentration of a few main