Using Anton Paar's Cora 5001 Raman spectrometer to analyze the quality of hand sanitizers

Relevant for: Cosmetics, Consumer goods.

As hand sanitizers are supposed to prevent infections their quality is of paramount importance. Uncovering adulteration with toxic methanol or sub-potent active ingredient concentrations is easily possible using Cora 5001 Raman spectrometers.

1 Introduction

Anton Paar's Cora 5001 Raman spectrometers offer a fast and non-destructive analysis to identify low-quality consumer products, e.g. in case of adulterated products. In times of a global pandemic like COVID-19, hand sanitizers have become a product for everyday use to prevent infections. Those products are intended to improve human health. Since the COVID-19 pandemic lead to shortages in the availability of hand sanitizers the FDA published a temporary and less restrictive production guideline. However, governmental agencies like the FDA had to subsequently ban several hand sanitizers as they presented a risk to consumers health instead of preventing harm. [1] Main reasons for such bans are

- Sub-potent active ingredient concentration (ethanol or isopropanol) that has no or less effect on germs.
- Adulteration or exchange of the active ingredient with toxic methanol. [1]

Raman spectroscopy is a useful and fast tool to offer a solution for those problems as it can identify the main component of hand sanitizers (for details see [2]), it can verify if it is contaminated with methanol and even sufficiently quantify the amount of methanol added to the hand sanitizer.

1.1 Properties and risks of methanol

Methanol is widely used in industry as a solvent. It is a colorless liquid that is miscible with water and most organic solvents and has an alcoholic smell. [3] According to the ECHA it is toxic if swallowed, toxic in contact with skin and toxic if inhaled as it is metabolized to toxic formaldehyde and formic acid. [4, 5] Methanol exposure can result in nausea, vomiting, headache, permanent blindness or even death. [6] It causes damage to organs and is a highly flammable liquid and vapor. [4] It is a restricted substance in most of the world's countries. Its maximum concentration in consumer products such as hand sanitizers is highly regulated due to its inherent toxicity. For example, in the US products with more than 4 % methanol need to be labeled as poison, while in the EU hygiene products may consist of only up to 5 % methanol. [5]

2 Instrumentation and Experimental

Experiments were performed using a laser class 1 Cora 5001 Raman spectrometer with sample compartment offering an easy-to-use and safe way to measure Raman spectra (Fig. 1). Two sample sets were prepared and bottled into standard glass vials (4 mL; N13):

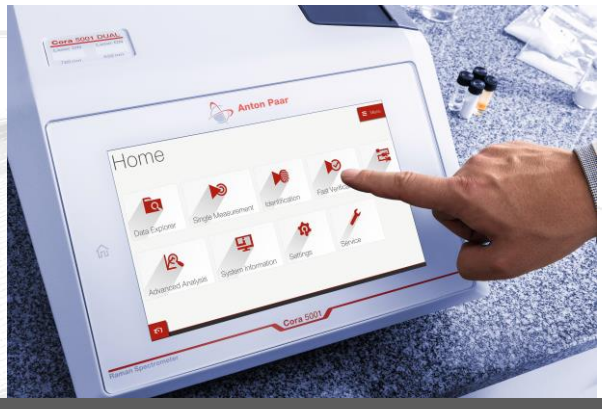

Fig. 1: Cora 5001 with sample compartment is an easy-to-use instrument due to its laser safety class 1, the implemented autofocus routine and its intuitive software

- Sample set A focusing on the active ingredient concentration: Samples were prepared with a variable concentration of 30–90 Vol% ethanol.
- Sample set B focusing on methanol adulteration: A commercial hand sanitizer based on ethanol as active ingredient was adulterated with methanol in a concentration range of 1–50 Vol%.

Focus optimization was performed on pure ethanol (set A) or pure hand sanitizer (set B) using the implemented autofocus option. Each sample was measured three times in random order with an excitation wavelength of 785 nm and a laser power of 450 mW. A baseline correction was applied and the resulting spectrum was analyzed with the implemented custom model “Simple Quantification Tool” focusing on the most intense Raman peaks at 882 cm^{-1} for ethanol and 1036 cm^{-1} for methanol.

3 Results

3.1 Quantification of active ingredient concentration (sample set A)

Using the Cora 5001 Raman, spectra of mixtures with varying content of the active ingredient ethanol were obtained as presented in Fig. 2. With decreasing ethanol concentration (and correspondingly higher water content), there is a peak shift of Raman peaks. The analysis in this report focusses on the C-C-O stretching vibration causing the most prominent signal. Its shift originates from increasing hydrogen bond interactions with rising amount of water molecules present in the mixture. Using the custom model “Simple Quantification Tool” it is possible to determine a linear correlation between the peak position of the C-C-O stretch vibration and the ethanol content (see Fig. 3). This correlation can be used to implement a quantification method for ethanol in hand sanitizer directly onto the device. Thus, the content of the active ingredient can be determined directly using Raman spectroscopy in a fast and non-destructive way, even through the container of the hand sanitizer.

3.2 Uncovering methanol adulteration of hand sanitizer (sample set B)

Using the Cora 5001 Raman, spectra of mixtures with varying content of methanol in hand sanitizer were obtained as presented in Fig. 4 focusing on the spectral region of 850-1200 cm^{-1} where the most prominent Raman peaks of methanol and ethanol are located. With increasing methanol concentration, the signal at 1036 cm^{-1} rises in intensity starting as a peak shoulder and increasing to an individual peak. Normalizing the data reveals a change in peak ratios of ethanol and methanol signals which can be used for quantification of the contaminants content in relation to the active ingredient of hand sanitizers. Analysis was performed using a python script but the implemented custom

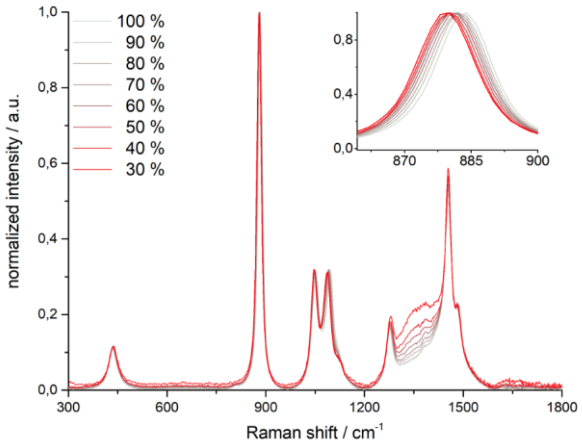

Fig. 2: Normalized Raman spectra of samples with varying ethanol content in the range of 30-100 Vol% ethanol. With decreasing ethanol content, the most intense signal shifts to lower wavenumbers which is presented in the close-up in the upper right corner

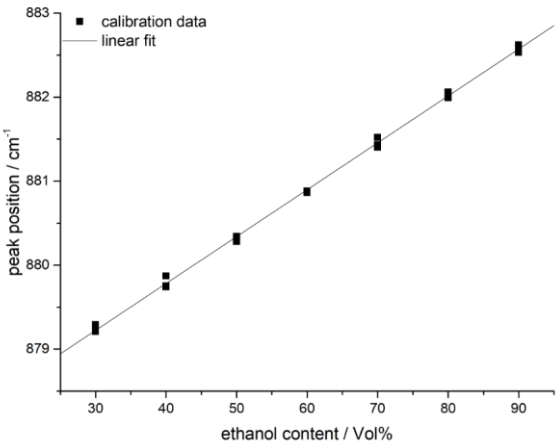

Fig. 3: Linear Correlation of ethanol concentration and peak position of most prominent Raman signal of ethanol

model “Simple Quantification Tool” can be used as well.

As shown in Fig. 5 there is a linear correlation between the peak height ratio of the peaks at 1036 cm^{-1} and 882 cm^{-1} originating from C-C-O stretch vibrations of methanol and ethanol, respectively. This correlation can be used to quantify the methanol content of hand sanitizers. Using a custom model, quantification is enabled directly on the device.

To evaluate the capabilities of this analysis the limit of detection (LoD) and the limit of quantification (LoQ) were determined as well. For the calculation of LoD and LoQ the following equation was used: [7]

$$limit = \frac{a \cdot \sigma_{s,ref}}{m}$$

a = 3 for LoD a = 10 for LoQ

$\sigma_{s,ref}$ = standard deviation of quantification metric of reference measurements

m = slope of linear calibration curve

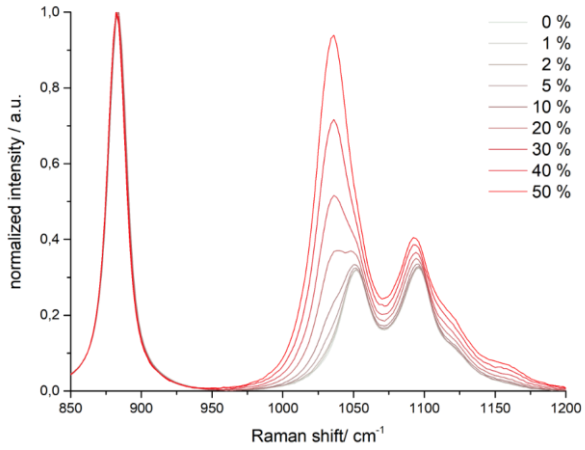

Fig. 4: Normalized Raman spectra of hand sanitizers adulterated with methanol in a concentration range of 1-50 Vol%. With increasing methanol content, the Raman signal at 1036 cm^{-1} rises

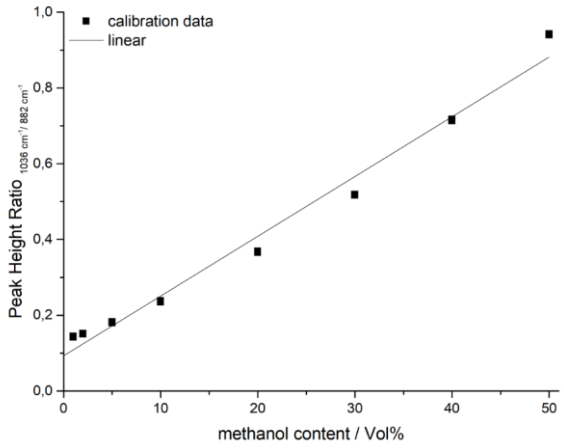

Fig. 5: Calibration curve for mixtures of methanol and hand sanitizer presenting a linear correlation of the peak intensity of the most prominent methanol signal and the methanol concentration

For the presented experiment the LoD was determined as 0.08 Vol% and a LoQ of 0.28 Vol%. Considering the ethanol content of the used hand sanitizer (here 95 %), this is equivalent to 0.7 g/L and 2.33 g/L related to pure ethanol, respectively. Since there are no specific regulations yet on the allowed methanol content in sanitizers, and as methanol poisoning usually arises from misuse of hand sanitizer as drinking alcohol substituent, those values are reviewed in the context of regulations for spirits. [6] Depending on the kind of spirits and the country the maximum amount of methanol allowed is in a range of 0.05–15 g/L. [8] With an LoD of 0.7 g/L the capabilities of the Cora 5001 rank in the lower concentration region of this range and will be sufficient in most scenarios. Evaluating its capabilities in the context of methanol in consumer products in general (limit 4-5 %) Cora 5001 is ideally suited for quality control. [5] Thus, Raman spectroscopy is a useful tool to prevent severe methanol poisoning and to protect consumers health.

4 Summary

The Cora 5001 Raman spectrometer is a useful tool to analyze the quality of hand sanitizers which are essential consumer goods in times of a pandemic to prevent infections. It enables fast, non-destructive measurements through bottles, and after an initial calibration, quantification is possible directly on the device. Two main quality issues leading to bans of hand sanitizers, as they pose a risk to consumers health, can be identified using Cora 5001. On the one hand, it can be used to ensure consumers use products with suitable active ingredient concentration, as it can detect Raman peak shifts caused by dilution with water. On the other hand, it not only uncovers adulteration with toxic methanol but also enables the quantification of the adulterant concentration with a limit of detection of 0.08 Vol% when analyzing peak height ratios of relevant Raman signals. Thus, Cora 5001 is a useful tool for evaluation of hand sanitizer quality which operates in a detection range of relevant adulterant limits in regulations & guidelines.

5 References

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[2] Application Report "How to Set Up a Functional Identification Method"; DocID E41IA033., 2020.

[3] https://www.epa.gov/sites/production/files/2016-09/documents/methanol. 02.06.21.

[4] https://echa.europa.eu/de/substance-information/-/substanceinfo/100.000.599. 02.06.21.

[5] https://www.methanol.org/wp-content/uploads/2020/04/Methanol-Safety-During-the-COVID-19-Pandemic-3.pdf 07.06.21.

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[7] K. Danzer, H. Hobert, C. Fischbacher und K.-U. Jagemann, Chemometrik-Grundlagen und Anwendungen, Springer-Verlag, 2001.

[8] European Union, „Regulation (EC) 2019/787 of the European Parliament and of the Council of 17 April 2019," *Official Journal of the European Union,* 2019.

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