Clean Hands and COVID: Keeping Hand Sanitizers Safe During a Pandemic

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Abstract

In response to increased demand for hand sanitizers due to the COVID-19 pandemic, the Agency released "Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) Guidance for Industry" (1) a guidance allowing non-traditional drug manufacturing sources to produce alcohol-based hand sanitizers (ABHS). As these manufacturers were previously unregulated by the Agency, quality assessment of their ABHS products due to safety and quality concerns was high priority. Label claim alcohol, percent alcohol content, and quantitation of impurities were determined as critical quality attributes for ABHS. Methanol (MeOH) was of particular concern due to the economically motivated adulteration with this toxic impurity. MeOH can replace ethanol (EtOH) or isopropanol (IPA) in ABHS, making its identification in surveyed samples vital. Additionally, the potential use of fuel grade ethanol by certain industry manufacturers, potentially introducing other impurities to their ABHS raised concerns and the need to test for these "fuel based" impurities. To ensure safety and quality of these products manufactured during the COVID-19 pandemic, two analytical methods for testing ABHS products were developed, validated, and employed by the Office of Testing and Research St. Louis (OTR-STL) in coordination with the Office of Quality Surveillance (OQS). One was a rapid semi-quantitative spectroscopic screening method capable of identifying and estimating alcohol content of sample (LOD MeOH = 3%), which allowed for the identification of non-conforming samples needing additional testing. The second was a gas chromatography-mass spectrometry (GC-MS) method which allowed for the quantitative and qualitative assessment of quality characteristics (alcohol identity, percent alcohol content, and impurities: LOD MeOH = 0.003%) of ABHS. To date over 345 samples have been collected by the Agency for laboratory testing. Both methods have been used successfully for the combined determination of alcohol identity, percent alcohol content, and impurity detection and quantitation.

Introduction

- ICH Q2B and USP guidelines were utilized to develop and validate these two methods for EtOH and IPA.
- Both testing methodologies were developed on a hand sanitizer manufactured in-house and then validated utilizing domestically manufactured ABHS.
- Spatially Offset Raman Spectroscopy (SORS) was utilized as an initial screen to prioritize samples for further laboratory testing by GC-MS.
- GC-MS was utilized both for Assay and Impurity testing.

Methods

RAMAN SPECTROSCOPY METHOD

A variant of Raman spectroscopy called spatially offset Raman spectroscopy (SORS), that is effective in through-container rapid screening of drug products was used for this method. USP general chapters <1120> and <858> (2,3) were followed for instrument qualification, procedure and method validation.

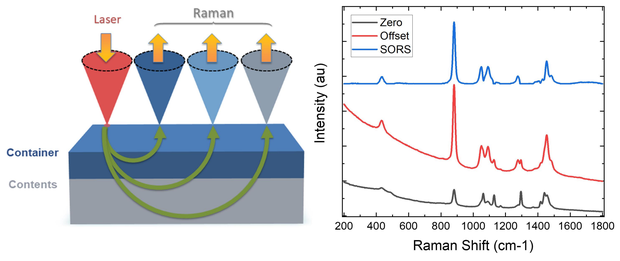

Figure 1. Diagram of SORS application

GC-MS Method

Instrument
Agilent 7010B GC-TQ with 7693 Autosampler and 8890 GC

Column
Agilent DB-624, 30m x 0.25mm x 1.4µm

Settings
Carrier Gas: Helium
Run Time: 15.667min
Flow Rate: 1.0mL/min
Injector Temp: 250°C
Injection Vol.: 1.0µL
Injection Type: Pulsed Split (50:1 split w/ 25psi pulse for 0.5min)
Oven Temp Gradient: 40°C(5min) to 240°C at 30°C/min (4min)
MSD Source Temp: 230°C
MSD Quad Temp: 150°C
Ionization Mode: EI (70eV)

Time (min)	Scan Range or SIM Ions	Gain	Dwell Time (ms)
0 - 2.6	30 - 45	5	100
2.6 - 4	30 - 65	1	100
4 - 6.8	30 - 105	1	100
6.8 - 7.3	78, 74, 51, 43 (Unit Resolution)	2	100,50,50,50
7.3 - 15.667	30 - 105	1	100

Table 1. MSD Settings

Results and Discussion

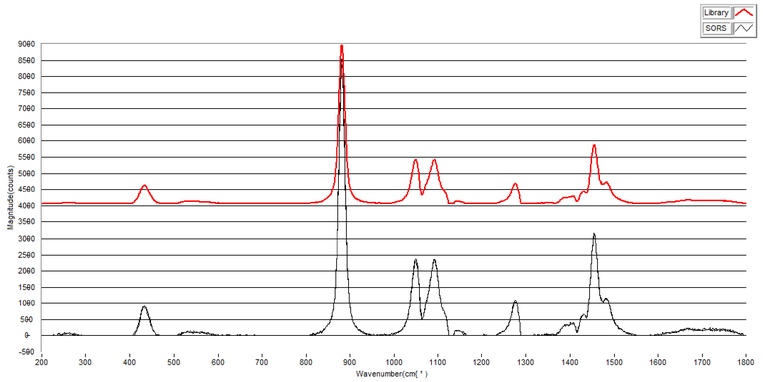

Figure 2. ABHS sample spectrum obtained by SORS. Confirmed for ethanol at 882 cm^{-1} (C-C stretching), 1049 cm^{-1} (C-O stretching), 1092 cm^{-1} (CH_3 rocking), and

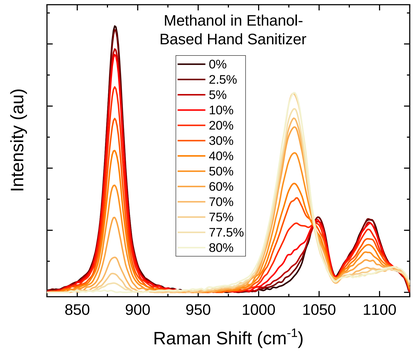

Figure 3. SORS spectra showing methanol detection. MeOH shift is at ~1030cm^{-1} (C-O stretching).

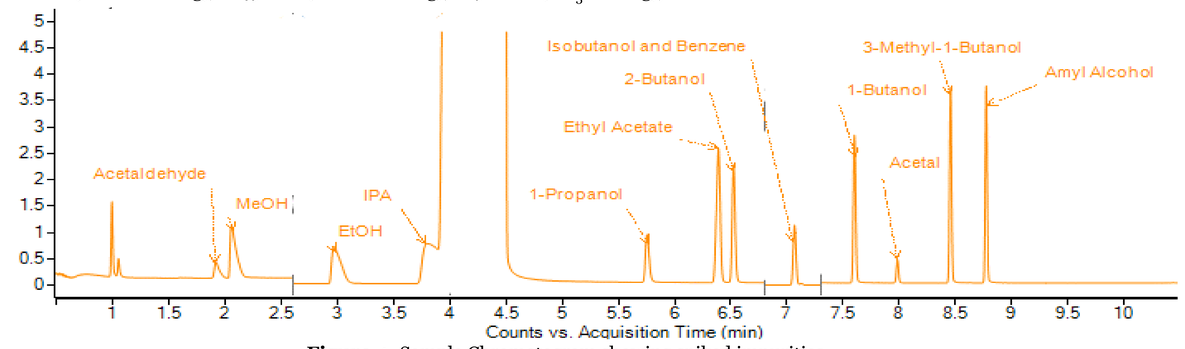

Figure 4. Sample Chromatogram showing spiked impurities.

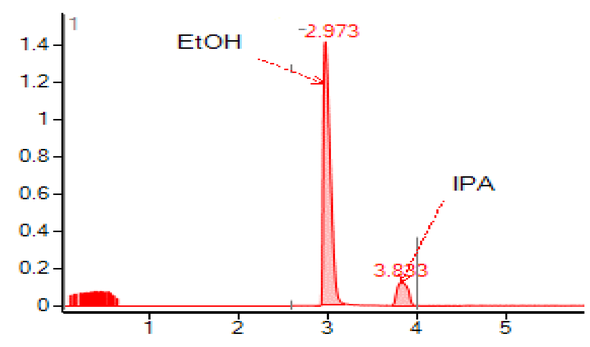

Figure 5. GC-MS Sample Chromatogram showing EtOH Assay

Conclusion

- Two analytical methods were developed, validated, and implemented to assess the safety and quality of ABHS manufactured domestically by non-traditional sources.
- These methods were used sequentially to successfully determine alcohol identity, percent alcohol content, and impurities of domestic ABHS.

References

(1) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-temporary-policy-preparation-certain-alcohol-based-hand-sanitizer-products-during
(2) USP43-NF38 – 7856
(3) USP43-NF38 1S - online