A protocol for ethanol or isopropanol dosage in hand rub gels

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Method Article

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Abstract

A method of determination of the ethanol or isopropanol content in hydro-alcoholics hand rub solutions is reported. Based on quantitative ^{1}HNMR (q^{1}HNMR), the results are obtained rapidly and accurately. The method is available for viscous solutions to which other simpler techniques do not apply.

Introduction

As the spread of the COVID-19 pandemic accelerates around the world, many low- and middle-income countries are still struggling to access the diagnostic tests they desperately need to control the disease. Moreover, passive protection methods such as masks and hydro-alcoholic gels are the first means of defence to avoid chaotic spread of the virus among the population. The World Health Organization (WHO) provides a protocol that was taken into consideration in many national legislations.[1] In France, at the beginning of the pandemic, we applied this protocol to fabricate several dozens of litres of hydro-alcoholic mixture at our institute and the contents of ethanol or isopropanol in grams per grams of solution was determined by ^{1}H quantitative NMR (qNMR). If the contents of alcohols in liquids gels can be approximatively measured using a simple alcohol-meter, this technic is less appropriate for viscous liquids containing gelling agents. We report here a method of ethanol content measurement using ^{1}H quantitative NMR (^{1}H qNMR). Our intention is to remind the scientific community of this well-known technic.

Reagents

D2O

3-(trimethylsilyl)-1-propanesulfonic acid di sodium salt (TSPA, CAS: 2039-96-5, 97% purity).

Equipment

NMR Brucker 400MHz.

3mm NMR tubes (Norell).

Balance (0.01 mg accuracy).

4 mL flat bottom screw neck vial equipped with a centred hole, screw closure closed by a silicone PTFE

syringe (Inject®-F 1 ml)

needle (Henke Sass Wolf, Germany, 0.6X25mm)

Procedure

Sample preparation:

- Masses are weighed using a Mettler Toledo balance (0.01 mg accuracy) into a 4 mL flat bottom screw neck vial equipped with a centred hole closed by a silicone PTFE (Macherey-Nagel, Germany).

- The standard is weighted first, then 2 mL of D_2O are introduced.

- The vial is then closed and gently shaken until all the solid dissolves.

- The gel is added into the vial with a syringe (Inject®-F 1 ml) equipped with a needle (Henke Sass Wolf, Germany, 0.6X25mm) through the silicone join in order to minimize the evaporation of ethanol. - The solution was shaken, then 600 mL were transferred into 3 mm standard NMR tubes (Norell) for analysis.

Pulse Program.

Single pulse, without carbon decoupling ('zg' with 90° pulse). Data Points (acquired): 64 K. NS=64. Relaxation delay: D1=60s. Acquisition Time: 4s. Spectral window for proton: SW=30ppm and O1: 7.5 ppm (the sample Temperature is fixed at 19 °C ± 0.1 K).

Post-Acquisition Processing.

Performed with ACDLABS software (1.2, academic version). Zero Filling: to 256K. Line Broadening: LB = 0.1 Hz. Phasing: manually. Baseline Correction: 6th order polynomial (for each signal measured a ratio signal/noise>100 is verified).

Troubleshooting

It is important to use a screw neck vial closed by a silicone PTFE and an appropriate syringe and needle to minimize ethanol evaporation during the sample preparation.

Time Taken

Sample preparation: 10 minutes

NMR acquisition: 1h

NMR processing: 10 minutes

Anticipated Results

Quantitative NMR is a valuable method because the measured signals represent a direct measurement of the composition if correct inter-pulse delay are adequately chosen.[2] Therefore, in presence of an internal

reference of known purity, the composition of a sample can be determined accurately using a single spectrum/ integration sequence (so-called absolute quantification). For this purpose, we used 3-(trimethylsilyl)-1-propanesulfonic acid di sodium salt (TSPA, CAS: 2039-96-5, 97% purity) as standard (also used as chemical shift reference) and D_2O for NMR solvent.

After proper weighting of the standard and the gel, the masses of ethanol or isopropanol contained in the samples are calculated by equations 1:

$$Masse = [\ 15 \times 0.97 \times M^{(Alc)} \times SInt^{Alc} \times m^{(Std)}\ ]/[\ 218.3 \times n^1H^{(Alc)} \times SInt^{(Std)}\ ]$$

$$= [\ 0.06665 \times M^{(Alc)} \times SInt^{Alc} \times m^{(Std)}\ ]/[\ n^1H^{(Alc)} \times SInt^{(Std)}\ ] \quad \text{Eq.1}$$

Where $M^{(Alc)}$, $n^1H^{(Alc)}$ and $m^{(Std)}$ are respectively the molecular mass, the number of integrated proton and the weighted masse of the chosen alcohol; $SInt^{(Alc)}$ and $SInt^{(Std)}$ being the sum of the integrals for the chosen alcohol and the standard; 15 and 218 and 0.97 being the total number of proton, the molecular mass and the purity of the standard.

For ethanol and isopropanol respectively, the equation resumes to:

$$Mass^{(ethanol)} = [\ 0.615 \times SInt^{(Alc)} \times m^{(Std)}\ ]/\ SInt^{(Std)} \quad \text{Eq. 2}$$

$$Mass^{(isopropanol)} = [\ 0.572 \times SInt^{(Alc)} \times m^{(Std)}\ ]/\ SInt^{(Std)} \quad \text{Eq. 3}$$

We found 75% and 68% for handrub solutions produced according to the WHO protocols. The weighted masses were TSPA, 18.14mg, ethanolic gel: 34.69mg (Figure 1) and TSPA: 41.85mg, isopropanol gel: 25.95mg (Figure 2).

References

1. https://www.who.int/gpsc/5may/Guide_to_Local_Production.pdf?ua=1

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