Citric acid - a precursor to a respiratory sensitiser in e-cigarettes?

S Costigan[1], C Rawlinson[2,*], J Frosina[2], K McAdam[1]

[1]Nicoventures and [2]BAT, R&D, Southampton, U.K.

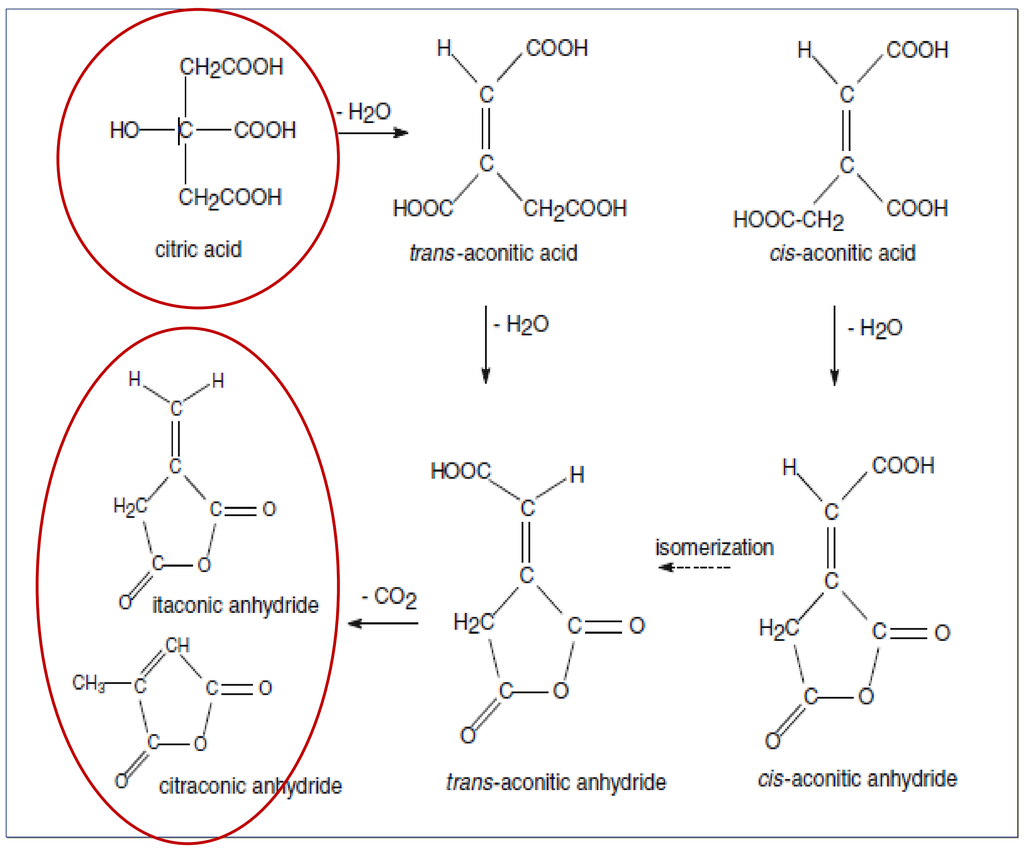
*Affiliation at the time of the research reported here

Poster **148** at SRNT Annual Meeting, 7th-11th March 2017, Florence, Italy.

WHAT COULD THEORETICALLY HAPPEN?

Citric acid can thermally degrade into itaconic and citraconic anhydrides

When citric acid is heated, dehydration and decarboxylation processes, depending on experimental circumstances reported to commence around 175°C [1] or 203°C [2], can result in the formation of aconitic acid, which further reacts to citraconic anhydride [1-3]. This is readily transformed to the isomeric itaconic anhydride. The two isomeric forms are difficult to separate chromatographically and have near-identical mass spectra. And so are often reported as a sum of both isomers.



1. Serban Moldeveanu. 2009. "Pyrolysis of Organic Molecules: Applications to Health and Environmental Issues“ Publisher: Elsevier Science. 744p. ISBN: 9780080932156.
2. D. Wyrzykowski, E. Hebanowska, G. Nowak-Wiczk, M. Makowski, L. Chmurzyński. 2011. Journal of Thermal Analysis and Calorimetry, Volume 104, Issue 2, pp 731–735.
3. Barbooti MM, Al-Sammerrai A. Thermochim Acta. 1986;98:119–26.

Itaconic and citraconic anhydrides are respiratory sensitisers

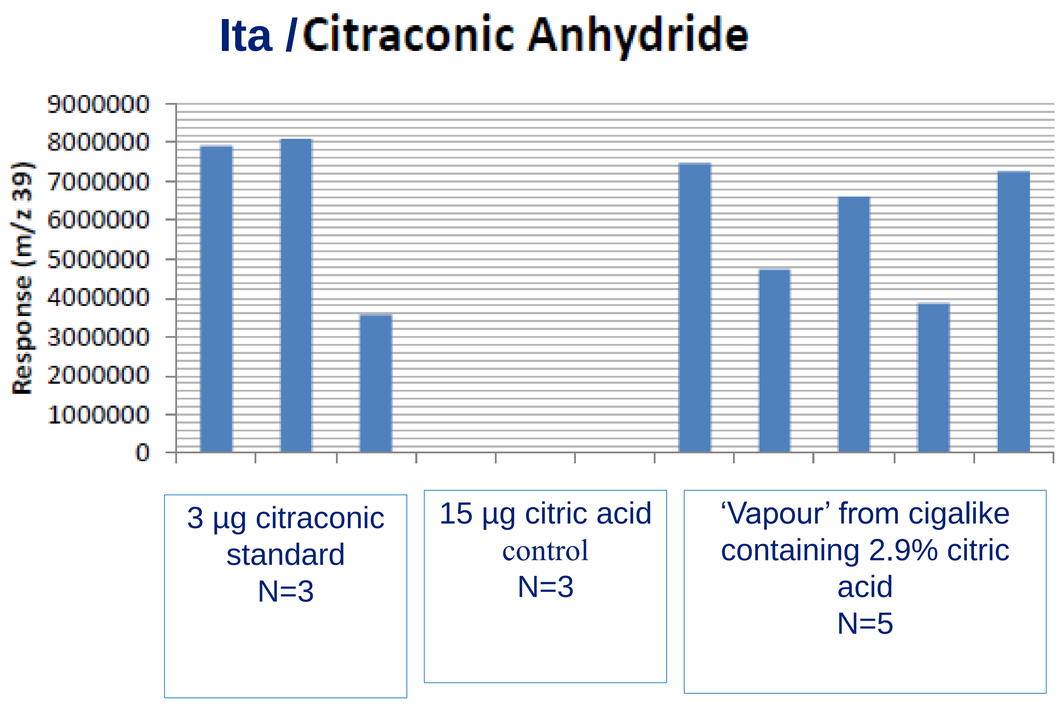
Several organic acid anhydrides are known to cause hypersensitivity and can induce both contact sensitisation and occupational asthma [1]. The respiratory sensitisation hazard was confirmed for, amongst others, citraconic anhydride in a guinea pig [2] and Brown Norway rat model [3]. Given ready conversion between citraconic and itaconic anhydrides and their close structural relationship, it is prudent to assume the citraconic data can be read across to itaconic as well.

1. Casarret and Doull (2013) Toxicology: the basic science of poisons. Mc Graw Hill Education.
2. Welinder H, Zhang X, Gustavsson C, Bjoerk B, Skerfving S (1995) Toxicology 103: 127-136.
3. Zhang XD, Welinder H, Jonsson BA, Skerfving S (1998) Scand J Work Environ Health 24: 220-227.

CAN THIS HAPPEN IN E-CIGARETTES?

Measured citraconic/itaconic anhydride in ‘vapour’ from cigalike containing e-liquid with citric acid

From an e-liquid containing 2.9% citric acid, the estimated amount of citraconic anhydride in the e-cigarette aerosol ranged between 51 mg/m^3 and 98 mg/m^3.



Method

Used a commercially available cigalike product. Filled cartridge with e-liquid consisting of PG/VG/water/nicotine and 2.90% mono hydrate citric acid.

The e-cigarette was sampled 5 times, using a single ‘square-wave’ 35 mL, 2 second puff. Captured aerosol in Tenax/Sulficarb thermal desorption (TD) tube and analysed gas chromatography coupled to time-of-flight mass spectrometry (GC-TOFMS).

Three blank TD tubes were fortified with 3 µg of citraconic anhydride standard as a positive control. Three more blank TD tubes were fortified with 15 µg of citric acid standard, to demonstrate the anhydrides were not artefactually formed in the presence of excess quantities of acid.

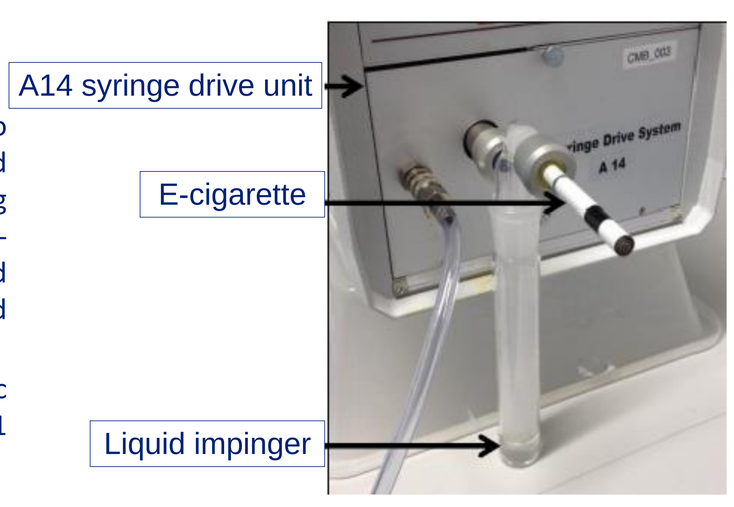
Confirmed presence of anhydride with second analytical method

Although the TD inlet was optimised to minimise the formation of citraconic anhydride, to confirm that the detected citraconic anhydride was not formed as an artefact of the analytical technique (TD being heavily reliant on thermal transfer), analysis of a liquid sample was also conducted. Itaconic/citraconic anhydride was confirmed in all 6 replicates.

Method

Used same cigalike product and e-liquid. Three replicates of two separate e-cigarettes were sampled into separate impingers containing 10ml diethyl ether, using 10 x ‘square-wave’ 80 mL, 3 second puffs (30 second puff interval). Analysed using liquid injection GC-TOFMS.

The limit of detection for citraconic anhydride was determined to be 1 µg/mL.



Inlet temperatures above 150°C resulted in detectable degradation of citric acid, resulting in the formation of citraconic anhydride. The optimised conditions used an inlet ramp from 55°C to 100°C, at 5°C/sec.

CONCLUSION & RECOMMENDATION

- Citric acid in an e-liquid can lead to significant amounts of citraconic and/or itaconic anhydride in the ‘vapour’ due to thermal degradation from the vaping process. These are known to be respiratory sensitisers.
- It is recommended that the potential for formation of citraconic and itaconic anhydrides should be investigated before commercialisation of e-liquids containing citric acid.
- Further work a current, higher power device is underway.

www.bat-science.com
@BAT_Sci
Correspondence: Sandra_Costigan@bat.com