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Short communication

# The total margin of exposure of ethanol and acetaldehyde for heavy drinkers consuming cider or vodka

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ABSTRACT

Heavy drinkers in Scotland may consume 1600 g ethanol per week. Due to its low price, cider may be preferred over other beverages. Anecdotal evidence has linked cider to specific health hazards beyond other alcoholic beverages. To examine this hypothesis, nine apple and pear cider samples were chemically analysed for constituents and contaminants. None of the products exceeded regulatory or toxicological thresholds, but the regular occurrence of acetaldehyde in cider was detected. To provide a quantitative risk assessment, two collectives of exclusive drinkers of cider and vodka were compared and the intake of acetaldehyde was estimated using probabilistic Monte–Carlo type analysis. The cider consumers were found to ingest more than 200-times the amount of acetaldehyde consumed by vodka consumers. The margins of exposure (MOE) of acetaldehyde were 224 for the cider and over 220,000 for vodka consumers. However, if the effects of ethanol were considered in a cumulative assessment of the combined MOE, the effect of acetaldehyde was minor and the combined MOE for both groups was 0.3. We suggest that alcohol policy priority should be given on reducing ethanol intake by measures such as minimum pricing, rather than to focus on acetaldehyde.



## 1. Introduction

Previous research has surveyed heavy drinkers in Scotland, who consume 200 UK units and more per week (1 UK unit being 8 g of ethanol), i.e. 1600 g ethanol per week. White cider made an important contribution to the weekly intake, likely facilitated by its low price per unit (ppu) of alcohol (Black et al., 2014). Because some ciders are among the cheapest forms of alcohol sold within the UK, some drinkers were observed who exclusively consumed white cider. During the survey, many drinkers confirmed that white cider represented their first choice of drink when funds are low (Black et al., 2014). Cider may also be consumed in more risky locations than other beverage types (Forsyth and Barnard, 2000).

Anecdotal evidence has linked cider consumption to gastric complaints (Black et al., 2014) and "Alcohol Concern" in England produced a recent report also providing anecdotal evidence of certain harmful effects of cider (Goodall, 2011). A study about the antioxidant potential of alcoholic beverages has indeed suggested that its low values in white drinks such as cider may pose an extra risk for liver cirrhosis (Gill et al., 2010).

Other reports (without substantiating evidence) suggested that "ciders have traditionally been regarded as high in 'fusel alcohols',

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particularly 2-phenyl ethanol, which has often been attributed to their low nutrient status" (Lea, 2004). A French study in the 1970s detected increased relative risks for oesophageal cancer for consumers of cider compared to other alcoholic beverages. The extra risk was speculated as being due to the presence of carcinogens in cider (Tuyns et al., 1979). However, the literature so far lacks any evidence that cider may be different in its content of "carcinogens" from other beverages (see e.g. Lachenmeier et al. (2012) for review about carcinogens in alcoholic beverages).

White cider's low price alone may promote high doses and this will have an impact on health. However, given the weight of anecdotal evidence, it seemed important to explore whether or not cider consumption may contain constituents or contaminants other than ethanol, which are potentially pathogenic. An official Scottish Government publication has suggested there is a need for more drink-specific data (Beeston et al., 2014). For this reason, we have analysed a collective of cider samples from Scotland for health-relevant constituents and contaminants, and provide a risk assessment for the cumulative effects using the combined margin of exposure ($MOE_T$) procedure (for background information on the margin of exposure approach see EFSA (2005) and US EPA (1995), the $MOE_T$ procedure has been reviewed by US EPA (2001) and Wilkinson et al. (2000)).

## 2. Materials and methods

Nine samples (7 apple and 2 pear ciders) were obtained from supermarkets during May 2014 in Scotland. The type and brands of cider were chosen to be typical of those reported as consumed by the participants of the Black et al. (2014) study including the different cider categories based on alcoholic strength. Details on sample type and purchase price are provided in Table 1. The samples were screened using Fourier transform infrared (FTIR) spectroscopy (Lachenmeier, 2007) and nuclear magnetic resonance (NMR) spectroscopy (Godelmann et al., 2013) for constituents and contaminants. A standard enzymatic assay was applied to determine total $SO_2$. Volatiles including acetaldehyde were analysed using gas chromatography (for details on parameter selection and chemical methodology, see Lachenmeier et al. (2011b)). For comparison, data on acetaldehyde content of vodka were taken from the literature (Lachenmeier and Sohnius, 2008) and additional data of vodka sampling and analysis in Germany between 2010 and 2014 (n = 106). Results for volatiles are reported in grams per hectolitre of pure (100%) alcohol (g/hl pa). The remaining results are reported in mg/L of the original beverage.

Alcohol consumption data were taken from two collectives of heavy drinkers, who exclusively consumed cider or vodka. In the sample of 639 participants, 161 reported white cider consumption and within those 72 drank it exclusively in the week recorded (=last week or in a typical week). 147 reported vodka consumption, from which 95 were exclusive vodka consumers. Briefly, in addition to demographic data participants responded to a questionnaire which documented a 'typical' or 'last week' alcohol consumption (type, brand, volume, price, place of purchase). Details on the epidemiologic study were previously published (Black et al., 2014). Average body weights for male and female adults were obtained from EFSA (2012).

The data of the chemical analysis and alcohol consumption were combined to estimate the exposure of the drinkers to the compounds ethanol and acetaldehyde. The methodology for quantitative risk assessment using the margin of exposure (MOE) approach (EFSA, 2005; US EPA, 1995) was based on a previous study conducted for compounds in alcoholic beverages (Lachenmeier et al., 2012) with the exception that probabilistic exposure estimation was conducted (Lachenmeier et al., 2014; Lachenmeier and Rehm, 2013b; Lachenmeier et al., 2013). The MOE is defined as the ratio between the lower one-sided confidence limit of the benchmark dose (BMDL) and estimated human intake of the same compound. BMDL values for acetaldehyde (Lachenmeier et al. (2009) based on Soffritti et al. (2002)) and ethanol (Lachenmeier et al. (2011a) based on NTP (2004) and Beland et al. (2005)) were taken from the literature.

In addition to the individual MOE values for ethanol and acetaldehyde, the combined margin of exposure ($MOE_T$) was calculated

**Table 1**
Sample description, purchase price and selected analytical results[a] of cider samples from Scotland.

| Sample number | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| Cider type | White | White | Pear | Pear | Cheap amber | Cheap amber | Cheap amber | Amber "quality cider" | Amber "quality cider" |
| Purchase price (pence per UK unit) | 15.3 | 29 | 21.6 | 33.3 | 18.8 | 23.8 | 25 | 32.5 | 31.9 |
| Alcoholic strength (% vol) (labelling) | 7.5 | 7.5 | 5.3 | 4.5 | 5.3 | 4.2 | 4 | 5 | 4.7 |
| Alcoholic strength (% vol) (analysis) | 7.4 | 7.3 | 5.2 | 4.2 | 5.2 | 4.2 | 4.1 | 5.0 | 4.8 |
| Total sugar (g/L) | 11 | 3 | 46 | 46 | 10 | 16 | 15 | 16 | 31 |
| Energy (kJ/L) | 1940 | 1750 | 2050 | 1810 | 1410 | 1240 | 1180 | 1410 | 1690 |
| Total $SO_2$ (mg/L) | 59 | 74 | 56 | 63 | 65 | 66 | 55 | 42 | 76 |
| Acetic acid (mg/L) | 180 | 168 | 123 | 177 | 131 | 114 | 229 | <100 | 112 |
| Fumaric acid (mg/L) | 17 | n.d. (<5) | 32 | 34 | 24 | 24 | 16 | 25 | 10 |
| HMF (mg/L) | n.d. (<5) | n.d. (<5) | n.d. (<5) | n.d. (<5) | 14 | 6 | 8 | n.d. (<5) | n.d. (<5) |
| Furfural (mg/L) | n.d. (<2) | n.d. (<2) | n.d. (<2) | n.d. (<2) | 3 | 3 | n.d. (<2) | n.d. (<2) | n.d. (<2) |
| Malic acid (g/L) | 3.3 | 0.8 | 4.4 | 4.4 | 3.8 | 3.6 | 2.5 | 3.2 | 2.3 |
| Lactic acid (mg/L) | n.d. (<200) | n.d. (<200) | n.d. (<200) | n.d. (<200) | n.d. (<200) | n.d. (<200) | 256 | 319 | n.d. (<200) |
| Acetaldehyde (g/hl pa) | 10 | 20 | 31 | 14 | 16 | 20 | 22 | 12 | 27 |
| Methanol (g/hl pa) | n.d. (<4) | 6 | 4 | 5 | n.d. (<4) | n.d. (<4) | 6 | 5 | 18 |
| 1-Propanol (g/hl pa) | 9 | 12 | 11 | 8 | 10 | 10 | 8 | 34 | 7 |
| Iso-butanol (g/hl pa) | 41 | 17 | 27 | 42 | 25 | 14 | 32 | 9 | 21 |
| Amyl alcohols (g/hl pa) | 200 | 96 | 143 | 225 | 131 | 120 | 166 | 132 | 170 |
| 2-Phenyl ethanol (g/hl pa) | 5 | n.d. (<2) | 5 | 8 | 4 | 5 | 7 | 4 | 7 |
| Ethyl acetate (g/hl pa) | 28 | 33 | 29 | 24 | 26 | 25 | 37 | 32 | 22 |
| Ethyl lactate (g/hl pa) | n.d. (<6) | n.d. (<6) | n.d. (<6) | n.d. (<6) | n.d. (<6) | n.d. (<6) | 12 | 11 | n.d. (<6) |

[a] Not detectable (n.d.) in all samples (detection limit in mg/L in brackets): citric acid (200 mg/L), tartaric acid (0.5 mg/L), acetoine (10 mg/L), formic acid (5 mg/L), gluconic acid (400 mg/L), putrescine (50 mg/L), cadaverine (50 mg/L), pyruvic acid (20 mg/L), 4-aminobutanoic acid (120 mg/L), alanine (35 mg/L), arginine (150 mg/L), proline (150 mg/L), caftaric acid (15 mg/L), epicatechin (30 mg/L), gallic acid (25 mg/L), shikimic acid (20 mg/L), trigonelline (10 mg/L), benzoic acid (10 mg/L), sorbic acid (10 mg/L), salicylic acid (10 mg/L), 1-butanol (2 g/hl pa), 2-butanol (2 g/hl pa), 1-hexanol (2 g/hl pa), benzyl alcohol (2 g/hl pa), methyl acetate (6 g/hl pa), benzyl acetate (1 g/hl pa), ethyl benzoate (1 g/hl pa), and benzaldehyde (1 g/hl pa).