Unrecorded alcohol – no worries besides ethanol: a population-based probabilistic risk assessment

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CHAPTER 11. UNRECORDED ALCOHOL – NO WORRIES BESIDES ETHANOL: A POPULATION-BASED PROBABILISTIC RISK ASSESSMENT

Dirk W. Lachenmeier & Jürgen Rehm

Summary

In the WHO European region, 22% of the total alcohol consumption was unrecorded in 2005, for example, in the form of illicit or counterfeited alcohol, home-produced or surrogate alcohol. According to conjectural evidence, unrecorded alcohol consumption has been associated with an increased toxicity due to regular contamination. The AMPHORA project has studied the contamination status by analysing samples of unrecorded alcohol from 16 countries in Europe. Using these data, this article provides a detailed population-based risk assessment using a Monte-Carlo type probabilistic methodology for the following substances, most regularly found in unrecorded alcohol (from an analysis of 50 substances in total): ethanol, ethyl carbamate, acetaldehyde, methanol, copper, lead, nickel, manganese, boron, and aluminium. By calculating the margin of exposure, ethanol was found to be the compound posing the highest risk, clearly above toxicological thresholds, while average scenarios for all other substances did not exceed such thresholds.

Our results show that the composition of unrecorded alcohol in the European region poses no public health risks beyond the ethanol-specific harms inherent to any type of alcoholic beverage. The probabilistic exposure assessment also clearly invalidates assumptions of contamination as a factor in increased alcohol-related mortality caused by unrecorded alcohol consumption. Instead, we think that this higher mortality might be due to more detrimental drinking patterns associated with unrecorded alcohol consumption, brought about by lower prices in combination with higher alcoholic strengths.

Policy measures should aim to reduce unrecorded consumption in general, rather than focusing on specific contamination problems.

This study uses the **Margin of Exposure** approach (**MOE**). The MOE is the ratio of the lower border of the toxic threshold of the consumed substance (for example ethanol or acetaldehyde) divided by the estimated intake of the substance. Thus, for example a MOE of 1 means that the amount consumed is the same as the dose that is considered toxic. An MOE of 10 means that the amount consumed is only ten times lower than the dose that is considered toxic. An MOE of 10,000 means that the amount consumed is ten thousand times lower than the dose that is considered toxic. For genotoxic carcinogens, (which ethanol, as well as acetaldehyde are), the European Food Safety Authority indicates an MOE of 10,000 as the cut off point for high public health risks. This means that the amount consumed should be at least 10,000 times lower than the level considered toxic.

Introduction

Unrecorded alcohol is any alcohol that is either not taxed as an alcoholic beverage and/or not registered in the jurisdiction where it is consumed (Lachenmeier, 2012; Rehm, Kanteres & Lachenmeier, 2010). Unrecorded alcohol products include alcoholic beverages brought into the country via cross-border shopping, homemade, informally-produced alcohol, illegally-produced or smuggled alcohol products, as well as surrogate alcohol that is not officially intended for human consumption (see classification in Lachenmeier, Sarsh & Rehm, 2009). Some common examples of surrogate alcohol include mouthwash, perfumes, and eau-de-colognes (Lachenmeier, Sarsh & Rehm, 2009). In the WHO European region, the average unrecorded alcohol consumption per capita for adults was 2.67 litres of pure ethanol in 2005, which is 22% of the total alcohol consumption in the region (Lachenmeier et al., 2011a). Surrogate alcohol is widely consumed in Russia and countries of central and eastern Europe (Lachenmeier, Rehm & Gmel, 2007).

One of the main problems with these unrecorded alcohol products is that some of them, such as homemade beverages, are not subject to regulatory controls to ensure that their composition is free of contaminants or toxic compounds which could potentially harm health, while others are produced without human consumption in mind entirely (Lachenmeier et al., 2011b).

Problematic compounds can come from spoilage during the fermentation (e.g. very high levels of higher alcohols (with more carbon atoms than ethanol, such as methylbutanol or propanol), ethyl acetate or acetaldehyde), contamination during processing (e.g. accumulation of metals such as lead) and/or the presence of chemical compounds related to the 'denaturing' of alcohol for non-beverage uses (e.g. methanol, diethyl phthalate). Some of these compounds can be carcinogenic, hepatotoxic, or teratogenic, if thresholds are exceeded. But, surprisingly, there is only a very limited scientific literature studying the composition of homemade and surrogate alcohols as well as examining their potential harm to health. Most of the alarmist reports about the "health threats" of unrecorded alcohol are based in conjecture rather than science (Lachenmeier & Rehm, 2009). To rectify the paucity of scientific data, the AMPHORA project has focused its efforts on analyzing the chemical composition of unrecorded types of alcohol. For this, samples of unrecorded alcohol were collected and analyzed from 16 European countries. A total number of 115 samples were analysed (81 spirits, 32 wine products and 2 beers). About half of the beverages presented abnormal parameters, the most common being ethyl carbamate contamination (n=29), and elevated levels of copper (n=20), manganese (n=16) and acetaldehyde (n=12). Apart from 10 of the samples, all other parameters (including methanol, higher alcohols, phthalates) did not exceed normative thresholds (Lachenmeier et al., 2011a).

At first sight, these results (i.e. non-compliance of 50% of samples) may sound alarming. However, exceeding normative thresholds cannot be directly interpreted as constituting an acute health risk for the consumer, as the thresholds are typically based on safety factors of 100 and higher. For example, the vodka methanol limit in the European spirits regulation (European Parliament and Council, 2008) is 500 times below that of the maximum concentration tolerable for humans (Lachenmeier et al., 2011b).

In this study, an approach other than the comparison with regulatory limits is applied for risk assessment, namely, the margin of exposure (MOE). To accomplish this, we combined the data from the AMPHORA project with other surveys on unrecorded alcohol, and applied a probabilistic Monte-Carlo-type method to provide a population-based exposure estimation. The exposure was then compared with the toxicological threshold for each compound to

calculate the MOE, which is an indicator that can be used to judge comparatively the risk of compounds in mixtures, and to facilitate the prioritization of risk management actions (EFSA, 2005; IPCS, 2009; Lachenmeier, Przybylski & Rehm, 2012). This approach allows us, for the first time, to make a judgement about the risk of unrecorded alcohol and how it compares with and contributes to the risk generated by legal and recorded ethanol. The results will be used to point out options for alcohol policy.

What we did

The first step in every risk assessment study of constituents and contaminants in foods and beverages is the selection of compounds. The selection of substances and the decision to examine their occurrence in unrecorded alcoholic beverages was based on results from surveys conducted as part of the AMPHORA project in several European countries (Lachenmeier et al., 2011a), and combined with data from other surveys conducted with similar research methodology in Poland (Lachenmeier et al., 2009), Ukraine (Lachenmeier et al., 2010b) and Russia (Solodun et al., 2011).

From the more than 1,000 different components that may occur in alcoholic beverages (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 1988), we had previously selected a sub-group of 50 compounds for chemical analysis in our samples of unrecorded alcohol by applying a risk-oriented approach (Lachenmeier et al., 2011b). From those compounds only 9 regularly exceeded the maximum limits available for drinking water or wine (Lachenmeier et al., 2011a), so we selected these substances for more detailed exposure assessment in this study. Ethanol was additionally included as major toxic compound of unrecorded alcohol, so that 10 substances in total were compared in this study.

The following list shows substances that were absent in most samples and did not exceed predefined thresholds of toxicity in any sample (see Lachenmeier et al. (2011b) for details), and were therefore excluded from our exposure assessment: 1-propanol, 1-butanol, 2-butanol, iso-butanol, amyl alcohols, 1-hexanol, benzyl alcohol, 2-phenyl ethanol, methyl acetate, benzyl acetate, ethyl lactate, ethyl caprylate, ethyl benzoate, benzaldehyde, thujone, chloride, nitrate, phosphate, sulphate, dimethyl phthalate, diallyl phthalate, dibutyl phthalate, n-butylbenzyl phthalate, diethylhexyl phthalate, diheptyl phthalate, di-n-octyl phthalate, di-ethylhexyl adipate, zinc, chromium, antimony, arsenic, tin, and selenium.

Furthermore, the following substances, occurring above limits in only single samples, were also excluded: ethyl acetate, cadmium, diethyl phthalate, diisobutyl phthalate, and polyhexamethyleneguanidine hydrochloride.

The remaining substances, included for assessment, were ethanol, ethyl carbamate, acetaldehyde, methanol, copper, lead, nickel, manganese, boron, and aluminium.

The methodology for comparative quantitative risk assessment was based on a previous study (Lachenmeier, Przybylski & Rehm, 2012) with the only difference being that probabilistic exposure estimation was conducted.

The toxicological thresholds for the selected substances, for which we used benchmark doses (BMD), where available, or ‘no observed effect levels’ (NOEL) or ‘no observed adverse effect levels’ (NOAEL), were typically identified in monographs of national and international risk assessments bodies such as WHO, International Programme on Chemical Safety (IPCS), JECFA, US Environmental Protection Agency (EPA) and EFSA (EFSA, 2010; IPCS, 1997; US EPA, 2005; Vavasour et al., 2006; WHO, 1982; WHO, 2003; WHO, 2005; WHO, 2011), and, if unavailable

from these sources, from our own studies (Lachenmeier, Kanteres & Rehm, 2009; Lachenmeier, Kanteres & Rehm, 2011).

The MOE approach was used for risk assessment (EFSA, 2005; US EPA, 1995). The MOE is defined as the ratio between the lower one-sided confidence limit of the BMD (BMDL) or NOEL/NOAEL and estimated human intake of the same compound.

Calculations of population-based exposure and of MOE require the following information: the amount of a substance found in unrecorded alcohol, per capita consumption of unrecorded alcohol and the bodyweight of consumers. Similarly to the approach of Medeiros Vinci et al. (2012) for probabilistic human exposure assessment of food contaminants, we applied best fit distributions to the lower limit scenario of substance contents (i.e., non-detectable samples were considered zero). For per capita unrecorded alcohol consumption, we selected a best fit distribution for the unrecorded alcohol consumption data, available from the WHO Global Information System on Alcohol and Health (GISAH) (WHO, 2012) for the countries with available sample survey data (Albania, Austria, Croatia, Czech Republic, Germany, Hungary, Italy, the Netherlands, Norway, Poland, Romania, Russia, Slovenia, Spain, Switzerland, UK and Ukraine). The bodyweight was assessed as normal distribution with average of 73.9 kg and standard deviation of 12 kg for males and females according to EFSA Scientific Committee (2012). The distribution fitting was conducted with a fixed lower limit of zero because negative values are factually impossible. Monte Carlo simulations were performed with 10,000 iterations using Latin Hypercube sampling and Mersenne Twister random number generator. Calculations were performed using the software package @Risk for Excel Version 5.5.0 (Palisade Corporation, Ithaca, NY, USA).

What we found

The toxicological thresholds of the 10 substances assessed are shown in Table 1. Where several endpoints were available, the most sensitive toxicological endpoint was chosen, in order to provide a conservative assessment. For four of the compounds, human epidemiological data were available as the basis for the assessments. For the rest of the compounds, the assessments had to be based on animal data. The thresholds of the compounds, as defined by lower benchmark dose limits, vary over a very wide range, from 0.0015 mg/kg bw/day for lead to 440 mg/kg bw/day for ethanol.

Table 2 gives an overview of the occurrence of the selected substances in unrecorded alcohol, as well as the best-fitting risk functions. In general, the contamination of unrecorded alcohol with the selected substances varied widely, depending on product category, raw material, or diligence during manufacturing. The non-normality of the fitted distributions can be explained by the presence of zero data below the limits of detection (LOD) of the analytical methodologies (especially in the case of ethyl carbamate or heavy metals). As the LODs of our analytical methodologies were quite low (e.g. 1 part per billion (ppb) for metals), the results when using other methods to deal with zero values (e.g. considering non-detectable values as LOD instead of zero) were not significantly different (data not shown). For this reason, we decided to leave the values at zero, thus giving a conservative estimate and avoiding exaggeration of the risk.

Table 1. Toxicological thresholds selected for calculating the margin of exposure (data updated from (Lachenmeier, Przybylski & Rehm, 2012) with permission from John Wiley and Sons)

Agent	Toxicological Endpoint [a]	Value [c] [mg/kg bw/day]	Type of endpoint [b]	Reference
Ethanol	Human epidemiology, liver cirrhosis mortality	440	$BMDL_{1.5}$	Lachenmeier, Kanteres & Rehm, 2011
Ethyl carbamate	Alveolar and bronchiolar neoplasms in mice	0.3	$BMDL_{10}$	Vavasour et al., 2006
Acetaldehyde	Tumour-bearing animals in male rats	56	$BMDL_{10}$	Lachenmeier, Kanteres & Rehm, 2009
Methanol	Blood formate accumulation in humans	20	Level deduced from endogenous concentrations	IPCS, 1997
Copper	Liver toxicity in dogs	5	NOEL	WHO, 1982
Lead	Cardiovascular effects in humans	0.0015	$BMDL_{1}$	EFSA, 2010
Nickel	Two-generation study on rats (NOAEL for all endpoints including perinatal lethality)	2.2	NOAEL	WHO, 2005
Manganese	Upper range manganese intake value from human dietary studies is considered NOAEL	0.18 [c]	NOAEL	WHO, 2011
Boron	Decrease in fetal body weight in rats	10.3	$BMDL_{05}$	US EPA, 2005
Aluminium	Histopathological changes in the spleen and liver in rats	52	NOAEL	WHO, 2003

[a] Human data was preferred over animal data, where available. The most sensitive endpoint was chosen if dose-response data for several organ sites were available.
[b] $BMDL_x$: lower one-sided confidence limit of the benchmark dose (BMD) for a x% incidence of health effect. The No Effect Level (NOEL) or No Observed Adverse Effect Level (NOAEL) are used in cases when no usable BMD-modelling for oral exposure was identified in the literature.
[c] Recalculated from the original value of 11 mg/day using a bodyweight of 60 kg.

Table 2. Overview of constituents and contaminants in European unrecorded alcohol with descriptive statistics and best fit distributions (original analytical survey data taken from Lachenmeier et al., 2009; Lachenmeier et al., 2010b; Lachenmeier et al., 2011a; Solodun et al., 2011)

Agent [a]	N [b]	Positive samples	Mean	Median	Standard Deviation	Best fitting risk function for concentration of agent in the beverage [c]
Ethanol (% vol)	232	100%	41.8	40.7	16.5	*RiskBetaGeneral(1.4588;4.2175;0.10)* [d]
Ethyl carbamate (mg/L pa)	228	41%	0.65	0.00	1.69	*RiskExpon(0.64943)*
Acetaldehyde (mg/L pa)	222	97%	226	100	671	*RiskGamma(0.68975;337.18)*
Methanol (mg/L pa)	222	99%	1977	121	3173	*RiskGamma(0.33647;5955)*
Copper (mg/L pa)	174	88%	8.27	0.69	15.92	*RiskGamma(0.32911;28.573)*
Lead (mg/L pa)	174	55%	0.14	0.01	0.66	*RiskGamma(0.33654;0.7801)*
Nickel (mg/L pa)	174	34%	0.23	0.00	1.43	*RiskGamma(0.3353;2.014)*
Manganese (mg/L pa)	174	47%	1.21	0.00	3.27	*RiskGamma(0.31699;8.0882)*
Boron (mg/L pa)	174	18%	3.70	0.00	10.79	*RiskExpon(3.6977)*
Aluminium (mg/L pa)	174	36%	0.68	0.00	2.39	*RiskGamma(0.44631;4.1782)*

[a] The results (besides ethanol) are reported as mg per litre of pure alcohol (mg/L pa) to ensure the comparability between the alcoholic beverages with highly variable alcoholic strengths.
[b] The differences in sample numbers is caused by the fact that not all samples were analyzed for all parameters (e.g. due to lack of samples volume)
[c] The best fit distributions were selected based on chi-squared statistics. The lower limit was set as zero. The upper limit was set as infinity.
[d] For ethanol, the risk function was modelled with unrecorded per capita consumption data taken from WHO GISAH WHO, 2012 for the countries with available survey data (Albania 2.1 L, Austria 0.6 L, Croatia 2.5 L, Czech Republic 1.5 L, Germany 1 L, Hungary 4 L, Italy 2.4 L, The Netherlands 0.5 L, Norway 1.6 L, Poland 3.7 L, Romania 4 L, Russia 4 L, Slovenia 3 L, Spain 1.4 L, Switzerland 0.5 L, UK 1.7 L and Ukraine 7.5 L of pure alcohol per capita).

Table 3 presents the point estimate as well as the probabilistic exposure estimates. In all cases, the highest exposure detected was for ethanol (average 77 mg/kg bodyweight (bw)/day), while the lowest found was for lead (average 2.5E-05 mg/kg bw/day). The probability density functions of the estimated exposures are shown in Figure 1 for all compounds. The results also underwent a sensitivity analysis, which allows a ranking of the input distributions which impact on exposure. In all cases, the concentration of the contaminant had the highest influence, followed by unrecorded consumption and a minor influence of bodyweight (normalized regression coefficient for concentration ranging between 0.71 and 0.79, for unrecorded consumption between 0.24 and 0.48, and for bodyweight between -0.08 and -0.12).

Table 3. Estimated exposure of the European population to constituents and contaminants found in unrecorded alcohol

Agent	Point Estimate [a] (mg/kg bw/day)	Probabilistic analysis [b] (mg/kg bw/day)			
		Mean	SD	P5	P95
Ethanol [c]	75	77	54	11	181
Ethyl carbamate	6.19E-05	6.40E-05	8.91E-05	1.58E-06	2.41E-04
Acetaldehyde	0.022	0.023	0.038	1.94E-04	0.088
Methanol	0.191	0.196	0.433	3.46E-05	0.920
Copper	8.96E-04	8.85E-04	1.88E-03	1.55E-07	4.09E-03
Lead	2.50E-05	2.52E-05	5.38E-05	5.39E-09	1.16E-04
Nickel	6.43E-05	6.77E-05	1.56E-04	1.12E-08	3.15E-04
Manganese	2.44E-04	2.49E-04	5.69E-04	3.04E-08	1.21E-03
Boron	3.52E-04	3.59E-04	4.89E-04	8.78E-06	1.31E-03
Aluminium	1.78E-04	1.84E-04	3.51E-04	2.41E-07	8.32E-04

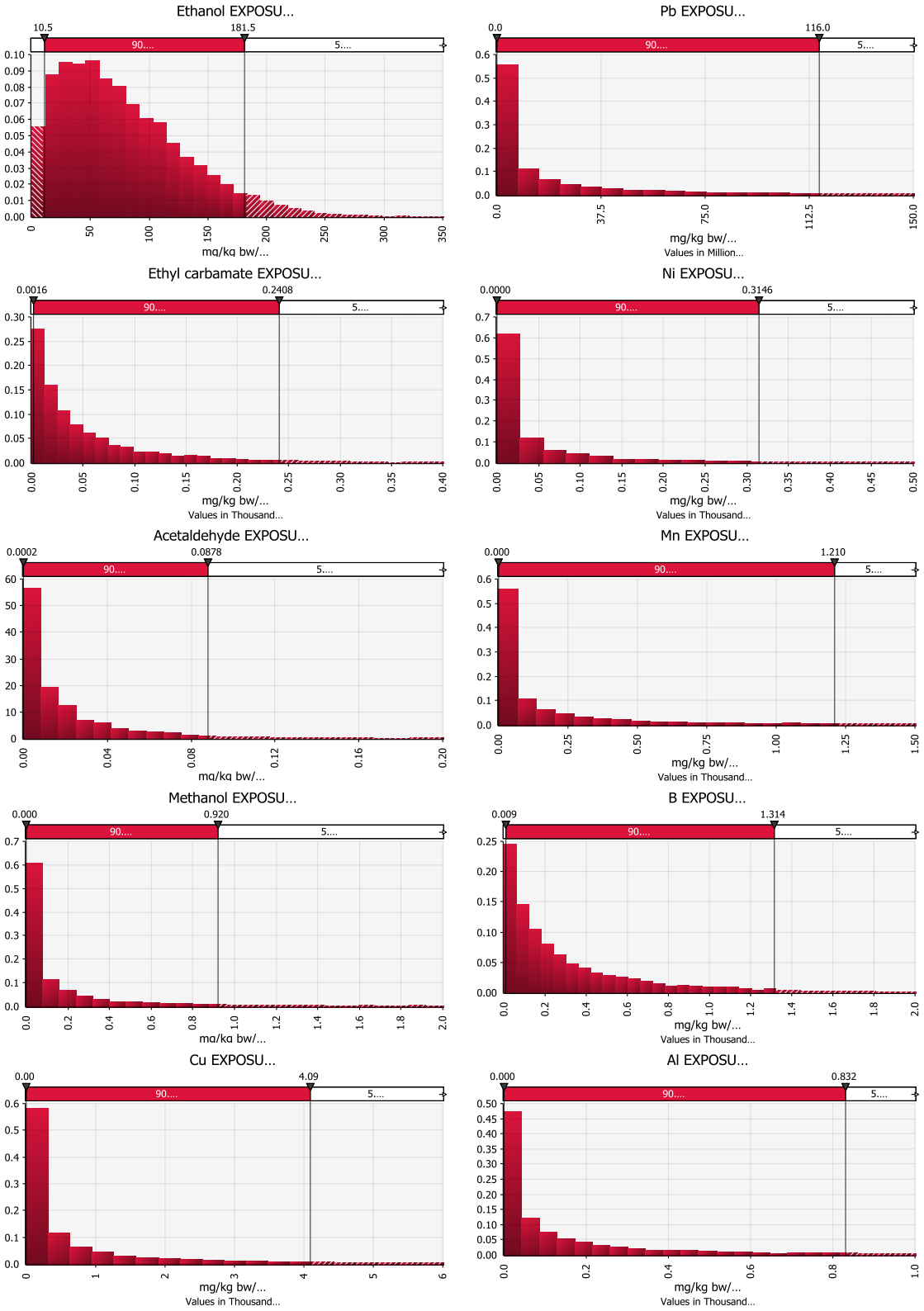
[a] Calculated with averages for all parameters

[b] Calculated for all agents except ethanol using the following formula with the risk functions defined in Table 2:
*Exposure = Risk function of unrecorded per capita consumption (L pa) / 365 days * risk function of concentration in beverage (mg/L pa) / risk function of bodyweight (kg).*
The risk function of bodyweight was *RiskNormal(73.9;12)* according to average and standard deviation from EFSA Scientific Committee, 2012.

[c] The exposure to ethanol was calculated using the following formula:
*Exposure = Risk function of unrecorded per capita consumption (L pa) / 365 days / risk function of bodyweight (kg) * 0.789 (kg/L) * 10^6.*

Finally, the margins of exposure (MOE) for all compounds are compared in Figure 2. Ethanol is the only compound for which the complete exposure distribution is below an MOE of 100, and, on average, below 10. From all other compounds, only methanol and lead reach MOEs below 100, but only in worst-case scenarios. All other compounds with a threshold-based mechanism of toxicity (e.g. Cu, Ni, Mn, B, Al) do not reach an MOE of below 100. From the genotoxic carcinogens, acetaldehyde and ethyl carbamate reached average exposures below the MOE threshold of 10,000 for this class of compounds (if the risk assessment has to be based on animal data).

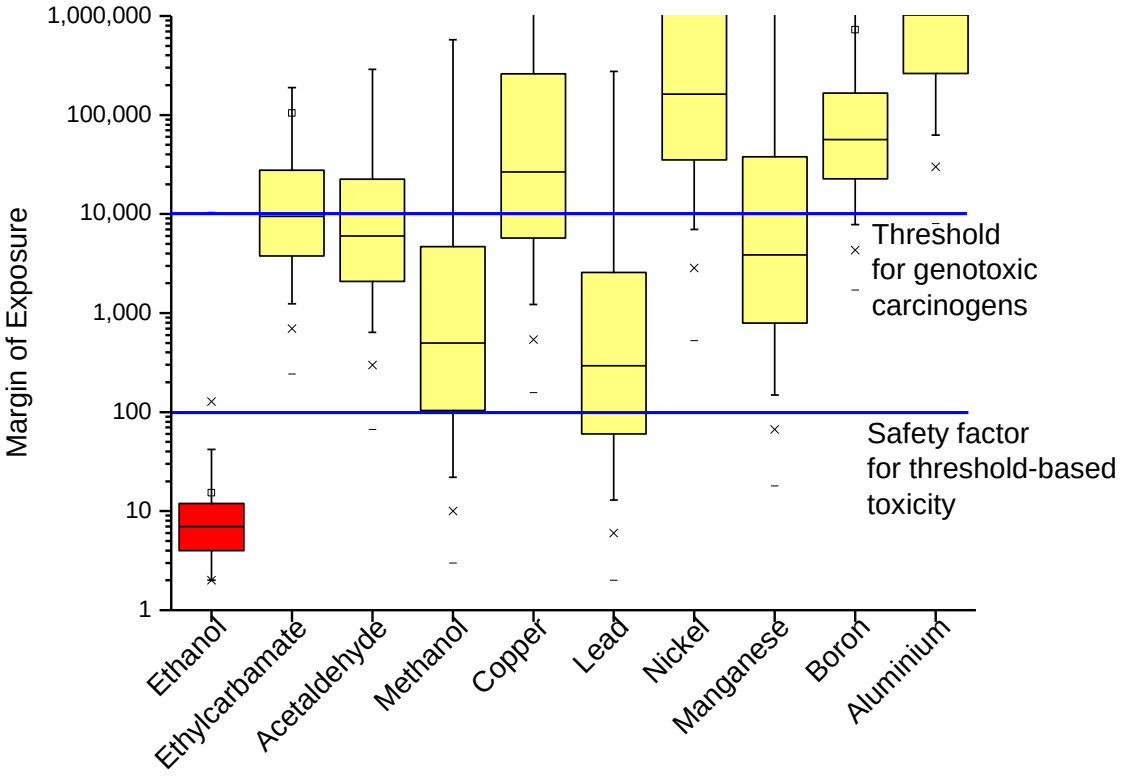
Figure 1. Histograms showing the probability density of estimated exposures using probabilistic simulation with 10,000 iterations (y-axis shows the relative frequency of a value in the range occurring)



What does this mean?

In traditional risk assessment studies, point-estimates are usually applied, which means that a fixed value for consumption (usually the mean population value) is multiplied by a fixed value for the chemical concentration (Lambe, 2002). In the past, we have done this, for example, to evaluate acetaldehyde or ethyl carbamate exposure from alcohol consumption (Lachenmeier et al., 2010a; Lachenmeier, Kanteres & Rehm, 2009). While point-estimates are easy to calculate and may provide a good first overview in assessing exposure, the uncertainty of what this means in terms of risk may be considerable, especially in the case of non-normal distributions, as in our case of contaminants in unrecorded alcohol samples. For this reason, we decided to additionally apply a probabilistic method, which takes account of every possible value that each variable can take, and weights each possible scenario by the probability of its occurrence (Lambe, 2002). To facilitate this, we applied the Monte-Carlo approach, which has been used in alcohol epidemiology for some time to estimate uncertainty of alcohol-attributable fractions (Gmel et al., 2011). Monte-Carlo methods have been also applied in food science to model dietary exposure to chemicals in food (Gibney & van der Voet, 2003; Lambe, 2002; Medeiros Vinci et al., 2012), but this study is the first to apply it to estimate the exposure to chemicals in alcoholic beverages. The advantage of the approach is that rather than single values for each scenario it generates distributions of the Margins of Exposure (MOE), which allow a direct visualization and comparison of all scenarios (Figure 2). The probabilistic approach also validates our previous point estimate approaches, conducted for single substances (Lachenmeier et al., 2010a; Lachenmeier, Kanteres & Rehm, 2009; Lachenmeier, Przybylski & Rehm, 2012), as the average point-estimates correspond closely to the average probabilistic estimates found in this study (Table 3).

Figure 2. Margin of Exposure (MOE) for compounds occurring in unrecorded alcohol based on probabilistic exposure estimation (simulation with 10,000 iterations). (The box is determined by the 25th and 75th percentiles. The whiskers are determined by the 5th and 95th percentiles. 1st and 99th percentiles are marked by x, while minimum and maximum are marked with dash. Values above 1,000,000 are not shown).



Coming back to our initial research question, our comparison clearly shows that ethanol represents by far the highest risk in unrecorded alcohol. The MOE of ethanol reaches down to below 10, which is the lowest level of all compounds under study (Figure 2). Both genotoxic carcinogens ethyl carbamate and acetaldehyde may reach MOEs below 10,000 in some scenarios, which according to EFSA indicates a concern for public health if the assessment has to be based on animal data (EFSA, 2005). Nevertheless, we think that compared to ethanol, which must also be treated as a genotoxic carcinogen (Baan et al., 2007; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2010; Secretan et al., 2009), the risks of ethyl carbamate and acetaldehyde appear to be minor in the case of these unrecorded alcohol samples (the average MOEs are above 10,000). In considering acetaldehyde as contaminant of alcoholic beverages, for example, the German Federal Institute for Risk Assessment holds the view that mitigation measures are not required (BfR, 2010).

For non genotoxic substances, a 100-fold uncertainty factor is routinely applied. The factor is based on scientific judgement and allows for species differences (where animal data are used) and human variability (EFSA, 2005). None of the average MOEs for the non-genotoxic substances would be below 100. For methanol and lead, where the MOE may be less than 100 in some cases below the 25th percentile (Figure 2), it must be considered that the toxicological assessment is based on human data, so that a safety factor of 10 should be sufficient. The MOE for these two compounds (methanol and lead) may fall below 10 only in extreme worst-case scenarios in the lowest 1st percentile of the distribution.

We conclude that the composition of unrecorded alcohol in the European Union poses no worries beyond the ethanol-specific harms inherent to any type of alcoholic beverage. Our probabilistic exposure assessment clearly invalidates assumptions of contamination as a factor in increased mortality due to unrecorded alcohol consumption (Razvodovsky, 2008). To provide an epidemiologically detectable increased risk of contaminants, their MOEs would have to range in the magnitude of the MOE of ethanol, which clearly is not the case.

As we have stressed before (Lachenmeier et al., 2011a; Lachenmeier, 2012; Rehm, Kanteres & Lachenmeier, 2010), the disproportionate health hazards of unrecorded alcohol, which are sometimes postulated but not clearly proven, could be purely explained by the fact that unrecorded alcohol is regularly sold at higher alcoholic strength (>45% vol.), but for half the price, of legal beverages, which may lead to more detrimental patterns of drinking (Lachenmeier, 2012). Empirical research to prove or disprove this hypothesis is lacking so far. The same is true of the alternative hypothesis; that the unrecorded alcohol drinker may adjust his drinking volume by either “tasting” the ethanol content or “titrating” to the required effect level, so that the outcome would be similar to drinking recorded alcohol.

Conclusions for policy and practice

Our suggestion for alcohol policy would be that unrecorded alcohol in Europe clearly poses a public health problem, which is not due to contaminants but due to its strength in terms of ethanol itself. Most of the contaminants studied also occur in recorded types of alcohol at similar levels, and we can confirm our previous finding that no substantial difference in risk from chemical contaminants between unrecorded and recorded alcohol exists (Lachenmeier, Przybylski & Rehm, 2012).

Nevertheless, the contamination problem appears to be highlighted in public opinion, and perhaps among policy makers, due to the large media attention that isolated intoxication cases receive. Such intoxication cases (typically from methanol) are, of course, tragic and should be avoided, but from the point of view of population health, they appear to be negligible in light of the alcohol-related mortality of over 120,000 deaths per year in Europeans between 15-64

years due to recorded consumption (estimates for 2004, based on WHO, 2009; Rehm et al., 2009, Rehm et al., 2012). The question is also how methanol intoxications could be prevented, as they are typically caused when chemically pure methanol is added to ethanol either out of ignorance or criminal intent.

In our judgement, the major policy focus should be to reduce unrecorded consumption *per se*, for which some options exist (Lachenmeier, Taylor & Rehm, 2011). The incentive for drinking surrogate alcohol, which appears to be the group of unrecorded alcohol posing the highest risk, could be reduced by abolishing the tax privileges for denatured alcohols. If that is not possible, more suitable denaturants such as bittering agents should be chosen, which would clearly prohibit human consumption and would especially impact on unintentional consumption when such products are relabelled (substances with no taste such as methanol and diethyl phthalate should be forbidden as denaturant). Unregulated forms of home production should be brought into some form of state control to ensure the conformity of alcohol composition. Actions limiting illegal trade and counterfeiting could include introduction of tax stamps and electronic surveillance systems of alcohol trade (Lachenmeier, Taylor & Rehm, 2011). The individual marking and traceability of legal alcohol bottles through the complete supply chain appears to be one of the most promising measures, as the customer is often unaware that he is consuming (counterfeited) unrecorded alcohol, and currently has no means to differentiate recorded from unrecorded products. This measure has already been introduced by some producers of premium-brand wine to prevent counterfeiting (Domaines Barons de Rothschild, 2012). The consumer can check the authenticity of the product at the point of sale by scanning a QR code with a mobile phone. Similar measures are currently being discussed to prevent counterfeiting of medicinal products and we believe that such systems could be feasible to protect the supply chain of alcoholic beverages in general.

Take home messages

1. The AMPHORA project studied the chemical composition of unrecorded alcohol, which has been thought to be extremely toxic due to various contaminants.
2. Some contaminants such as acetaldehyde, ethyl carbamate, copper or lead were indeed found above regulatory limits set for legal products.
3. To consider the “dose makes the poison” principle, we have conducted a detailed exposure assessment using probabilistic methods to compare the risks between the different compounds in unrecorded alcohols.
4. Ethanol was the most dangerous toxic substance in unrecorded alcohol, while all other substances were below toxicological thresholds in average scenarios.
5. Policy measures should aim to reduce unrecorded consumption in general rather than focusing on specific contamination problems.

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