vitamin C is an unproven treatment. Our report is useful because it describes a method for overcoming the technical problem of analyzing oxalic acid in the presence of extremely high ascorbic acid concentrations and because of the surprisingly small fractional conversion of ascorbic acid to oxalic acid under the conditions of our study.

We cannot agree with the claim that intravenous vitamin C is equivalent to ethylene glycol poisoning simply because urinary oxalic acid concentrations may be only moderate after suicidal ethylene glycol ingestion. In such cases, the rapid development of oxalate nephropathy prevents the kidneys from excreting the large amounts of oxalic acid generated from ethylene glycol. In contrast, our data indicate that very little oxalic acid is formed after rapid intravenous ascorbic acid in people with normal renal function, a very different situation.

The possibility that oxalic acid can be formed intracellularly as well as extracellularly is speculative, and the data in our article do not address it. We agree that urine samples containing ascorbic acid should be acidified and refrigerated at pH less than 2.0 as soon a possible to avoid ex vivo formation of oxalic acid. Our observation of oxalic acid formation at pH 1.7 was in samples with extremely high ascorbic acid concentrations left at room temperature for 24 hours.

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The effect of phytophenols in alcoholic beverages on alcohol dehydrogenase 1: is there really evidence for an inhibition of metabolic toxicity of alcohol?

To the Editor:

We read with great interest the article by Haseba et al [1] on the influence of polyphenols in whisky on the alcohol metabolism, specifically, the reduction of acetaldehyde levels through inhibition of liver alcohol dehydrogenase (ADH). The findings could be important because the authors conclude that the intake of alcohol together with phytophenols may not only diminish the metabolic toxicity of alcohol by reducing both the blood acetaldehyde level and oxidative stress, but also help limit the amount of alcohol a person drinks by depressing alcohol metabolism. However, we have major concerns that both conclusions cannot be derived from the experimental data and are purely conjectural.

The major restriction of the study is the interpolation of results gathered using experimental animals (mice) to humans, the potential problems of which are not even mentioned. We have no evidence to date regarding if and how the results from mice can be transferred to humans. Thus, conclusions on the link between phytophenols in whisky or other foods and the metabolic toxicity of alcohol due to acetaldehyde and oxidative stress are simply not supported. There is a general lack of data on bioavailability of polyphenols in humans [2]. Concentrations of the nonvolatile whisky fraction in the percentage range as used in the in vitro experiment on liver extract are highly unlikely to occur in vivo in the human liver. The in vivo animal experiments with blood acetaldehyde concentration between 20 and 50 μmol/L also appear to be outside of the parameters of human alcoholic beverage consumption, which seldom leads to measurable blood acetaldehyde concentrations. It is generally accepted that no significant (>0.5 μmol/L) acetaldehyde concentrations occur in venous blood during normal conditions, that is, with no deficiency in, or inhibition of, aldehyde dehydrogenase [3,4]. The in vivo experiments also used a concentrate of the whisky nonvolatile fraction (10:1), which was added to ethanol solution in 10% or 20% amounts leading to considerably higher dosages than those expected in humans drinking whisky. All in all, we think that the situation used in mice is not directly comparable with humans. The short-term design of the animal experiments was also problematic because chronic-toxic effects (eg, carcinogenic effects) of ethanol and acetaldehyde are evident only in long-term or lifetime studies [5,6].

Thus, phytophenols may or may not have a positive effect on health. As explained above, this currently is a hypothesis without empirical evidence; however, hypothetically, if phytophenols really had an effect on ADH1 in humans, then ethanol would be expected to stay in the blood and other tissues longer and at higher concentrations. One of the well-established major pathways for carcinogenesis of ethanol in the gastrointestinal tract is the local formation of acetaldehyde by the microbial flora in the oral cavity and colon [7,8]. With reference to genetic-epidemiologic evidence available from humans with reduced ADH1 activity, the ADH1B*1/*1 genotype (activity only 1/40 of the normal) was reported to increase relative risk for head and neck cancers [9], which was in fact explained by a longer exposure time to the microbially formed salivary acetaldehyde after alcohol consumption [10]. The same effect would be expected by the inactivation of ADH1 through polyphenols.

The conclusion that the effect of polyphenols on ADH1 reduces the likelihood of binge drinking by depressing alcohol metabolism is completely unfounded. First, the study did not include a component investigating the behavioral effects of the experimental animals. Second, there is no evidence in humans that such an effect may even arise. Although there is evidence that the pharmacokinetics of

alcohol metabolism can be influenced by factors such as food consumption [11] leading to the reduction of peak blood ethanol concentrations (similar to the results in the current animal study and a previous study by Haseba et al [12]), there is no evidence in the literature that the consumption of food with alcoholic beverages has a causal impact on binge drinking.

Finally, a recent risk assessment has shown that acetaldehyde constitutes a potential public health risk—even without consideration for the metabolically produced acetaldehyde [13]. Whisky (along with other alcoholic beverages) contains acetaldehyde as a normal constituent (≈30 mg/L on average) [14]. The International Agency for Research on Cancer also recently stated that ethanol in alcoholic beverages is carcinogenic, independent of beverage type [15,16]. Therefore, with no conclusive epidemiologic evidence proving differences between beverages on carcinogenicity or other major disease end points [17,18], we think it is currently not possible but irresponsible for alcohol industry–supported research to give consumer recommendations that one type of alcoholic beverage may be less detrimental to health.

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