

## Commentary

## The importance of hangover research

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Alcohol hangover is defined as the combination of mental and physical symptoms experienced the day after a single episode of alcohol consumption starting when the blood alcohol concentrations approaches zero [1]. Despite being a major economic and public health problem, research into hangover remains neglected. A recent Google search found 53,600,000 references to hangover, while a PubMed search identified only 618 publications that indexed the word. A significant section of the community appears to consider hangover as divine retribution and a useful deterrent to excessive drinking, although the evidence available appears to indicate that experiencing a hangover has little impact on drinking habits [2].

Nonetheless, hangover accounted for A\$6 billion in lost productivity in 2012 in Australia [3]. In addition, impaired cognition and psychomotor performance during hangover appear to be of importance in impairment of motor vehicle driving and poor work performance [4,5]. It is clear that more importance should be given to resolving the problem of hangover in our societies both by promoting responsible drinking and by the development of therapies to prevent the adverse effects of hangover.

The search for a preventative treatment for hangover has so far not produced a practical, comprehensive effective therapy. Ethics Committees are often not supportive of hangover research, particularly for potential remedies, and relatively few research groups have appreciated the importance of this area. There is considerable evidence that many of the toxic effects of alcohol, including hangover, are mediated by its' metabolite acetaldehyde [6]. Alcohol is metabolised to acetaldehyde by the enzyme alcohol reductase. Acetaldehyde is subsequently metabolised by the enzyme aldehyde reductase, which is dependent on the potent antioxidant glutathione [7].

Glutathione may become depleted during alcohol consumption leading to an accumulation of acetaldehyde. In addition, there is evidence that the generation of oxygen free radicals which increase oxidative stress, plus activation of the immune system and inflammation play a role in the pathogenesis of hangover [8-11]. These may result from the high levels of oxidative stress produced by alcohol per se. However, it is also possible that these effects may be related to a lack of glutathione and the effects of increased exposure to acetaldehyde.

In addition to its' putative role in the pathogenesis of hangover, acetaldehyde has been implicated in the development of several diseases associated with alcohol consumption including cirrhosis of the liver, cardiomyopathy and oesophageal cancer

[12-14]. It is therefore possible that therapies that are potent antioxidants, particularly if they counteract the toxic effects of acetaldehyde, may not only prevent hangover symptoms but also have longer term effects in the prevention of some diseases associated with excessive alcohol consumption.

Studies of the effects of potent antioxidants and compounds that regenerate glutathione in hangover are lacking. A study of a polyphenolic extract from clove buds (250 mg single dose) has been recently reported to reduce hangover symptoms by about 50% in 16 male subjects in a double blind placebo controlled crossover trial. Inflammatory markers were also significantly reduced [15]. However, the significance of the study was uncertain as the dosing of the alcohol was vague and the plasma levels of alcohol reported did not appear to be consistent with known pharmacokinetics of alcohol. Another study of a combination of potent antioxidants including cysteine (which regenerates glutathione) and ascorbic acid given as 2 doses (one at the end of a drinking session and one approximately 4 hours later) to 19 normal volunteers using a double blind placebo controlled design reported an improved wellbeing in the active group and improvements in some hangover symptoms (difficulty concentrating, nausea and headache) the day following heavy alcohol consumption [16]. Further work is required to confirm these results.

Several other studies have shown partial effects of compounds in reducing hangover symptoms. These include Korean Pear juice and Red Ginseng which appear to mainly act by lowering plasma alcohol levels and therefore must be given prior to drinking [17,18]. A comprehensive review of all of the compounds that have been claimed to have hangover relieving effects has been published by Jayawardena et al. [19].

There is a professional society dedicated to hangover research called the Alcohol Hangover Research Group and they have produced best practice guidelines for research in the field [20]. It is important now that more groups become involved in this field and more funding be made available for hangover research.

**Disclosure**

Dr. Jan Quinton is CEO of Phoenix Pharmaceuticals Australia Pty Ltd which markets a hangover treatment in Australia.

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