The elusive hangover cure

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Recently the news reported that the best remedy for a hangover is common soft drink. This was, however, only a hypothesis based the in vitro finding of accelerated metabolism of ethanol and its toxic product, acetaldehyde.¹ With winter holidays approaching, pharmacists are likely to encounter patients seeking relief from alcohol overindulgence.

Veisalgia - aka hangover

A hangover can mean any of a constellation of unpleasant signs and symptoms that occur when the blood alcohol concentration (BAC) falls. It usually begins 6 to 8 hours after consumption of an intoxicating amount of alcohol, peaks when the BAC reaches zero, and lasts about 24 hours.² There is no consensus on what constitutes a hangover.²⁻⁵ In the largest survey of hangover symptoms, fatigue was the most common symptom (reported by almost 96%), followed by thirst, drowsiness, sleepiness, headache, dry mouth, nausea, weakness, reduced alertness and concentration problems (symptoms reported by at least 75%).⁵ They were usually the most severe symptoms too, in addition to vomiting, apathy, and reduced appetite.

The pathophysiology of hangovers is not fully understood. During hangovers there are a number of abnormalities - dehydration, pH and electrolyte imbalance, hypoglycemia, sleep disturbances; alteration in hormones including serotonin, histamine, prostaglandins and cytokines; and inflammation such as gastric irritation.²⁻⁵ There is no clear correlation between these abnormalities and symptoms.- "no two hangovers are the same".⁶ The relative role of ethanol, its metabolite acetaldehyde, congeners (other alcohols and organic compounds produced during fermentation or introduced during beverage production), co-exposures such as tobacco smoke, other substances, and dancing is also unclear. Psychosocial factors, personality traits, and individual biology may play a role. An estimated 25 - 30% of adults are resistant to developing hangovers.⁷
The economic burden of hangovers is significant. One estimate of the cost to the Canadian economy of alcohol-related short-term disability (days in bed or with reduced activity) is $40 million per year.\textsuperscript{8} The estimated cost of lost productivity in other countries is in the billions.\textsuperscript{9} Studies have shown impaired cognitive and psychomotor performance in the hungover state. In one study the decrease in attention performance was similar between the acute intoxication and hangover states while reaction times were worse in the hangover state, raising safety concerns.\textsuperscript{10}

**Treatments**

There is no experimental evidence of an effective treatment for hangovers, the only sure-fire prevention is abstinence. Home treatments, folk-cures, herbal and homeopathic hangover remedies abound, as do tales of their effectiveness. While rehydrating, refuelling, and resting are good things, very few specific hangover treatments have been scientifically studied (Table 1). The few published are small and methodologically flawed (a consensus document on best practices in hangover research has recently been published\textsuperscript{11}).
Safety concerns

While most remedies are likely harmless, some treatments are potentially hazardous. "Hair of the dog" (more alcohol) only delays the onset of hangover symptoms, may enhance the existing toxicity of alcohol already consumed, and increases the likelihood of continued drinking. Analgesics may provide relief from headache, but care must be taken not to overuse. Some hangover remedies available for purchase on the internet contain analgesics - patients should check labels. NSAIDs may worsen gastric irritation, and the rare patient may be at increased risk of liver toxicity from acetaminophen due to depleted glutathione stores and induction of hepatic metabolism. Caffeine may create a false sense of safety, but data shows that judgement and psychomotor performance remain impaired during acute intoxication, and there is no evidence of improved performance during hangovers.

| Table 1. Purported mechanisms and effects of some hangover treatments |
|----------------------------------------|---------------------------------------------------------------------------------------|
| **Soft drinks (Sprite), fructose or glucose beverages (Gatorade, Ryzel, others)** | Raises activity of alcohol dehydrogenase and aldehyde dehydrogenase, increasing clearance of ethanol and acetaldehyde. Fructose enhances regeneration of NAD+, a cofactor in the metabolism of ethanol. Clinical studies: no effect on hangover symptoms. (REF 18) |
| **Borage oil** | Basis of treatment unclear - likely related to mediation of prostaglandin synthesis. No effect on over-the-counter drugs. (REF 19) |
| **Artichoke extract** | Antioxidant and choleretic activity. No effect on physiological changes. Cognitive function test score: unaltered. (REF 20) |
| **Prickly pear (Opuntia ficus indica) (NOHO, Pronto, others)** | Antioxidant; increases protective stress proteins. Extract reduced nausea, anorexia, and dry mouth in no other symptoms. Reduced risk of a severe hangover and markers of inflammation. (REF 21) |
| **After Effect® (borage oil, prickly pear, milk thistle extract, fish oil, vitamins and magnesium)** | Combined antioxidant, prostaglandin, immune system and miscellaneous effects. Symptom score appeared to show benefit, but there was no placebo control (only subjects expected severity was treated). (n=103) (REF 22) |
| **Party Smart® (Himalayan Drug Company)** | Mechanism unknown. Contains date palm, cherrv, Indian gooseberry, grape, and other Ayurvedic herbs. Four small trials (n=10 to 19) conducted by the manufacturer showed better mood and reduced hangover symptoms compared to placebo. (REF 23) |
| **Tangerine pith/ginger/sugar** | Unclear; traditional Chinese remedy, regulates "qi". Reduced gastrointestinal symptoms when taken before alcohol consumption. No difference using placebo after. (REF 24) |
| **Kudzu (Pueraria lobata; Drinkwel, Last Round, others)** | Kudzu flower increases elimination of acetaldehyde. However, some remedies contain kudzu root that reduces acetaldehyde clearance similar to disulfiram. No clinical studies on hangover symptoms. (REF 25) |
| **B vitamins and derivatives (pyridoxine, metadoxone, pyritinol) (Hangover Guardian, Modj Synergy, others)** | Pyridoxine and metadoxone are purported to increase alcohol metabolism, protect the liver and balance the immune system. Equivocal effects on alcohol clearance but larger studies show pyridoxine does not affect ethanol clearance or level of consciousness during intoxication; hangover symptoms not assessed. Pyritinol is a pyridoxine derivative touted as nootropic, may reduce prostaglandins, promote glucose uptake into the brain. One small study reported reduced hangover symptoms. (REF 26) |
| **Cysteine and other "biologically active" sulfur compounds (Xo3, others)** | Cysteine, N-acetylcysteine, and glutathione are purported to replenish hepatic glutathione stores, related to hangover symptoms is unclear. One patient application for methylsulfonylmethane (MSM) as a hangover cure purported that MSM softens cell walls, allowing alcohol to be flushed out faster, increasing cell oxygenation. No clinical trials on relieving hangover symptoms. (REF 27) |
| **Caffeine** | Caffeine has alerting and analgesic effects. Subjects given caffeinated beer reported better perceived sleep quality, but there were no significant differences in morning sleepiness, hangover incidence, and hangover severity. (REF 54) (REF 28) |
| **Propranolol** | Increased adrenergic tone may cause hangover symptoms. 160 mg long-acting propranolol taken before drinking reduced HR but no effect on BP; no benefit for tremor, headache, overall severity. (REF 10) |
| **NSAIDs** | Inhibition of prostaglandin synthesis. 200 mg ibuprofen taken before drinking and then be reduced headache, dry mouth, thirst, tremor, nausea and vomiting. (REF 30) |
| **Tropisetron (plus diazepam)** | Tropisetron eluted GI symptoms; diazepam for withdrawal. Tropisetron did not have any effect on symptoms or headache. (REF 11) |

\( \text{C} = \text{crossover} \quad \text{RCT} = \text{randomized controlled trial} \)
Summary

There is no evidence of an effective hangover remedy. Pharmacists can help patients avoid worthless and potentially dangerous treatments. However, the best prevention is avoiding over-indulgence in the first place, and the most effective cure is likely the tincture of time.

References:


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