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# Papers

## Interventions for preventing or treating alcohol hangover: systematic review of randomised controlled trials

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### Abstract

**Objective** To assess the clinical evidence on the effectiveness of any medical intervention for preventing or treating alcohol hangover.

**Data sources** Systematic searches on Medline, Embase, Amed, Cochrane Central, the National Research Register (UK), and ClinicalTrials.gov (USA); hand searches of conference proceedings and bibliographies; contact with experts and manufacturers of commercial preparations. Language of publication was not restricted.

**Study selection and data extraction** All randomised controlled trials of any medical intervention for preventing or treating alcohol hangover were included. Trials were considered if they were placebo controlled or controlled against a comparator intervention. Titles and abstracts of identified articles were read and hard copies were obtained. The selection of studies, data extraction, and validation were done independently by two reviewers. The Jadad score was used to evaluate methodological quality.

**Results** Fifteen potentially relevant trials were identified. Seven publications failed to meet all inclusion criteria. Eight randomised controlled trials assessing eight different interventions were reviewed. The agents tested were propranolol, tropisetron, tolfenamic acid, fructose or glucose, and the dietary supplements *Borago officinalis* (borage), *Cynara scolymus* (artichoke), *Opuntia ficus-indica* (prickly pear), and a yeast based preparation. All studies were double blind. Significant intergroup differences for overall symptom scores and individual symptoms were reported only for tolfenamic acid,  $\gamma$  linolenic acid from *B officinalis*, and a yeast based preparation.

**Conclusion** No compelling evidence exists to suggest that any conventional or complementary intervention is effective for preventing or treating alcohol hangover. The most effective way to avoid the symptoms of alcohol induced hangover is to practise abstinence or moderation.

### Introduction

The alcohol hangover has substantial economic and health consequences.<sup>1,2</sup> In Britain, the associated problems have been estimated to account for about £2 billion in lost wages each year, mostly due to sickness absence.<sup>3</sup> With binge drinking on the rise, these figures are likely to increase.<sup>4</sup> In the United States, the total cost of alcohol use has been estimated at \$12-30 billion per year, although other figures criticised for being inflated range as high as \$148 billion per year.<sup>1,5</sup> The rates of medically certified sickness absence seem to be higher in never drinkers, former

drinkers, and current heavy drinkers than in current light drinkers.<sup>6</sup> In the workplace, a person with a hangover may experience impaired memory and visual-spatial skills and may be at risk.<sup>7,8</sup> Other symptoms in varying combinations may include lightheadedness, nausea, and concentration difficulties. The symptoms seem to be due to a combination of ethanol's main metabolic product acetaldehyde, congeners including methanol, endocrine and immune system disturbances, dehydration, and sleep disturbance.<sup>1,9</sup> Substantially increased risks of all cause mortality can occur even in people drinking less than recommended maximums, particularly among younger adults.<sup>10,11</sup> An increased risk of strokes has been observed in young adults, particularly on occasions when alcohol intake is higher than average.<sup>12</sup> In addition, during celebrations at Christmas, for instance, alcohol consumption increases and may lead to a rise in fatal alcohol poisonings by 0.4% for every 1% increase in the sales of spirits.<sup>13</sup>

These considerations emphasise the need for safe and effective preventive and therapeutic measures. A plethora of "hangover cures" is on offer.<sup>14-16</sup> Searching the internet on Google.com (search term: hangover cure, accessed 20 Jan 2005) retrieved in excess of 325 000 hits. The box gives a flavour of what is on offer. The aim of this systematic review was to assess the clinical evidence on the effectiveness of any medical intervention for preventing or treating alcohol hangover.

### Methods

#### Searching

We searched Medline (1951 to January 2005), Embase (1974 to January 2005), Amed (1985 to January 2005), the Cochrane Library (issue 1, 2005), the National Research Register, United Kingdom ([www.update-software.com/projects/nrr/](http://www.update-software.com/projects/nrr/)—accessed 20 Jan 2005), and ClinicalTrials.gov, United States ([clinicaltrials.gov/](http://clinicaltrials.gov/)—accessed 20 Jan 2005). We designed the search strategy to retrieve all articles on the topic (strategy: hangover, alcohol and hangover, hangover adj cure). In addition, we hand searched conference proceedings (*FACT - Focus on Alternative and Complementary Therapies* 1996-2005) and our own collection of papers and medical journals (*Phytomedicine* 1994-2005, *Alternative and Complementary Therapies* 1995-2005, and *Forschende Komplementärmedizin Klassische Naturheilkunde* 1994-2005). We also hand searched the bibliographies of all retrieved articles. We contacted six manufacturers of commercial preparations for alcohol hangover and five experts on the subject and asked them to contribute further studies. We imposed no restrictions on the language of publication.

**Interventions for alcohol hangover reported on the internet\***

- Aspirin
- Bananas
- Barley grass
- Berocca containing vitamin B complex, vitamin C, calcium
- Blend containing cardamom, amomum, tangerine peel, citrus peel, ginseng, atractylodes, poria, massa fermentata, dried ginger, polyporus
- Bloody Mary (that is, alcoholic drinks)
- Cabbage
- Calcium carbonate
- Charcoal tablets
- Chaser (that is, alcoholic drinks)
- Coffee
- Cysteine
- Eggs
- Exercise
- Fresh air
- Fruit juice
- Ginseng
- Glutamine
- Green tea
- Hair of the dog (that is, alcoholic drinks)
- Honey
- Hot bath
- Ibuprofen
- Ice pack
- Kidney dialysis
- Milkshake
- Multivitamins
- Paracetamol
- Pizza
- RU 21
- Russia Party
- Shower
- Sleep
- Sob'r-K HangoverStopper
- Succinic acid
- Various recipes containing ingredients such as olive oil, raw egg yolk, tomato ketchup, Tabasco sauce, Worcester sauce, lemon juice, buttermilk
- Vegemite on toast
- Water

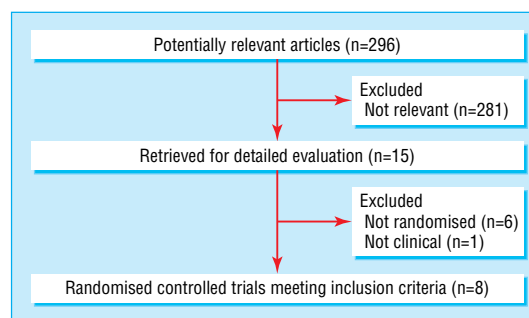
\*Results from the first 20 websites retrieved by Google.com with the search term "hangover cure" (accessed 20 Jan 2005).

**Selection**

We included all trials reporting that the sequence of allocation was randomised and testing any medical intervention for preventing or treating alcohol hangover. We included trials reported as placebo controlled or controlled against a comparator intervention. Titles and abstracts of identified articles were independently assessed and hard copies of all potentially relevant articles were obtained for further evaluation (MHP, EE).

**Validity assessment**

We used the system developed by Jadad to evaluate methodological quality.<sup>17</sup> Two authors (MHP, EE) independently assessed the quality of trials.



Flowchart of trial selection process

**Data abstraction**

MHP and JCV abstracted data systematically and independently according to design, quality, sample size, alcohol challenge, intervention and brand name, dose, results, adverse events, and control of lifestyle factors. We planned quantitative data synthesis but abandoned it because of the heterogeneity of the data.

**Results**

The literature searches identified 15 potentially relevant trials (figure).<sup>18–32</sup> We also identified one unpublished study.<sup>25</sup> We excluded seven publications because they were either not reported as randomised<sup>18–23</sup> or did not test an intervention in a clinical trial.<sup>24</sup> Eight trials met the inclusion criteria and were reviewed.<sup>25–32</sup> These trials tested eight different conventional agents and dietary supplements (table). Disagreements during the assessments were settled by discussion.

Four randomised controlled trials tested dietary supplements: *Borago officinalis* (borage), *Cynara scolymus* (artichoke), *Opuntia ficus-indica* (prickly pear), and a yeast based preparation. Two trials reported intergroup differences for an overall symptom score and for the individual symptoms restlessness, discomfort, and impatience.<sup>25–28</sup> In the first of these trials the effectiveness of  $\gamma$  linolenic acid from *B officinalis* was tested in people who attended a private party.<sup>25</sup> The results indicated a significant reduction in the overall severity of hangover and in the individual symptoms of headache, laziness, and tiredness compared with placebo ( $P < 0.01$ ). Another trial tested a combination preparation containing 250 mg dried yeast, 0.5 mg thiamine nitrate, 0.5 mg pyridoxine hydrochloride, and 0.5 mg riboflavin per tablet in participants who consumed vodka (40% volume alcohol) amounting to a total of 100 g absolute alcohol.<sup>28</sup> The difference in the change for the symptoms discomfort, restlessness, and impatience was statistically significant in favour of the yeast preparation. Two other trials that tested extracts of *C scolymus* and *O ficus-indica* reported no intergroup differences for their main outcome measures.<sup>26–27</sup>

Four trials tested conventional agents: tropisetron, propranolol, tolfenamic acid, and fructose or glucose (table). One trial reported intergroup differences for an overall symptom score ( $P < 0.01$ ).<sup>31</sup> This trial tested the prophylactic effectiveness of tolfenamic acid, an inhibitor of prostaglandin biosynthesis. Each participant consumed alcohol in small groups and drank at his own pace. The amount of alcohol and food ingested was not measured. The overall symptom score and the individual symptoms headache, nausea, vomiting, thirst, dry mouth, tremor, and irritation were significantly reduced compared with placebo. Three other trials, which tested propranolol, tropisetron, and fructose or glucose, reported no beneficial intergroup differences.

## Randomised controlled trials of interventions for alcohol hangover

First author	Design; Jadad score	Alcohol challenge	Intervention (brand name)	Dose and regimen	Control; duration	No randomised/No analysed	Main outcome measure	Main result	Adverse events in intervention group (cases)	Control of lifestyle factors
Moesgaard <sup>25</sup>	Parallel, double blind; 3	140-160 ml	$\gamma$ linolenic acid from <i>Borago officinalis</i> (Bio-Glandin 25)	1000 mg before alcohol challenge	Placebo; 1 day	40/18 healthy volunteers	Overall hangover symptom score	Intergroup difference (P<0.01)	Not reported	Participants were recruited at a private party; no restrictions on food and drink reported
Pittler <sup>26</sup>	Crossover, double blind; 5	1.2 g/kg BW	<i>Cynara scolymus</i> extract L1120 (Cynara Artichoke)	960 mg before and after alcohol challenge	Placebo; 1 day	15/15 healthy volunteers	Overall hangover symptom score	No intergroup difference (P>0.05)	Redness in the face (1)	A meal was taken before alcohol challenge
Wiese <sup>27</sup>	Crossover, double blind; 4	1.75 g/kg BW	<i>Opuntia ficus-indica</i> (not reported)	1600 IU before alcohol challenge	Placebo; 1 day	64/55 healthy volunteers	Overall hangover symptom score	No intergroup difference (P>0.05)	Not reported	A meal was taken before alcohol challenge
Laas <sup>28</sup>	Parallel, double blind; 3	100 g	Dried yeast (Morning Fit)	750 mg after alcohol challenge	Placebo; 1 day	61/58 healthy volunteers	Hangover symptom scores	Intergroup differences for discomfort, restlessness, impatience (P<0.05)	Not reported	After alcohol challenge soft drinks, water, and a low fat lunch were offered; no caffeine intake
Muhonen <sup>29</sup>	Parallel, double blind; 2	Not reported	Tropisetron (not reported)	5 mg tropisetron and diazepam when patients reached 0% BAC	Placebo; 1 day	11/not reported alcoholics (DSM-III-R)	VAS scores for vomiting, nausea, appetite, headache	No intergroup differences (P>0.05)	Not reported	Participants were patients in hospital for detoxification
Bogin <sup>30</sup>	Crossover, double blind; 4	Not reported; calculated for each patient to estimated BAC levels of 0.1%)	Propranolol, long acting (not reported)	160 mg 2 hours before alcohol challenge	Placebo; 1 day	10/10 healthy volunteers	Overall hangover symptom score	No intergroup difference (P>0.05)	Not reported	No analgesics or water were allowed after alcohol challenge
Kaivola <sup>31</sup>	Crossover, double blind; 3	Self determined, not assessed	Tolfenamic acid (not reported)	200 mg before and after alcohol challenge	Placebo; 1 day	30/not reported healthy volunteers	Overall hangover symptom score	Intergroup difference (P<0.01)	Swollen eyes, slight dysuria (2)	Challenge was done in small groups; restrictions on non-alcoholic beverages and food intake not reported
Ylikahri <sup>32</sup>	Parallel, double blind; 2	1.75 g/kg BW	Fructose (not reported)	1 g/kg BW fructose or glucose during or 0.5 g/kg BW fructose or glucose after drinking	Glucose; 1 day	109/not reported healthy volunteers	Overall hangover symptom score	No intergroup difference (P>0.05)	Not reported	During the challenge the participants did not receive food but could drink water freely

BAC = blood alcohol concentration; BW = bodyweight; VAS=visual analogue scale.

## Discussion

The paucity of randomised controlled trials is in stark contrast to the plethora of "hangover cures" marketed on the internet. This confirms the unreliability of the internet in healthcare matters.<sup>33</sup> Our findings show that no compelling evidence exists to suggest that any conventional or complementary intervention is effective for preventing or treating alcohol hangover. Encouraging findings for their main outcome measures exist for  $\gamma$  linolenic acid from *B. officinalis*, a yeast based combination preparation, and tolfenamic acid. However, only single randomised controlled trials for each of the tested interventions were available, most were of small sample size, and all used unvalidated symptom scores. Independent replications of these studies are therefore necessary. The lack of a sensitive standard outcome measure to assess the physiological and subjective effects of alcohol hangover may be one of the reasons for the small body of evidence. The development and initial validation of the hangover symptoms scale will hopefully encourage further systematic research and will aid the integration of trial data.<sup>34</sup>

Future studies should also investigate the biological changes that occur during alcohol hangover. The trial of *O. ficus-indica* reported that the extract had some effects on individual symptoms, which received some media attention.<sup>27, 35</sup> The

authors suggested that *O. ficus-indica* exerts its action by acting on prostaglandin synthesis and cytokines that are deregulated during alcohol hangover.<sup>36</sup> This view is supported by the improvement reported for tolfenamic acid,<sup>31</sup> a potent inhibitor of prostaglandin synthesis. However, other data also reported beneficial effects for pyritinol, a nootropic agent that seems to enhance cognitive performance, and Liv.52, an Ayurvedic herbal preparation containing eight extracts with possible effects on alcohol metabolism.<sup>18, 19</sup> These agents seem not to act directly on the prostaglandin system. Future studies should disentangle the pathology of alcohol hangover to enable the development of effective hangover interventions.

Ethical concerns may relate to research in this area. It is conceivable that positive trials might lead to considerable media interest and industry marketing, which ultimately might lead to an increase in alcohol consumption. However, little evidence exists to show that alleviation of hangover symptoms results in increased alcohol consumption.<sup>1</sup> Conversely, no conclusive evidence shows that hangover effectively deters alcohol consumption.

Limitations of our review pertain to the potential incompleteness of the reviewed evidence. We aimed to identify all randomised controlled trials on the topic. The distorting

### What is already known on this topic

The alcohol hangover has substantial economic and health consequences

Compliance with moderation to prevent alcohol hangover is poor

### What this study adds

Eight randomised controlled trials assessing eight different medical interventions for preventing or treating the symptoms of alcohol hangover were reviewed

No compelling evidence exists to suggest that any conventional or complementary intervention is effective for preventing or treating alcohol hangover

effects on systematic reviews arising from publication bias and location bias are well documented.<sup>37-40</sup> For this study we searched databases with a focus on the American and European literature and those that specialise in complementary medicine, and we included hand searches. We imposed no restrictions on language of publication, and the two reviewers independently appraised the clinical evidence. We are therefore confident that our search strategy located the published trials on the subject. However, whether we identified all unpublished trials has to remain uncertain.

### Conclusions

Our findings show that no compelling evidence exists to suggest that any complementary or conventional intervention is effective for treating or preventing the alcohol hangover. Future studies should investigate the biological changes that occur during alcohol hangover. Until the pathology of alcohol hangover is understood in more detail, an effective intervention is likely to remain elusive. The most effective way to avoid the symptoms of alcohol induced hangover is thus to practise abstinence or moderation.

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