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REVIEW ARTICLE

Interventions for treatment and/or prevention of alcohol hangover: Systematic review

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Abstract

Objective: To evaluate new research conducted over the past few years (2009–2016) assessing the effectiveness of potentially curative and/or preventive methods of alcohol hangover.

Methods: Data were retrieved by a 4-stage systematic search process. A search of the online Pubmed and Scopus databases were performed, using a combination of keywords: "Alcohol," "Ethanol," and "C_2H_5OH," in combination with the terms "Hangover," "Treatment," and "Prevention." The search comprised studies listed between January 1, 2009 and June 30, 2016. Findings were synthesized using a systematic approach. Quantitative analysis was not done because of the heterogeneity of the included studies.

Results: Six controlled human studies were identified (placebo controlled—3, controlled studies with a comparator intervention—3). Of the interventions, the use of polysaccharide rich extract of *Acanthopanax senticosus*, red ginseng antihangover drink, Korean pear juice, KSS formula, and the After-Effect© were associated with a significant improvement of hangover symptoms ($p < .05$). The highest improvement was observed for the following symptoms: tiredness, nausea/vomiting, and stomachache. None of the methods were effective for all the symptoms.

Conclusion: The available evidence suggests that several products are capable of significantly improving some, but not all, of the symptoms related to alcohol hangover. Therefore, further research is necessary to develop clinically effective hangover treatments.

KEYWORDS

alcohol, cure, hangover, prevention, treatment

1 | INTRODUCTION

Alcohol hangover is a set of disturbing symptoms experienced by alcohol consumers the day after a session of excessive drinking. Alcohol hangover states may last for up to 24 hr after drinking (Verster, 2008). The mechanism of hangover is not fully understood even though multiple causes have been suggested. Alcohol itself is responsible for some hangover symptoms (Prat, Adan, & Sánchez-Turet, 2009; Swift & Davidson, 1998). However, most hangover symptoms appear when the blood alcohol level is low and their severity peaks when the blood alcohol level becomes 0 (Verster, 2008). Evidence suggests that alcohol

metabolites and other biological factors such as hormonal alterations and de-regulations in cytokine pathways, nonalcoholic compounds in alcoholic beverages (e.g., congeners), use of other drugs, family history, and even the personality of a person play a role in manifestation of hangover symptoms (Prat et al., 2009; Swift & Davidson, 1998; Verster, 2008).

Irrespective of the mechanism, it is generally accepted that hangover is the most frequently experienced negative effect of alcohol consumption (Verster, Van Herwijnen, Olivier, & Kahler, 2009; Wiese, Shlipak, & Browner, 2000). Five out of the top 10 consequences of alcohol consumption are linked to hangover (Verster et al., 2009). According to a national survey conducted in the United States, 9.2%

of the workers experienced hangover at least once while working, and 10.2% of the workers were either under the influence of alcohol or had hangover at least once within the last 12 months (Frone, 2006). The high prevalence of hangover together with its unpleasant symptoms has become a significant problem for those who consume alcohol. The symptoms of hangover demonstrate a wide variation in expression and severity. The most commonly experienced symptoms of hangover include tiredness (95.5%), increased thirst (89.1%), sleepiness (87.7%), headache (87.2%), dry mouth (83%), and nausea (81%; Penning, Mckinney, & Verster, 2012). Hangovers may adversely affect the productivity, job performance, academic achievements, and normal day-to-day activities of an individual, with negative economic consequences (Frone & Verster, 2013; Verster et al., 2010). In the United States, about 2,000 dollars per employee is lost annually because of alcohol-related absenteeism and impaired working ability (Verster et al., 2010). Hence, it is clear that hangover has detrimental effects not only on physical health, psychological well-being, and social life of an individual but also on the economy of a country. This raises the necessity for discovering an effective treatment and/or preventive strategy for alcohol hangover (Verster, 2012).

In order to develop an effective treatment for hangover, many studies have been conducted testing the efficacy of various herbal and nonherbal products. However, most of these remedies provide symptomatic relief only for one or few of the symptoms of hangover. Two systematic reviews of controlled studies on prevention and/or treatment of alcohol hangover done in 2005 and 2010 has tested the effectiveness of several drugs (propranolol, tropisetron, tolfenamic acid, aspirin and paracetamol, and chlormethiazole), herbal preparations (*Borago officinalis*, *Cynara scolymus*, and *Opuntia ficus-indica*) and other formulations (KSS formula, Liv.52) on alcohol hangover (Pittler, Verster, & Ernst, 2005; Verster & Penning, 2010). In both studies, the authors concluded that there was no effective treatment or a preventive method that cures all the hangover symptoms. Since 2009, several new studies have examined potential new hangover treatments and therefore it is a necessity to relook at the evidence on treatment and/or prevention of alcohol hangover in order to find an effective cure. Our systematic review aims to systematically evaluate and summarize the new literature on treatment and/or prevention of alcohol hangover during the past few years (2009–2016).

2 | METHODS

We performed a systematic review, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for reporting of systematic reviews and meta-analyses (Liberati et al., 2009).

2.1 | Search strategy, inclusion, and exclusion criteria

Data on research related to treatment of alcohol hangover were obtained by a four-stage stepwise process. In the first stage, we began our literature review by searching the online Pubmed and SciVerse Scopus databases using the search terms "Alcohol," "Ethanol," and "C_2H_5OH," in combination with the terms "Hangover," "Treatment," and "Prevention." The search comprised studies listed between January 1, 2009 and June 30, 2016. The search limits were language

("English" [at least in abstracts]), species ("Humans"), and age ("all adults: 19+ years"). All controlled clinical trials on humans that evaluated any one of the following outcome measures were included: overall hangover severity or the severity of selected hangover symptoms. Animal studies and in vitro studies were excluded.

2.2 | Study selection

The total articles obtained from searching the above databases were pooled together and duplicate records were removed. Then, according to the above prespecified criteria, we examined the title, abstract, and descriptors of the articles in order to identify potentially relevant studies for full review. In the second and third stages, the articles were screened by reading the title and abstract, respectively, using the same inclusion/exclusion criteria defined above. The remaining studies were then screened for suitability during stage four by reading the full-text article according to the same criteria. To obtain additional data a manual search was performed using the reference lists of selected articles. This process was conducted by two independent reviewers (RJ and TT) and the final group of articles to be included in the review was determined after an iterative consensus process among the reviewers.

2.3 | Quality assessment, data extraction, and analysis

The methodological quality of the included studies were assessed by two authors independently (PR and TT), using the Jadad scoring system (Jadad et al., 1996). RJ and TT abstracted data systematically and independently according to design, quality, sample size, alcohol challenge, intervention, dose, and results. Quantitative data synthesis was not done because of the heterogeneity of the data ($I^2 > 90\%$).

3 | RESULTS

3.1 | Study selection

The literature search yielded 827 citations (Pubmed—307 and Scopus—520). After removing duplicates, 584 papers remained. The title and abstract of these papers were screened to identify potentially relevant papers for full review. The full texts were obtained for 22 papers deemed to be relevant, from which six studies were eligible to be included as per the inclusions or exclusion criteria. The number of articles identified using the above methodology is summarized in Figure 1.

3.2 | Study characteristics

The characteristics of the six studies included in the present review are summarized in Table 1. The Jadad scores of the studies vary from 1 to 5. Three were placebo controlled (Bang et al., 2015; Lee et al., 2013; Lee et al., 2014b), whereas the rest were controlled studies against a comparator intervention. Four of the studies were randomized (Bang et al., 2015; Lee et al., 2013; Lee et al., 2014b; Verster & Berthélemy, 2012), whereas in the remaining studies, the details of randomization were not described. Five of the studies were conducted in a cross-over fashion (Bang et al., 2015; Lee et al., 2013; Lee et al., 2014b; Noh et al., 2009; Takahashi, Li, Koike, & Sadamoto, 2010). Only males were
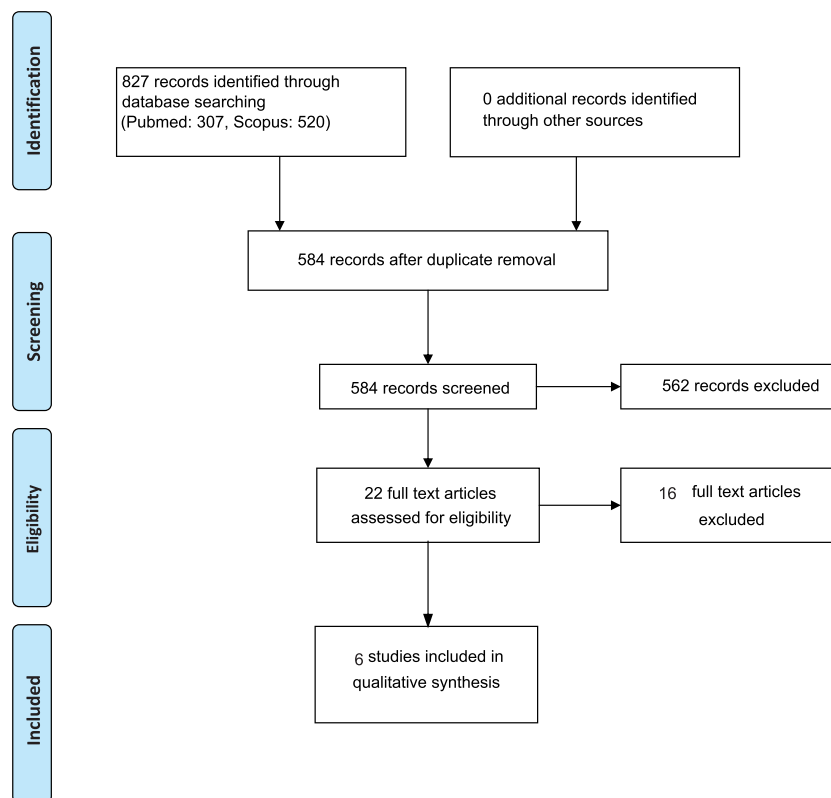
FIGURE 1 Summarized search strategy

included in four studies (Bang et al., 2015; Lee et al., 2013; Lee et al., 2014b; Noh et al., 2009), whereas in the remaining two, both males and females were included. All the participants were healthy adults between 19 and 58 years. Number of participants in each study varied from 9 to 28, except for one long distance study conducted via postal mail, which included 103 participants (Verster & Berthélemy, 2012).

The studies tested the effectiveness of a plant-based product or formula, namely, (a) polysaccharide rich extract of *Acanthopanax senticosus* (Bang et al., 2015), (b) Korean pear juice (Lee et al., 2013), (c) red ginseng antihangover drink (Lee et al., 2014b), (d) dandelion juice (Noh et al., 2009), (e) KSS formula (Takahashi et al., 2010), and (f) After-Effect© (Verster & Berthélemy, 2012). Three types of alcohol administration methods were used: amount depending on the body weight (Bang et al., 2015), specific amount of alcohol for all the participants (Lee et al., 2013; Lee et al., 2014b; Noh et al., 2009), and alcohol amount preferred by individual participant (Takahashi et al., 2010; Verster & Berthélemy, 2012).

In four studies, only a single substance was used as the intervention (Bang et al., 2015; Lee et al., 2013; Lee et al., 2014b; Noh et al., 2009); in the remaining two studies, a compound preparation made of several substances was used (Takahashi et al., 2010; Verster & Berthélemy, 2012). The interventions were administered either after alcohol (Lee et al., 2014b), before alcohol (Lee et al., 2013; Noh et al., 2009; Takahashi et al., 2010), or both before and after alcohol ingestion (Bang et al., 2015; Takahashi et al., 2010; Verster & Berthélemy, 2012). In one study, the intervention substrate was given daily for 7 days prior to alcohol consumption (Noh et al., 2009). In another study, four doses of the intervention substrate were given over 2 days after alcohol consumption (Takahashi et al., 2010). In the same study,

different regimens of the substrate (only a prophylactic dose, prophylactic dose and only therapeutic doses, and both prophylactic and therapeutic doses) were also evaluated. In the three placebo controlled studies, a substance that is similar in taste and quantity to the intervention substrate was used in two studies (Bang et al., 2015; Lee et al., 2013); in the remaining study, water was used as placebo (Lee et al., 2014b). In one study, alcohol without an intervention substrate was used as the control (Takahashi et al., 2010) and in the long distance study participants past experiences regarding hangover has been used as the control (Verster & Berthélemy, 2012). In one study, the control group was not clearly defined (Noh et al., 2009).

3.3 | Study outcomes

The main outcomes of the studies are summarized in Table 2. In all six studies, hangover severity has improved significantly following the respective interventions. Statistical significance ($p < .05$) was noted in five studies (Bang et al., 2015; Lee et al., 2013; Lee et al., 2014b; Takahashi et al., 2010; Verster & Berthélemy, 2012). In one of those studies, improvement was noted only when a prophylactic dose of the intervention was given (Takahashi et al., 2010). In five studies, central nervous system symptoms (headache, tiredness, dizziness, difficulty in concentration, memory loss, trouble in sleeping, and sleepiness) were shown to be improved (Bang et al., 2015; Lee et al., 2013; Lee et al., 2014b; Noh et al., 2009; Verster & Berthélemy, 2012). Five studies have also noted improvement of gastro-intestinal symptom (stomachache, nausea, vomiting, diarrhea, and loss of appetite; Bang et al., 2015; Lee et al., 2014b; Noh et al., 2009; Takahashi et al., 2010; Verster & Berthélemy, 2012), whereas in three studies

TABLE 1 Characteristics of included studies

Study	Sample	Study design	Jadad score	Amount of alcohol	Intervention	Control	Primary outcome measures	Comments
Bang et al. (2015)	28 Men 19–55 years	R PC DB CO WO-1 week	5	1.75 g/kg over 2 hr	Polysaccharide rich extract of *Acanthopanax senticosus* (PEA); 30 min before and soon after alcohol consumption	Product with same color and shape as the extract; 30 min before and soon after alcohol consumption	Acute hangover scale (9 item)	A prepared meal is given with alcohol
Lee et al. (2013)	14 Men Average 25.8 years Average BMI 22.93 kg/m2	R PC SB CO WO-2 weeks	4	540 ml of 20.1 v/v% (108.6 ml) (85.7 g)	220 ml of pear juice; 30 min before alcohol consumption	220 ml of artificial pear flavor and fructose; 30 min before alcohol consumption	Hangover severity (14 item); blood alcohol and acetaldehyde level	A low fat meal is given 2 hr prior to pear juice
Lee et al. (2014b)	25 Men 25–49 years BMI-18.5 to 29.9 kg/m2	R PC CO WO-2 weeks	2	100 ml of 40% v/v% (whiskey) (40 ml) (31.6 g)	100 ml of red ginseng antihangover drink (RGD); within 5 min of consuming alcohol	100 ml water; within 5 min of consuming alcohol	Hangover symptoms (15 items); blood alcohol and acetaldehyde level; alcohol concentration in expired air	One piece of cheese is given with alcohol
Noh et al. (2009)*	9 Men 24–28 years	C CO WO-2 weeks		360 ml 20% (72 g) over 1 hr	Dandelion juice 220 ml daily for 7 days	Not mentioned	Hangover symptoms (38 items); blood alcohol and acetaldehyde level	
Takahashi et al. (2010)	10 Men 40% 21–58 years	C CO WO- 1 week	1	>44 g	KSS[a] given in three regimes Regime 1: KSS two doses/day for 2 days. Regime 2: KSS one dose administered 5 hr before and four doses after alcohol consumption. Regime3: KSS one dose administered 5 hr before alcohol consumption	Alcohol without KSS	Hangover symptoms (VAS-22 item); time taken for disappearance of all symptoms; overall well-being assessment	No restriction in food and fluid intake
Verster & Berthélemy (2012)	103 Men-21% 25–40 years	R C	2	Sufficient quantity of alcohol to leave them feeling unpleasant the next day	After-Effect®[b] two capsules before consuming alcohol & two capsules at bed time.	Patients past experience without after effect	Hangover symptoms (9 item)	

Note. R = randomized; PC = placebo controlled; C = controlled; SB = single blinded; DB = double blinded; CO = cross-over study; WO = washout period.

[a]KSS formula contains Kitsuraku, Shokyo, brown sugar, and dextrin.

[b]After-Effect© comprises borage oil (gamma linolenic acid), fish oil (omega-3), vitamins B1, B6, and C, magnesium, Silybummarianum (silymarin), and *Opuntia ficus-indica*.

*published year.

TABLE 2 The main outcomes of the studies

Study	Total/mean hangover severity (control vs. intervention)	Symptoms improved (control vs. intervention)	Symptoms no improved	Blood alcohol concentration	Blood acetaldehyde concentration	Other parameter (clinical and investigation)
Bang et al. (2015)	Improved 14 hr after alcohol (2.3 ± 0.2 versus 1.7 ± 0.1) ($p < .05$)	Tiredness (2.5 ± 0.2 vs. 1.6 ± 0.1; $p < .01$) Headache (2.8 ± 0.2 vs. 1.9 ± 0.2; $p < .01$) Nausea (2.4 ± 0.3 vs. 1.5 ± 0.2; $p < .01$) Stomachache (1.9 ± 0.2 vs. 1.4 ± 0.1; $p < .05$) Dizziness (2.8 ± 0.2 vs. 2.0 ± 0.2; $p < .05$)	Thirst Loss of appetite Palpitations	No significant difference between placebo and intervention group	Not measured	
Lee et al. (2013)	Mean and sum of total hangover severity improved by 16% and 20% respectively by 15 hr after alcohol in intervention group ($p < .05$)	Trouble concentrating (NR; $p < .05$) Sleepiness/dizziness (NR; $p < .10$)	NR	Significantly reduced 15 min after alcohol ($p < .05$) and 30 min after alcohol ($p < .01$)	Reduced at 0.25, 0.5, 1, 2, 4, 6, and 15 hr after alcohol (P-NR)	Borderline positive correlation between AUC of acetaldehyde and hangover severity 3 hr after alcohol ($p = .03$)
Lee et al. (2014b)	Significantly improved 24 hr after alcohol (13.8 ± 1.75 vs. 8.40 ± 1.27; $P < 0.05$)	Stomachache (1.12 ± 0.27 vs. 0.40 ± 0.17; P-NR) Thirst/dehydration (2.12 ± 0.20 vs. 1.32 ± 0.16; P-NR) Concentration (1.48 ± 0.23 vs. 0.96 ± 0.18; P-NR) Memory loss (0.48 ± 0.16 vs. 0.08 ± 0.06; P-NR)	Nausea Vomiting Light sensitivity Sleeping difficult Excessive sweating Anxiety Depression Trembling/shaking Dizziness	Reduced at 30, 45, and 60 min after alcohol ($p < 0.05$)	Increased at 120 and 180 min after alcohol ($p > 0.05$)	Expiratory air alcohol level—significantly reduced at 30 and 60 min after alcohol ($p = .058$)
Noh et al. (2009)	Improved (p-NR)	Digestive muscle, eye, skin and central nervous system symptoms (P-NR)	Symptoms related to circulation	Reduced 150 min after alcohol (P-NR)	Reduced 150 min after alcohol (P-NR)	
Takahashi et al. (2010)	No difference between test 1 group and control group; significant improvement in test 2 and 3 groups on next day morning and evening ($p < .05$)	Nausea (P-NR) Vomiting (P-NR) Diarrhea (P-NR)	Increased sweating bloating sensation	Not measured	Not measured	Time taken for disappearance of all symptoms—no significant difference overall wellbeing assessment— significant improvement in test 2 and 3 ($p < .05$)
Verster & Berthélemy, (2012)	Significantly improved on next day (5.18 ± 1.9 vs. 2.33 ± 1.6; $p < .01$)	Thirst (6.62 ± 2.4 vs. 3.96 ± 2.5; $p < .001$) Headache (6.42 ± 2.5 vs. 2.71 ± 2.5; $p < .001$) Tiredness (6.96 ± 2.0 vs. 4.34 ± 2.6; $p < .001$) Dizziness (3.35 ± 2.9 vs. 1.34 ± 2.0; $p < .001$) Loss of appetite (4.39 ± 3.1 vs. 1.79 ± 2.3; $p < .001$) Stomachache (4.57 ± 3.2 vs. 1.60 ± 2.2; $p < .001$) Nausea (4.81 ± 3.0 vs. 1.50 ± 2.1; $p < .001$)	Palpitations	Not measured	Not measured	Not measured

Note. AUC = area under the curve; NR = not reported.

tiredness and thirst or dehydration were improved (Bang et al., 2015; Lee et al., 2014b; Verster & Berthélemy, 2012). In one study, there was a significant improvement in the overall well-being assessment, but no difference in time taken for disappearance of all symptoms (Takahashi et al., 2010). However, no intervention was able to relieve all the symptoms of hangover. Palpitations or cardiovascular symptoms were the commonest symptoms that have not shown any improvement in the studies (Bang et al., 2015; Noh et al., 2009; Verster & Berthélemy, 2012). Anxiety, depression, trembling or shaking (Lee et al., 2013), and increased sweating (Lee et al., 2013; Takahashi et al., 2010) were among the symptoms that did not improve. In one study, bloating sensation of the abdomen was more in the treatment group than in the control group (Takahashi et al., 2010).

4 | DISCUSSION

This systematic review pools scientific data on alcohol hangover treatment and/or prevention, published since 2009. All controlled human studies were considered and were systematically analyzed in areas of methodology and the test results. Six potentially effective herbal products and/or formulas were identified, which includes (a) a polysaccharide rich extract of *A. senticosus*, (b) Korean pear juice, (c) red ginseng antihangover drink, (d) dandelion juice, (e) KSS formula, and (f) After-Effect©. According to evidence available, all these products significantly reduces the hangover severity especially central nervous system, gastro-intestinal symptoms and dehydration. However, none of the interventions were effective in relieving all the hangover symptoms.

4.1 | Potential mechanisms that explain the effects of the treatments

The hangover treatments reviewed in this paper claim to have different mechanisms in alleviating hangover, either by altering the metabolism of alcohol or altering other factors that might cause hangover. Although the authors may claim these mechanisms, they have not been well investigated. Alcohol is metabolized into acetaldehyde by alcohol dehydrogenase and then in to acetate by acetaldehyde dehydrogenase via an oxidative process (Swift & Davidson, 1998). Korean pear juice stimulates key alcohol metabolizing enzymes: alcohol dehydrogenase and aldehyde dehydrogenase, resulting in reduction of acetaldehyde levels (Lee et al., 2012). There is a lot of individual variation in hangover severity and frequency to which genetic factors are known to contribute by about 40–45% (Slutske, Piasecki, Nathanson, Statham, & Martin, 2014). Mutations in the aldehyde dehydrogenase (ALDH2) gene are a main factor and individuals with ALDH2*2 allele experience severe hangover than others (Park et al., 2005). Korean pear juice is shown to be effective in reducing hangover where ALDH2*1/*1 or ALDH2*1/*2 genotypes are present but not with ALDH2*2/*2 genotype (Lee et al., 2013).

Furthermore, the oxidative processes involved in alcohol metabolism generates a lot of free radicals increasing the oxidative stress (Masalkar & Abhang, 2005). Fermented *Akebia quinatai* and red ginseng have a strong antioxidant action (Lee et al., 2014a; Park et al., 2009). The "morning effect" pill also contains antioxidants and

antiinflammatory agents such as gamma linolenic acid, omega-3, vitamins B1, B6, and C, magnesium, and *Opuntia ficus-indica*. Immunological changes are considered important in pathogenesis of hangover, as increased cytokine production is noted (Penning, Van Nuland, Fliervoet, Olivier, & Verster, 2010; Verster, 2008). Cytokine action on several parts of the brain including hippocampus could be the reason for memory impairment and set of symptoms known as sickness behavior (general weakness, difficulty in concentrate, reduced appetite, loss of interest, and reduced activity level, and increased sleepiness; Verster, 2008). A polysaccharide that has been isolated from *A. senticosus* has shown to be having some immune modulatory actions, especially in B lymphocytes and macrophages (Han et al., 2003).

4.2 | Importance of high-quality research and the limitations of the reviewed papers

Sample size is an important factor in clinical trials where hangover severity is measured (Verster et al., 2010). The response to alcohol varies significantly among individuals (Ramchandani, Bosron, & Li, 2001; Swift & Davidson, 1998; Verster et al., 2010). Hence, the results generated from smaller samples may not be able to be generalizable. Furthermore, alcohol metabolism also differs according to the age, gender, and body mass index (Parlesak, Billinger, Bode, & Bode, 2002; Ramchandani et al., 2001; Thomasson, 1995). Hence, using a mixture of males and females with gender and weight adjusted doses of alcohol given to the participants is more suitable in hangover studies (Verster et al., 2010). In addition, studies have shown an interracial variation in alcohol metabolism, due to difference in key enzymes involved in alcohol metabolism (Peng & Yin, 2009). This can also result in differences in patterns, frequency, and severity of alcohol hangover amongst the different ethnic groups, which also needs to be kept in mind when conducting alcohol hangover research. An effective hangover preventive or treatment strategy in one ethnic group might not demonstrate the same efficacy in another ethnic group due to these interracial variations. As most of the alcohol consumers are young adults and clinical trials should focus on that age group (Naimi et al., 2003). Cross-over designs help to eliminate the intersubject variability. Proper randomization and placebo selection is important. The results of the studies with low Jadad scores should be interpreted with caution and such studies should be redone with a more scientifically thorough design.

Four of the selected studies were experimental studies where a specific amount of alcohol was given to the participant in controlled conditions. These studies can measure the hangover severity without being affected by other confounding factors affecting alcohol absorption or metabolism such as food intake, hydration, sleep level, and other activities (Ramchandani et al., 2001; Verster et al., 2010). Yet emotional hangover symptoms such as embarrassment, misery, and guilt might not manifest as in normal setting (Verster et al., 2010). As the amount of alcohol causing hangover varies among individuals (Verster, 2008; Verster et al., 2010), giving the same amount of alcohol to all the participants may cause different levels of hangover causing difficulty in interpretation of the results. Also the amount of alcohol that can be consumed is limited because of ethical constraints. Regardless of the calculated correct alcohol doses given, hangover severity

varies with alcoholic beverages due to the presence of different types of congeners (Prat et al., 2009; Swift & Davidson, 1998; Verster et al., 2010). Hence, even if a substance is proven to be effective for one type of alcohol beverage it is difficult to generalize the result for other types. Two studies have used naturalistic method where participants consume alcohol at their own pace, amount, and type of choice. This mimics real-life drinking and subsequent hangover more than drinking in a controlled hospital or laboratory setting (Verster et al., 2010).

Using patients past experience as the control is also not suitable due to recall bias. The timing of substrate administration is another crucial factor. A substrate which has to be taken daily for 7 days prior to alcohol consumption is neither convenient nor practical. When the substrate is to be taken after alcohol consumption, the compliance might decline. In that aspect, prophylactic doses could be more beneficial. The methods of assessing hangover includes, hangover frequency, hangover symptom count, hangover duration, hangover susceptibility, and hangover severity (Verster et al., 2010). Most of the studies have used symptom count to measure hangover. Wide variety of symptoms are known to occur in hangover with lot of individual variations, making it impossible to evaluate all the symptoms (Verster et al., 2010). A better approach would be to use a validated symptom score such as hangover severity scale (Slutske, Piasecki, & Hunt-Carter, 2003), acute hangover scale (Rohsenow, Howland, Minsky, Almeida, & Roehrs, 2007), and alcohol hangover severity scale (Wall, Horn, Johnson, Smith, & Carr, 2000).

The considerable heterogeneity amongst the studies included in this review is a limitation, which stem from (a) factors associated with alcohol administration (different alcohol doses and types), (b) participants (predominantly males and young adults, and racial differences), and (c) intervention (limited details of the mechanistic explanations, most of studies have used various methods to assess the hangover level).

Finally, in future studies, it would be useful to explore the mechanistic reason for favorable action of some substance on alcohol hangover and individual response for different alcohol types and antihangover substances. In other words, more insight in the pathology and bio-behavioral correlates of the alcohol hangover is needed in order to develop an effective hangover treatment.

5 | CONCLUSIONS

The available evidence suggests that several products are capable of significantly improving some, but not all, of the symptoms related to alcohol hangover. Therefore, further research is necessary to develop clinically effective hangover treatments.

CONFLICT OF INTEREST

REFERENCES

Bang, J. S., Chung, Y. H., Chung, S. J., Lee, H. S., Song, E. H., Shin, Y. K., ... Jeong, J. H. (2015). Clinical effect of a polysaccharide-rich extract of *Acanthopanax senticosus* on alcohol hangover. *Pharmazie*, 70, 269–273.

Frone, M. R. (2006). Prevalence and distribution of alcohol use and impairment in the workplace: A U.S. national survey. *Journal of Studies on Alcohol*, 67, 147–156.

Frone, M. R., & Verster, J. C. (2013). Alcohol hangover and the workplace: A need for research. *Current Drug Abuse Reviews*, 6, 177–179.

Han, S. B., Yoon, Y. D., Ahn, H. J., Lee, H. S., Lee, C. W., Yoon, W. K., ... Kim, H. M. (2003). Toll-like receptor-mediated activation of B cells and macrophages by polysaccharide isolated from cell culture of *Acanthopanax senticosus*. *International Immunopharmacology*, 3, 1301–1312.

Jadad, A. R., Moore, R. A., Carroll, D., Jenkinson, C., Reynolds, D. J., Gavaghan, D. J., & Mcquay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials*, 17, 1–12.

Lee, H. S., Isse, T., Kawamoto, T., Baik, H. W., Park, J. Y., & Yang, M. (2013). Effect of Korean pear (Pyruspyrifolia cv. Shingo) juice on hangover severity following alcohol consumption. *Food and Chemical Toxicology*, 58, 101–106.

Lee, H. S., Isse, T., Kawamoto, T., Woo, H. S., Kim, A. K., Park, J. Y., & Yang, M. (2012). Effects and action mechanisms of Korean pear (*Pyrus pyrifolia* cv. Shingo) on alcohol detoxification. *Phytotherapy Research*, 26, 1753–1758.

Lee, M. H., Kwak, J. H., Jeon, G., Lee, J. W., Seo, J. H., Lee, H. S., & Lee, J. H. (2014b). Red ginseng relieves the effects of alcohol consumption and hangover symptoms in healthy men: A randomized crossover study. *Food and Function*, 5, 528–534.

Lee, E. K., Kwon, W. Y., Lee, J. W., Yoon, J. A., Chung, K. H., Song, B. C., & An, J. H. (2014a). Quality characteristics and antioxidant activity of vinegar supplemented added with *Akebia quinata* fruit during fermentation. *Journal of the Korean Society of Food Science and Nutrition*, 43, 1217–1227.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gotzsche, P. C., Ioannidis, J. P., ... Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ*, 339, b2700.

Masalkar, P. D., & Abhang, S. A. (2005). Oxidative stress and antioxidant status in patients with alcoholic liver disease. *Clinica Chimica Acta*, 355, 61–65.

Naimi, T. S., Brewer, R. D., Mokdad, A., Denny, C., Serdula, M. K., & Marks, J. S. (2003). Binge drinking among US adults. *JAMA*, 289, 70–75.

Noh, K. H., Jang, J. H., Kim, J. J., Shin, J. H., Kim, D. K., & Song, Y. S. (2009). Effect of dandelion juice supplementation on alcohol-induced oxidative stress and hangover in healthy male college students. *Journal of the Korean Society of Food Science and Nutrition*, 38, 683–693.

Park, J. C., Cha, J. Y., Lee, C. H., Doh, E. S., Kang, I. H., & Cho, Y. S. (2009). Biological activities and chemical characteristics of Monascus-fermented Korean red ginseng. *Journal of Life Science*, 19, 1553–1561.

Park, Y. M., Won, J. H., Kim, Y. H., Choi, J. W., Park, H. J., & Lee, K. T. (2005). In vivo and in vitro anti-inflammatory and anti-nociceptive effects of the methanol extract of Inonotus obliquus. *Journal of Ethnopharmacology*, 101, 120–128.

Parlesak, A., Billinger, M. H., Bode, C., & Bode, J. C. (2002). Gastric alcohol dehydrogenase activity in man: Influence of gender, age, alcohol consumption and smoking in a Caucasian population. *Alcohol and Alcoholism*, 37, 388–393.

Peng, G. S., & Yin, S. H. (2009). Effect of the allelic variants of aldehyde dehydrogenase ALDH2*2 and alcohol dehydrogenase ADH1B*2on blood acetaldehyde concentrations. *Human Genomics*, 3, 121.

Penning, R., Mckinney, A., & Verster, J. C. (2012). Alcohol hangover symptoms and their contribution to the overall hangover severity. *Alcohol and Alcoholism*, 47, 248–252.

Penning, R., Van Nuland, M., Fliervoet, A. L., Olivier, B., & Verster, J. C. (2010). The pathology of alcohol hangover. *Current Drug Abuse Reviews*, *3*, 68–75.

Pittler, M. H., Verster, J. C., & Ernst, E. (2005). Interventions for preventing or treating alcohol hangover: Systematic review of randomised controlled trials. *British Medical Journal*, *331*, 1515–1517.

Prat, G., Adan, A., & Sánchez-Turet, M. (2009). Alcohol hangover: A critical review of explanatory factors. *Human Psychopharmacology*, *24*, 259–267.

Ramchandani, V. A., Bosron, W. F., & Li, T. K. (2001). Research advances in ethanol metabolism. *Pathologie Biologie*, *49*, 676–682.

Rohsenow, D. J., Howland, J., Minsky, S. J., Almeida, A., & Roehrs, T. A. (2007). The acute hangover scale: A new measure of immediate hangover symptoms. *Addictive Behaviors*, *32*, 1314–1320.

Slutske, W. S., Piasecki, T. M., & Hunt-Carter, E. E. (2003). Development and initial validation of the hangover symptoms scale: Prevalence and correlates of hangover symptoms in college students. *Alcoholism: Clinical and Experimental Research*, *27*, 1442–1450.

Slutske, W. S., Piasecki, T. M., Nathanson, L., Statham, D. J., & Martin, N. G. (2014). Genetic influences on alcohol-related hangover. *Addiction*, *109*, 2027–2034.

Swift, R., & Davidson, D. (1998). Alcohol hangover. *Alcohol Health and Research World*, *22*, 54–60.

Takahashi, M., Li, W., Koike, K., & Sadamoto, K. (2010). Clinical effectiveness of KSS formula, a traditional folk remedy for alcohol hangover symptoms. *Journal of Natural Medicines*, *64*, 487–491.

Thomasson, H. R. (1995). Gender differences in alcohol metabolism. Physiological responses to ethanol. *Recent Developments in Alcoholism*, *12*, 163–179.

Verster, J. C. (2008). The alcohol hangover—a puzzling phenomenon. *Alcohol and Alcoholism*, *43*, 124–126.

Verster, J. C. (2012). Editorial: The need for an effective hangover cure. *Current Drug Abuse Reviews*, *5*, 1–2.

Verster, J. C., & Berthélemy, O. (2012). Consumer satisfaction and efficacy of the hangover cure After-effect(©). *Advances in Preventive Medicine*, *2012*, 617942–617942.

Verster, J. C., & Penning, R. (2010). Treatment and prevention of alcohol hangover. *Current Drug Abuse Reviews*, *3*, 103–109.

Verster, J. C., Stephens, R., Penning, R., Rohsenow, D., Mcgeary, J., Levy, D., ... T. & Adan, A. (2010). The alcohol hangover research group consensus statement on best practice in alcohol hangover research. *Current Drug Abuse Reviews*, *3*, 116–126.

Verster, J. C., Van Herwijnen, J., Olivier, B., & Kahler, C. W. (2009). Validation of the Dutch version of the brief young adult alcohol consequences questionnaire (B-YAACQ). *Addictive Behaviors*, *34*, 411–414.

Wall, T. L., Horn, S. M., Johnson, M. L., Smith, T. L., & Carr, L. G. (2000). Hangover symptoms in Asian Americans with variations in the aldehyde dehydrogenase (ALDH2) gene. *Journal of Studies on Alcohol*, *61*, 13–17.

Wiese, J. G., Shlipak, M. G., & Browner, W. S. (2000). The alcohol hangover. *Annals of Internal Medicine*, *132*, 897–902.