Hangover remedies

OH NO... NOT THE FESTIVE SPIRIT

Google 'hangover cure' and 2.37m hits come back: coffee, a hot bath, aspirin, ginseng and 'hair of the dog' are just a few. But is there any scientific basis to these remedies? asks Anthony King

The main symptom of a hangover is described in scholarly tracts as 'general misery', compounded by headache, tiredness, thirst, mood changes, diziness or even concentration problems. And there are longer-term effects that are often overlooked. 'People underestimate the consequences of alcohol hangovers. For example, reduced productivity at work, absenteeism, and increased risk of traffic accidents,' says hangover expert Joris Verster at the University of Utrecht in the Netherlands.

As for a one fix 'cure all' remedy, it's not that simple. The pathology of alcohol hangovers is not clear. Alcohol (and its metabolite) may cause the hangover, but there are many other factors that may aggravate alcohol severity, for example cogeners,' Verster notes.

Cogeners associated with alcoholic beverages are substances formed during the production process, rather than the chemically related compounds that chemists typically think of when they encounter the term.

'Congeners are toxins such as acetone, acetaldehyde, fusel oil, polyphenols, histamines, esters, tannins, amines and amides,' explains Damaris Rothsenov, a researcher at the Center for Alcohol and Addiction Studies at Brown University, Rhode Island, US. The originate from the various different grains, oak barrels and wine skins, and end up in alcoholic beverages as a result of fermentation, distillation and ageing processes.

Many of these chemicals impart colour, flavour and smell to alcoholic drinks; that waft of pungent brandy on plum pudding or burst of festive spice when a bottle of Módelo is uncorked. But they have a dark side too. While most of these chemicals are present in minute amounts, they are nevertheless believed to have a toxic effect on the central nervous system and contribute to a hangover, says Rothsenov.

According to Rothsenov, of all liquors, bourbon has the most cogeners and vodka or gin the least — bourbon has around 37 times the cogeners as vodka. Brandy has the second highest number of cogeners, followed by whisky. Even beer does not escape from these toxins — many beers in fact have more cogeners per standard drink than any liquor. Port, red wines and dry vermouth are all high in cogeners, while dry white wines tend to have the fewest cogeners of any wine.

In an experiment, Rothsenov gave students either bourbon, vodka or placebo prior to them going to bed to see what effects these drinks had on the intensity of their hangover, sleep and next day performance. The students were woken at 7am and given breakfast, but no coffee. Between 8am and 9.30am they completed cognitive tests. 'While alcohol was the best predictor
of how hangover the students reported feeling the next morning, compared to drinking placebo, bourbon had a worse effect than vodka," Rohsenow explains. "Beverage congeners in bourbon versus vodka did significantly increase the intensity of hangover," the study noted. Hangover was rated as more intense in those who slept poorly, so that an alcohol-induced sleep deficit impacts on the experience of a hangover. However, the type of alcohol did not affect performance in tests requiring attention and speed: vodka and whisky drinkers performed equally poorly. "People's sleep was more disrupted after drinking to intoxication than after drinking placebo drinks," Rohsenow added. They woke up more, were restive, and spent less time asleep. "People with more sleep disruptions felt more hungover." Ultimately, however, the severity of a hangover is determined by the amount of alcohol. Once in the stomach, the alcohol moves, via the small intestine, into the bloodstream, with peak levels 30 to 45 minutes later. Fatty foods like milk can slow absorption by about three-fold. Food, like turkey dinners and mince pies, has a similar effect. However, as Diane Bunce, a chemist at the Catholic University of America, Washington DC, points out, "If you drink any kind of carbonated beverage with the alcohol, this helps the alcohol move into your bloodstream quicker and your alcohol blood levels rise much faster." Champagne and other bubbly beverages, she explains, increase alcohol blood concentration by speeding up the emptying of the stomach into the small intestine, where alcohol is absorbed faster. The alcohol eventually distributes itself evenly throughout all body tissues in proportion to their water content. A man's total body water is about 68% of his total weight, while for a woman it's only 55%. Give a man and woman of equal weight the same amount of alcohol to drink and the woman will end up with a higher blood alcohol level. The constant thirst you get with a hangover comes from the dehydrating effects of alcohol in the body, so one way to lessen the effect would be to drink plenty of water whenever you drink alcohol," says Bunce. Although dehydration is often blamed for hangovers, Vestler adds: "The mechanism is unknown, but it is clear that hangovers are not simply caused by dehydration. Dehydration is a consequence of alcohol consumption, but cannot explain the general misery observed during hangovers." Nevertheless, rehydrating with fruit juice can only benefit you the next morning. Once in the liver, alcohol is broken down by the enzyme alcohol dehydrogenase into acetaldehyde. The speed of breakdown varies between individuals, but acetaldehyde is an
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extremely reactive molecule and it can cause deletions to proteins, nucleic acids and neurotransmitters: it is a prime suspect in many hangover studies. Acetaldehyde is broken down to acetate in mitochondria, where most of the cell’s energy, in the form of adenosine triphosphate (ATP), is made. In both steps, NAD+ is reduced to NADH. An abundance of NADH and acetaldehyde can lead to disbalances in other metabolic pathways. People with a faulty aldehyde dehydrogenase enzyme, for example, are slow to clear acetaldehyde and suffer from the effects of this toxic compound—flushing of the skin, headaches, stomach cramps, profound sweating and general malaise. 40–50% of people of Asian descent have such a defective enzyme.

SCIENTIFIC EVIDENCE
Some herbal products are reported by manufacturers to speed up alcohol and acetaldehyde metabolism, but there is no independent scientific evidence to support this. Verster suggests this is a red herring, and that ‘future research should not be focusing on alcohol metabolism.’ John Connolly at Strathclyde University in Scotland, author of a book chapter entitled ‘The toxic and toxic effects of alcohol and its metabolites’, agrees that revving up alcohol breakdown is probably not the way forward: ‘Trying to speed up alcohol metabolism is not too realistic. Various vitamins have been tried, but the effect is marginal.’

Indeed, there are myriad hangover cure stockists available online, containing a mix of herbal ingredients, vitamins or foods; again, most have no scientific studies to support their claims.

In 2009, in the British Medical Journal (2009; 313:1515), Verster published a review of all the randomised controlled trials of medical interventions for preventing or treating hangovers.

He found only 15 trials, and only one for treatment ‘intervention’. Seven of these, he stamped as ‘fail’ for various reasons, including the omission of a placebo group.

The remaining eight were propanolol, topiramate, an antiepileptic used to treat nausea and vomiting, tolcapone acid, an antiviral antifungal and antiinflammatory used in the treatment of migraines, fructose or glucose, and the dietary supplements borax (Borax officinalis), arthroc (Oxycod nobile), a yeast-based preparation, and quercetin (Quercus rubra).

There is no mention in many of these trials as to what was considered to be the active ingredient, which is a reflection of the level of these studies, and all used symptom scores that were not validated.

Three reported some relief for a few symptoms, but were laden with caveats. None were full-proof cures.

A more recent review by Verster (Current Drug Abuse Reviews, 2010, 3, 103) came to similar conclusions.

Verster doesn’t spread much festive cheer in his tidings: ‘There is no scientific evidence that any of the cures on the internet are effective in treating or preventing alcohol hangover. In most cases, some false research is just absent!’ The few products that have been scientifically investigated were shown to be ineffective in treating alcohol hangover, Verster adds.

Moreover, there is still a way to go, as scientists found to even study the range of symptoms experienced the morning after. ‘There is no animal model for alcohol hangover yet,’ he adds.

MIGRAINE CLUE
But rats suffering from chronic headache are available. Neuroscientist Michael Oshinsky at Thomas Jefferson University in the US is interested in migraine headaches and has created animal models for this debilitating condition. In a 2016 paper in PLoS One (2016, 5, 12, e15963), Oshinsky gave alcohol to such rats to find out what causes hangover headaches. He noted that hangover headache has been blamed on congestion, dehydration or the alcohol metabolite acetaldehyde, but his research points elsewhere. ‘Alcohol when broken down initially goes to acetaldehyde, but acetaldehyde is a very toxic compound and the body doesn’t like having it hang around. The liver quickly converts it to acetate,’ Oshinsky says. The high levels of acetate in the blood following drinking are the true cause of hangover headache, he explains. ‘We gave these rats acetate in the absence of alcohol and sure enough the acetate itself induced headache.’

A literature search revealed that persons on kidney dialysis suffered similarly when acetate had been used as a buffer. Acetate is ubiquitous in the body and is used as a substrate for the Krebs cycle, an essential cog in the body’s machinery to produce energy. The whole system is off killer if too much acetate becomes available after alcohol consumption, Oshinsky argues. ‘People prone to migraine suffer after just two or three alcoholic drinks, perhaps because of a dysfunction in their mitochondria,’ he says.

High levels of acetate leads to an increase in adenosine in many tissues, including the brain, so blocking adenosine receptors—with caffeine, for example—reduced hangover headaches in the lab rats. ‘Four hours after the consumption of alcohol, we gave the rats caffeine, an adenosine receptor antagonist, and it blocked the headache in all rats.’ However, pain was blocked only until the caffeine was broken down. Oshinsky hopes his plan could result in a cure for headaches in those prone to migraine but also hangovers. For now, it seems coffee or lots of tea may be one easily administered self-treatment option.

There are other theories as to the cause of hangovers, which may open paths to cure. ‘Recent research suggests a role for the immune system and cytokines in the genesis of alcohol hangover,’ notes Verster. In their 2014 review of hangover ‘cures’, Verster and his colleague Renate Penning noted that treatments showing a reduction in hangover severity were also involved in prostaglandin synthesis. This includes tolcapone acid and pricky pear, which offer partial relief. ‘Together with the observation that prostaglandin levels are elevated during alcohol hangover, this strengthens the idea that alcohol hangover is in fact an inflammatory process,’ they conclude.

These are the more traditional hangover cures. Fried egg and bacon is one, taking an aspirin before you go to bed is another. Such cures have gotten short shift from serious labs. ‘Surprisingly, various obvious and frequently applied remedies to relieve hangover symptoms, such as aspirin, drinking water, a heavy breakfast and extensive sleeping, have not been the subject of scientific research,’ Verster and Penning noted in their review. And neither has the ‘hair of the dog’ received any scientific evaluation, which Connolly says does provide some relief, but warns that ‘this remedy is really a good sign of impending dependence.’

‘If there was a real hangover cure out there, someone would have already marketed it,’ adds Connolly, dispensing any ghosts of Christmas hope.

There’s a need to understand the ‘why’ behind the hangover misery. Solving this puzzle could allow an effective cure to be developed. But this is by no means a consensus view. Some medical experts comment that if you’ve got a hangover you deserve it. Removal of hangovers might, they argue, encourage more regular excessive drinking, a lean closer to alcoholism. Connolly notes that binge drinking is a very real problem, adding: ‘I’d rather people just drink a sensible amount.’

For now, if moderation fails, an intake of juice, some breakfast, a cup of tea or coffee and a return to bed offers some hope the morning after.

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