Evaluation of the Efficacy and Safety of “PartySmart” in the Prevention of Alcohol-induced Hangover: A Prospective, Randomized, Double Blind, Comparative, Phase III Clinical Trial

Abstract

“Alcohol-induced hangover”, is a poorly understood physiological manifestation of the biochemical effects of alcohol on the body. There are various formulations, which are being promoted as a cure for alcohol-induced hangover; but these formulations have not been evaluated for their efficacy and safety, in controlled clinical trials. This study was planned to evaluate the comparative efficacy and safety of “PartySmart” in the prevention of the alcohol-induced hangover symptoms, with one of the formulations, which is being promoted as a cure for alcohol-induced hangover.

The present study was a prospective, randomized, double blind, comparative, phase III clinical trial.

Abbreviations

| ADH | Alcohol dehydrogenase |
| ALDH | Aldehyde dehydrogenase |
| BAC | Blood alcohol concentration |
| BMI | Body mass index |
| CRF | Case record form |
| HCl | Hydrochloric acid |
| HS | Highly significant |
| NAD | Nicotinamide adenine dinucleotide |
| NS | Not significant |
| POMS | Profile of mood states questionnaire |
| S | Significant |
Clinical Study

were willing to give informed consent were included in the study. The “PartySmart” group received a capsule of “PartySmart” before alcohol consumption, and the volunteers from the compared drug group consumed the other drug as per the recommended dose. All the volunteers were assessed at baseline and at 2 and 10 hours after receiving the study drugs for physical changes, and blood and urinary alcohol and acetaldehyde levels. All the participants had their food from the same restaurant, where they had same type of food, on the study day after consuming alcohol. All the participants consumed same brand and type of alcohol; and the details of number of alcoholic drinks consumed by each volunteer, the time of ‘going to bed’ and ‘rising in the morning’ were recorded in a structured case record form (CRF). The profile of mood states questionnaire (POMS questionnaire), predefined symptom score scale, and visual analog score scale were used to assess the intensity of hangover, and the final hangover scores were derived after averaging these scores. The predefined primary efficacy endpoints were the difference in the mean final hangover score, which was significantly lower in the “PartySmart” group than in the compared drug group. There was a significant difference in the mean blood alcohol levels after 10 hours, a highly significant difference in the mean blood acetaldehyde levels after 2 hours and a significant difference after 10 hours, in both the groups. There was a significant difference in the mean urinary alcohol levels after 2 and 10 hours, in both the groups. There was also a significant difference in the mean urinary acetaldehyde levels after 2 and 10 hours, in both the groups. There were no clinically significant adverse reactions, in both the groups and the overall compliance was good. These results suggest that “PartySmart” prevents the binding of acetaldehyde to cell proteins, causing a higher initial blood level and a subsequent rapid elimination, and the subsequent lower levels of alcohol and acetaldehyde in the blood reflected in the decreased final hangover score. Therefore, it may be concluded that “PartySmart” is effective and safe for usage in the prevention of alcohol-induced hangover, as compared to the other formulation.

Introduction

Hangover, over?

Doesn’t matter hard or soft, They will both leave you lost!
You could be coming, going or staying;
You’ll never know, just keep on praying.
All those brain cells had to die, the question is,
Was it worth the high?

Alcohol-induced hangover, also referred as “veisalgia” (from the Norwegian kveis for “uneasiness following debauchery” and Greek “algia” for “pain”), is a poorly understood physiological manifestation of the biochemical effects of alcoholic beverages on the body. Researchers suspect that both the breakdown products of alcohol metabolism (esp. acetylaldehyde), and other chemicals commonly found in alcoholic beverages (i.e., congeners) are in part responsible for the hangover. Secondary causes include the altered sleep patterns induced by drinking, and other recreational drugs used in conjunction with alcohol. While the causes of the hangover may vary from person to person, hangovers can occur in light, moderate and heavy drinkers, and have major repercussions not only for individuals, but also for the society at large. Alcohol hangover is commonly characterized by headache, nausea, polyuria, polydipsia, and fatigue.

There are various formulations, which are being promoted as a cure for alcohol-induced hangover, but these formulations have not been evaluated for the efficacy and safety, in controlled clinical trials, however, neither the changes in various biochemical parameters
and cognitive impairments on
treatment with these drugs have
been monitored.

“PartySmart” is a polyherbal
formulation containing the extracts
of Phoenix dactylifera, Cichorium
intybus, Andrographis paniculata,
Vitis vinifera, Phyllanthus amarus
and Emblica officinalis. Some
studies have shown that
“PartySmart” is useful in
preventing alcohol-induced
hangover; and previous studies
have demonstrated that pre-
treatment with “PartySmart” before
alcohol ingestion was associated
with rapid elimination of alcohol
and acetaldehyde3-5.

This study was planned to
evaluate the comparative efficacy
and safety of “PartySmart” in the
prevention of the alcohol-induced
hangover, with one of the
formulations, which is promoted
as a cure for alcohol-induced
hangover. This formulation with
which the activity of “PartySmart”
was compared is recommended in
a serving size of one capsule, and
each capsule contains Thiamin
(3 mg), Riboflavin (3.4 mg), Niacin
(940 mg), Vitamin B₆ (4 mg),
Pantothenic acid (20 mg) and
Opuntia ficus indica fruit extract
(800 IU). The recommended dose
is one-capsule/130 lbs. of body
weight, with water, at least 2 hours
before consuming alcohol.

Aim of the study

This study was planned to
evaluate the effect of “PartySmart”
on blood and urinary levels of
alcohol and acetaldehyde, after
alcohol ingestion, and to assess
the comparative efficacy and safety
of “PartySmart” over the compared
drug in the prevention of
the alcohol-induced hangover
symptoms.

Study design

The present study was a
prospective, randomized, double
blind, comparative, phase III
clinical trial. The duration of the
study was 12 hours on a night, and
the ‘Institutional Ethics Committee’
approved the study.

Materials and
methods

Inclusion criteria

A total of 10 healthy male
participants (from the pool of
volunteers of the R&D Center,
The Himalaya Drug Company,
Bangalore, India), who were
occasional social alcohol
drinkers, aged between
25-45 years, in the body weight
range of 50-70 kg, and were
willing to give informed consent
were included in the study.

Exclusion criteria

Exclusion criteria were
volunteers with acid peptic
disorder, diabetes mellitus,
neurological and psychiatric
disorders, chronic alcoholism,
history of drug abuse, history of
alcohol abuse, and a score of more
than 2 points on the validated brief
Michigan Alcoholism Screening
Test (MAST)6. Similarly,
volunteers
consuming certain concomitant
medications like antibiotics
(furazolidone, griseofulvin,
imidazoles), anticoagulants
(warfarin), antidepressants
(tricyclic antidepressants),
antihistamines, anticonvulsants
(phenytoin), cardiovascular
medications (nitroglycerin,
reserpine, methyldopa,
hydralazine and guanethidine),
sedatives and hypnotics
(benzodiazepines), and those
volunteers, who had known
hypersensitivity to alcohol and
were unwilling to give informed
consent were excluded from the
study.

Randomization and
blinding

A person unconnected with the
study did the randomization in
blocks of 4, by using a computer
generated random number
allocation. Double blinding was
done, and neither the volunteers,
nor the investigators were aware
of the block size, and therefore
were unable to predict the
treatment allocation. The codes
were kept in sealed envelopes
at a secure location to ensure the
double blinding of the treatment
allocation.

Study drugs

Randomly allocated volunteers
were divided into 2 groups:
“PartySmart” group and the
“Compared drug group”. The
“PartySmart” group received one
capsule of “PartySmart” before
alcohol consumption (Batch No.
41/2/R&D/HDC/2004) (Daily dose
of a capsule of “PartySmart” has
been shown to be safe and
effective, therefore was considered
adequate for this study). The
compared drug group was given
the other formulation. The
volunteers from the compared drug
group consumed the other
formulation as per the
recommended dose.
**Clinical Study**

**Study procedure**

All the volunteers were instructed to refrain from consuming any alcoholic beverage at least 48 hours before the study. To induce hangover symptoms, but prevent excessive drinking, all the volunteers were asked to quantify their usual alcohol consumption that will reliably result in hangover symptoms the next day, based on their previous personal experience.

All the volunteers were assessed at baseline (before taking the study drugs) and at 2 and 10 hours after receiving the study drugs for the physical changes, and for blood and urinary alcohol and acetaldehyde levels. The alcohol and acetaldehyde levels were measured by gas chromatography (*Michro-9100, NETEL Chromatograph*), which is a reliable and sensitive method for estimating blood and urinary levels of alcohol and acetaldehyde. All the investigations were performed at the R&D Center, The Himalaya Drug Company, Bangalore, India.

The investigators supervised the intake of the “PartySmart” capsules and the other compared formulation (caplets) by the volunteers. All the participants had their food from the same restaurant, where they had the same type of food, on the study day after consuming alcohol. To prevent excessive drinking, all the participants were reminded to limit their alcohol consumption to the predefined quantity. All the participants consumed same brand and type of alcohol (48w/v, 75% proof whisky), and the details of number of alcoholic drinks consumed by each volunteer, the time of ‘going to bed’ and ‘rising in the morning’ were recorded in a structured CRF. Local accommodation and taxi transport were provided to all the participants.

Various studies have been conducted on psychoactive drugs and also on alcohol-induced hangover by using the POMS. POMS questionnaire is a self-administered questionnaire and the objective of POMS is to measure the effects on mood of various therapeutic approaches. One limitation of the POMS questionnaire is that the complete POMS has 65 different questions, perhaps a few too many to evaluate and therefore an abbreviated version, which included 12 questions was used for this study. The volunteers were asked these 12 questions in the local language (Kannada) by the investigators the next morning, after the blood was withdrawn (before breakfast). The volunteers were asked to tick-mark on a paper, on which checking boxes of 10 cm length were drawn, which was calibrated every 2 cm. One end of the row was marked as one and the other end was marked as 5. The volunteer’s were asked to tick-mark on that predefined scale in the particular box, rating each question in the following manner: 1 = strongly disagree; 2 = disagree; 3 = neutral; 4 = agree; 5 = strongly agree.

The POMS questionnaire, which was used to evaluate the alcohol-induced hangover state in this study included the following 12 questions to evaluate the concerned parameter, which were as follows: (a) “Tension” - Do you feel emotionally stretched out or as being under some kind of unusual nervous strain or pressure? (b) “Anxiety” - Do you have a feeling of being generalized and vague, uneasy or apprehensive? (c) “Depression” - Do you have a feeling of sadness or helplessness? (d) “Dejection” - Are you feeling somewhat hopeless with low spirits? (e) “Anger” - Do you have a feeling of generalized displeasure or irritation or hostility about things happening around you? (f) “Hostility” - Do you have a feeling of non-specific or generalized aggressiveness? (g) “Activity” - Are you feeling energetic and lively enough, as you feel usually? (h) “Vigor” - Do you have enough strength of the body and mind for your routine activities? (i) “Fatigue” - Do you feel physically and mentally tired due to exertion? (j) “Inertia” - Do you feel like lacking enough inclination and willingness, for your routine daily activities? (k) “Confusion” - Do you feel strange or impaired regarding time, place or people around you? (l) “Bewilderment” - Are you feeling too disturbed due to inability to understand or comprehend these questions?

Each volunteer also indicated the severity of each symptom experienced during the alcohol-induced hangover, on a predefined symptom score scale, and another visual analog score scale. The physical parameters for the evaluation of hangover included (1) headache, (2) facial and dermal...
flushing, (3) nausea, (4) burning sensation in the stomach, (5) tachycardia, (6) body ache, (7) burning sensation in the eyes, (8) drowsiness and (9) overall feelings (euphoric/dysphoric and fresh/lousy). The volunteers were asked to tick-mark on these predefined score scales their rating of each symptom in the following manner: 1 = nil; 2 = negligible; 3 = mild; 4 = moderate; 5 = severe. The final hangover scores was derived after averaging the scores of POMS, symptom score scale, and visual analog score scale.

**Primary and secondary endpoints**

The predefined primary endpoints were the difference in hangover scores, physical parameters and blood and urinary alcohol and acetaldehyde levels. The primary outcome measures were assessed at baseline and after 2 and 10 hours after alcohol exposure, on the next day. The predefined secondary endpoints were reduced incidence of adverse effects and overall compliance to the formulations under investigation.

**Intercurrent illness and concomitant medication**

The investigators recorded any information about intercurrent illness, therapeutic interventions and concomitant medication. Antacid or any other drug given for symptomatic relief from acute alcohol-induced gastritis was allowed concomitantly with the study medication.

**Adverse events**

All the adverse events reported by the subjects or observed by the investigators were recorded with information about severity, date of onset, duration and action taken regarding study drugs. Relation of adverse events to study medication was predefined as “Unrelated”, “Possible”, and “Probable”.

**Analysis of data**

The data analysis was performed according to intent-to-treat principles. The “Independent Sample’s Unpaired ‘t’ Test” was used to compare both the groups for baseline parameters, predefined amount of alcohol to induce hangover, actual alcohol consumption and changes in various biochemical parameters. A two-sided “p” value of <0.05 was considered significant, and a power of 80% was considered for this trial.

**Results**

There were 5 volunteers in each group (“PartySmart group” and “the compared drug group”). There was no significant difference in the age and body mass index (BMI) of the volunteers in both the groups (t = 1.146, R² = 0.1411, p = 0.2848; NS) (Table 1 and Fig. 1). Similarly, there was no significant different in the mean predefined amount of alcohol consumption to experience the hangover (t = 0.00, R² = 0.00, p = 1; NS) (Table 1 and Fig. 2), and also in the mean amount of alcohol actually consumed by the volunteers (t = 0.6325, R² = 0.04762, p = 0.5447; NS) (Table 1) from the both groups.

There was a significant difference in the mean final hangover score, which was significantly higher in the compared drug group, as compared to the PartySmart group (t = 3.578, R² = 0.6154, p = 0.0072; S) (Table 1 and Fig. 3).

There was no significant difference in both the groups, in the mean blood alcohol levels after 2 hours (t = 0.9253, R² = 0.09668, p = 0.3819; NS) (Table 1 and Fig. 4); but there was a significant difference in the mean blood alcohol levels after 10 hours (t = 4.817, R² = 0.7436, p = 0.0013; S) (Table 1 and Fig. 5). There was a highly significant difference in both the groups, in the mean blood acetaldehyde levels after 2 hours (t = 5.754, R² = 0.8054, p = 0.0004; HS) (Table 1 and Fig. 6) and a significant difference after 10 hours (t = 3.679, R² = 0.6285, p = 0.0062; S) (Table 1 and Fig. 7).

There was a significant difference in both the groups, in the mean urinary alcohol levels after 2 hours (t = 2.425, R² = 0.4236, p = 0.0415; S) (Table 1 and Fig. 8) and 10 hours (t = 4.463, R² = 0.7134, p = 0.0021; S) (Table 1 and Fig. 9). There was a significant difference in both the groups, in the mean urinary acetaldehyde levels after 2 hours (t = 3.034, R² = 0.535, p = 0.0162; S) (Table 1 and Fig. 10) and after 10 hours (t = 4.337, R² = 0.7016, p = 0.0025) (Table 1 and Fig. 11).

There were no clinically significant adverse reactions, either observed by the investigators or reported by the volunteers, in the both groups and the overall compliance was good.
### Discussion

Alcohols are organic compounds consisting of a carbon skeleton with a hydroxyl group, and ethanol (grain alcohol), methanol (wood alcohol), and isopropanol (rubbing alcohol) are common examples. Ethanol is produced by yeast maintained in anaerobic conditions by “fermentation”, and the reaction is catalyzed by the yeast enzyme zymase, which is analogous to the human production of lactic acid ($\text{C}_6\text{H}_{12}\text{O}_6 \rightarrow 2\text{CH}_3\text{CH}_2\text{OH} + 2\text{CO}_2$)$^{10}$.

Researchers estimate that 20% of alcohol ingested passes through the stomach to the blood, and this absorption is relatively slow and is also unique in that few substances are absorbed in the stomach. The remaining 80% of alcohol ingested is absorbed quickly into the blood from the small intestine, and the presence of food in the stomach increases the time it takes for alcohol to be absorbed into the blood$^{10}$.

Between 2% (at low BAC) and 10% (at high BAC) of ethanol is excreted directly through the lungs, urine or sweat, but the greater part is metabolized to acetaldehyde in the liver. At least 2 metabolic routes (each with different optimal concentrations of ethanol), result in the metabolism of approximately one drink per hour. The most important pathway occurs in the cell cytosol where alcohol dehydrogenase (ADH) produces acetaldehyde, which is then rapidly destroyed by aldehyde dehydrogenase (ALDH) in the cytosol and mitochondria. Each of these steps requires nicotinamide adenine dinucleotide (NAD) as a cofactor, and it is the increased ratio of the reduced cofactor (NADH) to NAD (NADH:NAD) that is responsible for many of the

### Table 1

**Analysis of various parameters of “PartySmart” and “Compared drug” groups**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>PartySmart group</th>
<th>Compared drug group</th>
<th>Unpaired ‘t’ test summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>24.06 ± 0.63</td>
<td>26.24 ± 1.79</td>
<td>$t = 1.146, R^2 = 0.1411$, $p = 0.2848$; NS</td>
</tr>
<tr>
<td>Predefined amount of alcohol (ml) consumed</td>
<td>198.00 ± 7.34</td>
<td>198.00 ± 12.00</td>
<td>$t = 0.00, R^2 = 0.00, p = 1; NS</td>
</tr>
<tr>
<td>Amount of alcohol consumed (ml)</td>
<td>186.00 ± 11.22</td>
<td>198.00 ± 15.30</td>
<td>$t = 0.6325, R^2 = 0.04762, $p = 0.5447; NS</td>
</tr>
<tr>
<td>Severity of mean hangover</td>
<td>0.80 ± 0.20</td>
<td>2.40 ± 0.40</td>
<td>$t = 0.9253, R^2 = 0.09668, $p = 0.3819; NS</td>
</tr>
<tr>
<td>Blood alcohol levels (mg/dl) after 2 hours</td>
<td>35.08 ± 4.86</td>
<td>29.32 ± 3.88</td>
<td>$t = 0.00, R^2 = 0.00, p = 1; NS</td>
</tr>
<tr>
<td>Blood alcohol levels (mg/dl) after 10 hours</td>
<td>1.14 ± 0.63</td>
<td>7.68 ± 2.97</td>
<td>$t = 4.817, R^2 = 0.7436, $p = 0.0013; S</td>
</tr>
<tr>
<td>Blood acetaldehyde levels (µg/dl) after 2 hours</td>
<td>214.90 ± 23.81</td>
<td>74.34 ± 5.44</td>
<td>$t = 5.754, R^2 = 0.8054, $p = 0.0004; HS</td>
</tr>
<tr>
<td>Blood acetaldehyde levels (µg/dl) after 10 hours</td>
<td>10.30 ± 1.59</td>
<td>37.69 ± 7.27</td>
<td>$t = 3.679, R^2 = 0.6285, $p = 0.0062; S</td>
</tr>
<tr>
<td>Urine alcohol levels (mg/dl) after 2 hours</td>
<td>17.42 ± 1.39</td>
<td>35.49 ± 7.32</td>
<td>$t = 2.425, R^2 = 0.4236, $p = 0.0415; S</td>
</tr>
<tr>
<td>Urine alcohol levels (mg/dl) after 10 hours</td>
<td>8.59 ± 0.99</td>
<td>34.80 ± 5.79</td>
<td>$t = 4.463, R^2 = 0.7134, $p = 0.0021; S</td>
</tr>
<tr>
<td>Urine acetaldehyde levels (µg/ml) after 2 hours</td>
<td>37.68 ± 6.35</td>
<td>17.05 ± 2.43</td>
<td>$t = 3.034, R^2 = 0.535, $p = 0.0162; S</td>
</tr>
<tr>
<td>Urine acetaldehyde levels (µg/ml) after 10 hours</td>
<td>59.78 ± 4.58</td>
<td>27.61 ± 5.84</td>
<td>$t = 4.337, R^2 = 0.7016, $p = 0.0025; S</td>
</tr>
</tbody>
</table>
metabolic derangements observed after drinking. A second pathway occurs in the microsomes of the smooth endoplasmic reticulum (the microsomal ethanol-oxidizing system, or MEOS), which is responsible for 10% of ethanol oxidation at high blood alcohol concentrations. Acetate combines with a proton to form acetic acid, which can be further broken down to carbon dioxide and water or used to form fatty acids in the liver.

Ethanol is a weakly charged molecule that moves easily through cell membranes, rapidly equilibrating between blood and tissues. The effects of drinking depend in part on the amount of ethanol consumed per unit of body weight. A level of 0.02-0.03 results from the ingestion of one to two typical drinks.

Ethanol is a central nervous system (CNS) depressant that decreases the activity of neurons, although some behavioral stimulation is observed at low blood alcohol concentration (BAC). Ethanol has cross-tolerance, and shares a similar pattern of behavioral problems with other brain depressants (benzodiazepines and barbiturates). The intoxicating effects of alcohol appear to be due to its actions at specific neurotransmitter receptors and transporters. Alcohol enhances γ-aminobutyric acid A (GABAA) receptors, and inhibits N-methyl-D-aspartate (NMDA) receptors. In vitro studies suggest that the additional effects involve the inhibition of adenosine uptake, and a translocation of the cyclic AMP-dependent protein kinase catalytic subunit from the cytoplasm to the nucleus. Neurons adapt quickly to these actions, and thus different effects may be present during chronic administration and withdrawal.

Approximately 35% of drinkers may experience a “blackout” (an episode of temporary anterograde amnesia), in which the person forgets all or part of what occurred during a drinking evening. Another common problem, one seen after as few as one or two drinks, is that while alcohol can help someone to fall asleep, it also “fragments” the sleep pattern causing alterations between sleep stages and a deficiency in deep sleep. At the same time, alcohol diminishes rapid eye movement sleep early in the night, resulting in prominent and sometimes disturbing dreams later in the night. Finally, alcohol relaxes the muscles in the pharynx, which can cause snoring and exacerbate sleep apnea.

The symptoms characteristic of the hangover usually commence several hours after the last ingestion of alcohol and peak at the time the BAC reaches zero. Epidemiological data suggests that approximately 75% of those who drink to intoxication will experience hangover symptoms. Alcohol directly irritates the stomach lining. It also causes increased production of HCl, most likely by causing increased blood flow to the oxyntic cells that secrete HCl. The afferent nerves of the vagus, and sympathetic innervation of the stomach relay this information to the vomiting center of the medulla, which then sends down motor stimulation to start the antiperistaltic waves necessary for propulsion of the stomach contents out of the mouth. Nausea is the “conscious recognition of subconscious excitation in an area of the medulla closely associated with the vomiting center”, commonly seen in hangover. The etiology of hangover headaches is
uncertain, but it is thought that the vasodilation effect of alcohol leads to increased pressure in the cranial cavity. Alcohol may also induce increased histamine and serotonin levels, which are correlated with headaches in some people. Alcohol decreases blood sugar level in many people, and this temporary hypoglycemia is thought to be a minor cause of the fatigue experienced during a hangover. Both insulin and glucagon levels are increased by acute alcohol ingestion, the exact mechanism by which these two antagonists reduce the availability of glucose after alcohol ingestion is unknown. This is more likely the major cause of hangover fatigue. Besides, the obvious fact that most recreational drinking occurs at night, prolongs the time until a person begins sleep, and hence alcohol-induced sleep may be of poorer quality due to the “rebound effect”12.

Congener refers to any other biologically active compound found in alcoholic beverages, and proteins to the surface of the tubular cells. Water can then be reabsorbed from the lumen of the tubule and preserved. This is especially important in the collecting duct, which is normally impermeable to water. When alcohol depresses the amount of antidiuretic hormone in the circulation, the kidneys fail to retain water and the person excretes large volumes of urine (polyuria). This can lead to dryness of the mouth and mucous membranes throughout the body. This can elicit an extreme thirst response (polydipsia) in order to stimulate the person to intake liquids to compensate for the loss of fluid through the urine. Aldosterone and renin levels rise during the hangover period to help combat the dehydration brought on by the inhibition of antidiuretic hormone13.

Alcohol depresses hypothalamic synthesis of vasopressin (antidiuretic hormone, or ADH) as well as secretion of this hormone by the posterior pituitary. Anti-diuretic hormone combines with membrane receptors on the surfaces of kidney tubular cells to induce a cyclic adenosine monophosphate (cAMP) pathway. This ultimately results in the recruitment of special aquaporin proteins to the surface of the tubular cells. Water can then be reabsorbed from the lumen of the tubule and preserved. This is especially important in the collecting duct, which is normally impermeable to water. When alcohol depresses the amount of antidiuretic hormone in the circulation, the kidneys fail to retain water and the person excretes large volumes of urine (polyuria). This can lead to dryness of the mouth and mucous membranes throughout the body. This can elicit an extreme thirst response (polydipsia) in order to stimulate the person to intake liquids to compensate for the loss of fluid through the urine. Aldosterone and renin levels rise during the hangover period to help combat the dehydration brought on by the inhibition of antidiuretic hormone13.

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Congeners contribute to body damage brought about by heavy drinking. Congeners include low-molecular-weight alcohols (e.g., methanol and butanol), aldehydes, esters, histamine, phenols, tannins, iron, lead and cobalt. These chemicals contribute to hangovers. Beverages that have few congeners (gin and vodka) produce less severe hangovers than those that contain many (whiskey, brandy and wine). Methanol is present in whiskey, brandy and red wine and is metabolized by the same enzymes as ethanol, only slower because it is competitively inhibited by the presence of ethanol, which has a higher affinity for the enzymes. It is thought that this lingering methanol may induce even greater increases in histamine, resulting in more severe headaches than in other hangovers14.

The only true preventative measure for a hangover is not to consume alcohol in the first place. However, if this is not an option, one may be able to reduce the severity of the hangover by paying attention to the amount and type of alcohol they consume. After a hangover has happened, however, researchers suggest that time is the best remedy. Consumption of fructose-containing foods and liquids will restore blood sugar and fluid levels and may help overcome the fatigue and dehydration of the hangover. Antacids can relieve the irritation of the stomach lining and alleviate nausea. Nonsteroidal anti-inflammatory drugs may reduce headache, but should be used cautiously. Consuming “the hair off the dog that bit you” i.e., more alcohol, will depress brain function and may help with the irritability due to rebound, but will ultimately only prolong the hangover15.

This study used the POMS questionnaire, which was developed in 1971, for people undergoing counseling or psychotherapy, and it quickly gained popularity. The objective of POMS is to measure the effects of various therapeutic approaches on mood. The POMS questionnaire is used extensively in athletics to evaluate the impact of training and to control overtraining. Increases in training load are associated with a decrease in vigor and increase in fatigue, and these

![Figure 4. Blood alcohol levels after 2 hours in the “PartySmart” and “Compared drug” groups.](image)

![Figure 5. Blood alcohol levels after 10 hours in the “PartySmart” and “Compared drug” groups.](image)
two states exhibit the largest and fastest change in response to staleness. Additionally, mood disturbance increases with decreased performance and increased muscle soreness7.

In an experimental study, “PartySmart” was evaluated for its effects on hepatic alcoholic metabolizing enzyme parameters, in rats. The first group received water as vehicle, for 3 days, while the second group received PartySmart, for the same duration. One hour after the respective assigned treatments the animals were euthanised, liver homogenized samples were prepared and centrifuged. The resultant supernatants were used for the estimation of hepatic alcohol, and ALDH using spectrophotometric method. The results showed that pretreatment with “PartySmart” showed a highly significant increase in ADH, and ALDH as compared to control16.

In another study, the administration of “PartySmart” caused higher blood alcohol levels at 2 hours, (possibly by inhibiting the presystemic metabolism of alcohol), and the blood acetaldehyde levels were also found to be higher. The rapid lowering of acetaldehyde concentration in the blood is reflected in significantly higher excretion of acetaldehyde in the urine over a 10-hour period17.

In previous studies with PartySmart, lower alcohol and higher acetaldehyde concentrations were reported in chronic alcohol users, and one study confirmed that regular users of alcohol had lower blood alcohol concentrations. This was interpreted to signify the inhibition of the presystemic metabolism of alcohol, as chronic ingestion of alcohol causes induction of enzymes involved in alcohol metabolism. The same study evaluated the cognitive functions after a standard drinking session before and after treatment for 2 weeks with a similar herbal formulation, and cognitive functions showed less impairment after drug pretreatment. These findings suggest that the rapid elimination of acetaldehyde might be responsible for this effect18,19.

These results also suggest that “PartySmart” prevents the binding of acetaldehyde to cell proteins, causing a higher initial blood level and a subsequent rapid elimination. Lower levels of alcohol and acetaldehyde in the blood at 10 hours were reflected in the

Figure 6. Blood acetaldehyde levels after 2 hours in the “PartySmart” and “Compared drug” groups.

Figure 7. Blood acetaldehyde levels after 10 hours in the “PartySmart” and “Compared drug” groups.
decreased symptom scores and the change in the visual analog score. These observations are indicative of a reduced hangover after “PartySmart” pretreatment. In the other drug group, increase in POMS scores for mood states indicated that the alcohol challenge had the anticipated effect.

In this study, there were no clinically significant adverse reactions either observed by investigators or reported by the volunteers in the “PartySmart” group, which indicates the excellent safety profile of “PartySmart”. “PartySmart” was also evaluated for acute and chronic toxicity, in vitro, and was found to be safe. The acute toxicity of “PartySmart” was evaluated in vitro, and one group was received 20 ml/kg body weight of water orally (control), while the other group received a single oral dose of “PartySmart” at 5000 mg/kg body weight, by gavage using a stomach tube. All the rats were observed for changes in skin and fur, eyes and mucous membranes, respiratory, circulatory and central nervous system, tremors and convulsions, salivation and diarrhea, and lethargy, sleep and coma. Necropsy of all the animals was carried out, and all gross pathological changes were recorded. There was no mortality observed in any of the “PartySmart” treated group, and general behavior and appearance of the animals were normal even at a dose of 5000 mg/kg body weight, and hence it was not possible to determine the median lethal dose (LD₅₀). There were no observable gross abnormalities that could be attributed to drug toxicity at the time of autopsy, and these findings confirm that “PartySmart” lacks toxicity following acute exposure in rats.

The subchronic toxicity of “PartySmart” was evaluated in vitro, and the control group received 10 ml/kg body weight of vehicle (water), while the other group received “PartySmart” at a dose of 1000 and 2000 mg/kg body weight. All the experimental animals were observed for general signs and symptoms of toxicity. The blood samples were collected before autopsy for hematological and biochemical parameters. On day 91, the surviving animals were sacrificed after an overnight fast, and all the organs were preserved, processed, sectioned and stained for routine histopathological

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**Figure 8.** Urine alcohol levels after 2 hours in the “PartySmart” and “Compared drug” groups.

**Figure 9.** Urine alcohol levels after 10 hours in the “PartySmart” and “Compared drug” groups.
examination. No changes in feed intake were observed in the “PartySmart” treated group as compared to control, while hematological and biochemical parameters were within normal range in all the drug treated groups. No gross abnormalities attributing to the drug toxicity were noticed in any of the test groups. There was no significant difference in the organ weight profile of the animals in the treated group as compared to control. Histopathological examination of all target organs showed no evidence of lesions attributing to drug toxicity. These findings confirm that “PartySmart” is completely devoid of toxicity even after repeated administration in rats.

**Conclusion**

Alcohol-induced hangover is a poorly understood physiological manifestation of the biochemical effects of alcoholic beverages on the body. There are various other formulations, which are being promoted as a cure for alcohol-induced hangover, but the tall claims made by these formulations have not been substantiated with evidence generated in controlled clinical trials. This study was planned to evaluate the comparative efficacy and safety of “PartySmart” in the prevention of the alcohol-induced hangover symptoms, with one of the formulations promoted as a cure for alcohol-induced hangover.

This study observed a significant difference in the mean final hangover score, which was significantly lower in the “PartySmart” group than in the compared drug group. There was a significant difference in the mean blood alcohol levels after 10 hours, a highly significant difference in the mean blood acetaldehyde levels after 2 hours and a significant difference after 10 hours, in both the groups. There was a significant difference in the mean urinary alcohol levels after 2 and 10 hours, in both the groups. There was also a significant difference in the mean urinary acetaldehyde levels after 2 and 10 hours, in both the groups. There were no clinically significant adverse reactions, either observed by the investigators or reported by the volunteers in the both groups and the overall compliance was good. These results suggest that “PartySmart” prevents the binding of acetaldehyde to cell proteins, causing a higher initial blood level and a subsequent rapid elimination.
Lower levels of alcohol and acetaldehyde in the blood were reflected in the decreased final hangover score. Therefore, it may be concluded that “PartySmart” is effective and safe for usage in the prevention of alcohol-induced hangover.

References
1. Helen D, Belmont and Teen Ink. The Young Authors Foundation, Inc. www.teenink.com/Past/1989/68.html

Improvement Should Begin at the Diagnostic Level
- Measures to improve sputum microscopy should be taken.
- Check the quality of microscopy.
- We need cultural sensitivity labs all over the country.
- Twenty-four centers have already been proposed with the help of World Bank.
- Measures taken should include people inflicted with TB at the field levels.
- Unless we ensure correction of the existing DOTS program, DOTS plus would not be a success.
- Relapse in HIV-TB has mainly been seen through a new infection than relapse of an existing infection. Therefore, it is a case of mistaken relapses.
- This would encourage doctors to focus on patient and persistent relapses may be avoided.
- Ongoing active transmission reports are encouraging, ensuring better patient treatment.