

CLINICAL STUDY REPORT

"A double-blind, placebo-controlled, comparative clinical study followed by an Open-label extension study to evaluate the efficacy and safety of Party Smart Soft Chews"

PROTOCOL NO.: HWC/MSCD/PP/003/2022

Version:1.0, Date: 14 April 2022

Clinical Study Report Version: 1.0

Version Date: 07 Oct 2022



SPONSOR

HIMALAYA WELLNESS COMPANY

Makali, Bengaluru – 562162

India

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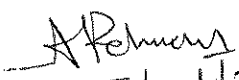


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07/10/2022
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APPROVED BY:

I, the undersigned, declare that I have reviewed the Clinical Study Report, and that to the best of my knowledge it is internally consistent and scientifically rational.

Dr. Rajesh Kumawat, MBBS, MD

Head-Medical Services and Clinical Development (R & D)

Himalaya Wellness Company

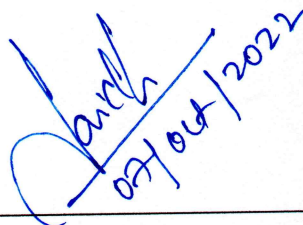


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INVESTIGATOR'S SIGNATURE PAGE

This study was conducted in compliance with the approved protocol & the ICMR ethical guidelines, the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-GCP) (Step 5) 'Guidance on Good Clinical Practice' (E6 R2), NDCT 2019 (The New Drugs and Clinical Trials), Declaration of Helsinki, Good Clinical Practice Guidelines for Clinical Trials in Ayurveda, Siddha, and Unani Medicine (GCP-ASU) & Central Council for Research in Ayurvedic Sciences (CCRAS) Research Policy.

I have read this Clinical Study Report for completeness, accuracy, compliance with the protocol, Standard Operating Procedures, Good Clinical Practices and confirmed that to the best of my knowledge it accurately describes the conduct and results of the study.

Principal Investigator	Signature and Date
Dr. Farida Khanum Abbasi, B.A.M.S, MD Healing Earth Multi-speciality Ayurveda hospital #419, sector-5, HSR Ring Road, HSR Layout, Bangalore- 560034	 07 Oct 2022

BIostatistician SIGNATURE

The undersigned confirm that the interpretation and presentation of data in this clinical study report are consistent with the results obtained.



07/oct/2022

Mr. Abdul Rehman

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Biostatistician

1.0 TITLE PAGE

Study Title:	"A double-blind, placebo-controlled, comparative clinical study followed by an Open-label extension study to evaluate the efficacy and safety of Party Smart Soft Chews"
Protocol Number:	HWC/MSCD/PP/003/2022
Investigational Product	PartySmart Soft Chews (Active & Placebo) PartySmart Capsule Cheers® Restore Capsule
Phase of Development:	Efficacy & Safety
Indication:	Alcohol hangover
Study Start Date:	23 rd May 2022
Study End Date:	17 th Jun 2022
Study Design:	Double-blind, Placebo-controlled comparative clinical study followed by an Open-label Extension.
Subject Population	Healthy adult subjects with previous history of social alcohol consumption
Number of Subjects:	40 Subjects
Sponsor:	Himalaya Wellness Company (HWC) Makali, Bengaluru. 562162, INDIA
Name and affiliation of principal or coordinating investigator(s) & Site	Principal Investigator: Dr Farida Khanum Abbasi, B.A.M.S, MD Healing Earth Multi-speciality Ayurveda hospital #419, sector-5, HSR Ring Road, HSR Layout, Bangalore-560034

Name of Sponsor Representative	Dr Rajesh Kumawat, MBBS, MD Head-Medical Services and Clinical Development (R & D) Himalaya Wellness Company
<p><i>Statement of Compliance:</i></p> <p>This study was conducted in compliance with the approved protocol, ICMR ethical guidelines, the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-GCP) (Step 5) 'Guidance on Good Clinical Practice' (E6 R2), NDCT Rule (The New Drugs and Clinical Trials), Declaration of Helsinki, Good Clinical Practice Guidelines for Clinical Trials in Ayurveda, Siddha, and Unani Medicine (GCP-ASU) & Central Council for Research in Ayurvedic Sciences (CCRAS) Research Policy.</p> <p>EC Approval Date: 11/05/2022</p> <p>CTRI Registration: CTRI/2022/05/042617</p>	

2.0 SYNOPSIS

Protocol Number	HWC/MSCD/PP/003/2022
Version Number and Date	1.0, Dated: 14 th April 2022
Title of Study	"A double-blind, placebo-controlled, comparative clinical study followed by an Open-label extension study to evaluate the efficacy and safety of PartySmart Soft Chews"
Study Type	Interventional
Investigational Product (IP)	PartySmart Soft Chews (Active & Placebo) PartySmart Capsule Cheers® Restore Capsule
Investigator/Site	Investigator who was interested to conduct study as per the protocol and ICH-GCP compliance. The study center was selected by Himalaya Wellness Company (HWC).
Sponsor	Himalaya Wellness Company (HWC), Bangalore, India.
Study Duration	Per Subject Duration of the Study: 3-4 weeks (including washout period)
Study Population	Healthy adult subjects with previous history of social alcohol consumption.
Study Design	A double-blind, placebo-controlled, comparative clinical study followed by an Open-label extension.
Study Methodology	After signing the informed consent form, subjects who fulfill the eligibility criteria were enrolled into the study. This was a double-blind placebo-controlled, comparative clinical study followed by an open-label extension study to evaluate the efficacy and safety of PartySmart Soft Chews. Subjects participated in all the four Periods, i.e., Period I, Period II, Period III and Period IV. Between each period there was a minimum 7 ± 2 days of washout period.

	<p>Period I (Active/Placebo Chews)</p> <p>Subjects received Active/Placebo PartySmart soft Chews as per dosages. 40 Subjects of either sex were enrolled to get at least 34 evaluable subjects.</p> <p>Dosage: Active/Placebo Chews – 20 subjects received two soft chews with first sip and remaining 20 subjects received 2 soft chews after last sip of alcohol consumption.</p> <p>Period II (Active/Placebo Chews) [after 7±2 days of Period I]</p> <p>All the 40 subjects from Period I received Active/Placebo PartySmart soft Chews.</p> <p>Dosage: Active/Placebo Chews – 20 subjects received two soft chews with first sip and remaining 20 subjects received 2 soft chews after last sip of alcohol consumption.</p> <p>Period III (PartySmart Capsule) [after 7±2 days of Period II]</p> <p>All the 40 subjects from Period II received PartySmart Capsule in this period.</p> <p>Dosage: PartySmart Capsule– 20 Subject received one capsule with first sip and remaining 20 subjects received one capsule after last sip of alcohol consumption.</p> <p>Period IV (Cheers® Restore capsule) [after 7±2 days of Period III]</p> <p>All the 40 subjects from Period III received Cheers® Restore capsule in this period.</p> <p>Dosage: Cheers® Restore Capsule– All 40 subjects received 2 capsules after last sip of alcohol consumption.</p> <p>Assessments:</p> <p>Subjects were assessed on the following time points in each Period.</p> <ul style="list-style-type: none"> • Blood investigations: Estimation of blood alcohol and acetaldehyde levels at,Pre-alcohol consumption (within one hour prior to first sip) (0hr) • At 1 hr post last sip • At 2 hr post last sip
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	<ul style="list-style-type: none"> At 12 hr post last sip
Objective	<ul style="list-style-type: none"> To evaluate the effect of PartySmart Soft chews on mitigation /prevention of alcohol hangover as evaluated by clinical symptoms, Acute Hangover Scale (AHS) and 1-item overall hangover severity scale. Safety and compliance of the study product.
Study End Point	<ul style="list-style-type: none"> Blood alcohol and acetaldehyde levels Clinical assessment of "Alcohol Hangover Symptoms" Assessment of Acute Hangover Scale (AHS) 1- item Overall Hangover Severity Scale Incidence of adverse effects
Target Sample Size	A total of 40 subjects were enrolled to get at least 34 evaluable subjects. Appropriate representation of male and female subjects were enrolled into the study.
Inclusion Criteria	<ol style="list-style-type: none"> Male and female subjects aged between 20-50 years, weighing more than 45 kgs. Subjects who were used to drink alcohol regularly (social drink, but not alcohol abuse) and is willing and able to comply with the alcohol consumption, blood withdrawal requirements and overnight stay as per the study requirements. Subjects who were judged by the Investigator to be in general good health based on medical history. Subjects who understood the study procedures and signed the informed consent forms participated in the study.
Exclusion Criteria	<ol style="list-style-type: none"> Subjects suspected of drug or alcohol abuse. A medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation.

	<ol style="list-style-type: none"> 3. Subjective sleep duration of less than 3 hours in the night before every study period. 4. Caffeine, nicotine on the day (from midnight) of every study period. 5. Alcohol consumption within 7 days of enrollment in the study 6. Use of psycho-active drugs during the past 30 days or any treatment that might interfere with the evaluation of the investigational product. 7. Subjects who were taking any drug known to interact with benzodiazepines and other drugs, e.g., antiepileptics, antihistamines, muscle relaxant drugs, antihypertensive drugs, drugs inhibiting cytochrome P450. 8. Subjects who were suffering from any clinically significant disorder that might interfere with his/her participation in this study and the evaluation of the efficacy or safety of the investigational product (e.g., renal insufficiency, hepatic or metabolic dysfunction, cardiovascular disease, neurological and or psychiatric disorder etc.). 9. Known hypersensitivity to any of the ingredients of the study products. 10. Participation in any other clinical trial within the past 30 days. 11. Pregnant and lactating women.
Dosage and route of Administration	<p>Period I (Active/Placebo chews)</p> <p>Active/Placebo Chews – 20 subjects received two soft chews with the first sip and remaining 20 subjects received 2 soft chews after the last sip of alcohol consumption.</p> <p>Period II (Active/Placebo chews)</p> <p>Active/Placebo Chews – 20 subjects received two soft chews with first sip and remaining 20 subjects received 2 soft chews after last sip of alcohol consumption. All subjects followed the same type of regimen (with first sip or after last sip). Ref: Figure 1: Study Flowchart</p>

	<p>Period III (PartySmart Capsule)</p> <p>PartySmart Capsule– 20 Subject received one capsule with first sip and remaining 20 subjects received one capsule after last sip of alcohol consumption. All subjects followed the same type of regimen (with first sip or after last sip). Ref: Figure 1: Study Flowchart</p> <p>Period IV (Cheers® Restore Capsule)</p> <p>Dosage: Cheers® Restore Capsule– Subjects received 2 capsules after the last sip of alcohol consumption.</p>
Alcohol Consumption	<p>Subjects were allowed to drink alcohol [42.8% of alcohol (Whiskey)] and the quantity of the alcohol exceeded or was greater than their normal drinking quantity (drunkenness standardization). The quantity of alcohol intake was maintained to be uniform across all the periods as far as possible.</p> <p>Note:</p> <ul style="list-style-type: none"> • During the washout period throughout the study, subjects was not allowed to drink alcohol. • Subjects were instructed to avoid heavy/ heavy fat content food at the day of study. • Subjects were provided with same kind of food on the day of study. • Study was conducted on different days for male and female subjects.
Concomitant Medication	<p>The Investigator treated the subjects as per the requirement and the details of rescue/concomitant medications used during the study was entered in the case report form (CRF).</p>

Results	<p>Safety Conclusion</p> <p>All the vitals were within the normal range, and there were no abnormality in physical assessment were recorded neither during the study conduct nor at the end of the study.</p> <p>The findings suggests that PartySmart soft chews have a good safety profile as they have a lower incidence of adverse effects compared to other groups.</p> <p>Efficacy Conclusions</p> <p>As per randomization of groups, first period was "Placebo Chews" and second period was "Active Chews". However, this was double blinded study for these two periods.</p> <p>The study revealed that the mean AHS score and the mean 1 item HSS scores were significantly lower after PartySmart soft chew consumption when compared to a placebo and that PartySmart soft chew is comparable to PartySmart capsules and the Cheers® Restore Capsule. The percentage of subjects who were symptom free was also recorded highest in Period 2. The blood alcohol and acetaldehyde levels at various timepoints were not significantly different among groups.</p>
Conclusion	<p>Based on the current study results, it can be concluded that PartySmart soft chews is safe and effective in reducing the symptoms of hangover.</p>

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5.0 LIST OF ABBREVIATIONS

Abbreviations	Full Form
ADH	Alcohol Dehydrogenase
ADR	Adverse Drug Reactions
AE	Adverse Event
AHS	Acute Hangover Scale
ALDH	Aldehyde Dehydrogenase
BAC	Blood Alcohol Concentration
CRF	Case Report Form
CSR	Clinical Study Report
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data capture
GCP	Good Clinical Practice
HWC	Himalaya Wellness Company
ICF	Informed consent form
ICH	International Council for Harmonization
IEC	Independent/ Institutional Ethics Committee
IP	Investigational Product
mITT	Modified Intent To Treat
SAE	Serious Adverse Event
SAF	Safety Analysis Set
SAP	Statistical Analysis Plan
UPT	Urine pregnancy Test
WHO	World Health Organization

6.0 ETHICS

6.1 Ethical Conduct for the Study – Declaration

This study was conducted in compliance with the ICMR ethical guidelines, the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) (Step 5) 'Guidance on Good Clinical Practice' (E6 R2), NDCT Rule (The New Drugs and Clinical Trials), Declaration of Helsinki, Good Clinical Practice Guidelines for Clinical Trials in Ayurveda, Siddha, and Unani Medicine (GCP-ASU) & Central Council for Research in Ayurvedic Sciences (CCRAS) Research Policy.

6.2 Independent Ethics Committee (IEC)

The ACE Independent Ethics Committee had reviewed and approved the protocol prior to commencement of the study. The study was initiated only after the approval of the study protocol (HWC/MSCD/PP/003/2022, Version 1.0, dated 14th April 2022) by ACE Independent Ethics committee.

It was required that the Principal Investigator (PI) must promptly report to the EC, if any new information that may adversely affect the safety of the subjects or the conduct of the study. Study Investigator was expected to follow the protocol in conformity with Good Clinical Practice (GCP) described in Guideline E6 of the International Council on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) and applicable regulatory requirements.

The Investigator had sent a copy of the approval from the IEC to the Sponsor or the Sponsor's designated representative. After approval from EC, the study was registered at CTRI via registration number CTRI/2022/05/042617.

6.3 EC Approvals and Notifications

Details are mentioned in the below

Site Code	Site Name	EC Name	Approval date
1	Healing Earth Multi - Specialty Ayurvedic Hospital	ACE Independent Ethics Committee	11/05/2022

6.4 Informed Consent Process

The site was provided with the standard format of Informed Consent Form and Subject Information Sheet in English, Kannada and Hindi as required by the EC. The necessary translations and back translations of these were made prior to beginning of study. The subject was given a copy of the Patient Information Sheet (in the language best understood by the subject) and was given sufficient time to consider the implications of the study before deciding whether or not to participate in the trial. The informed consent form was signed and dated by the subject and the Investigator. At this time, the subject had legal capacity and was able to comprehend the nature, meaning, importance and risks of the study and to make up his mind accordingly. Most of the Subjects used the English & Kannada consent forms. All the necessary elements of consent were explained to the Subjects including but not limited to

- The details of the research study
- The procedures involved
- Voluntary nature of the study
- Any possible benefits
- Known possible risks
- Alternatives to participation
- Confidentiality of personal information
- Compensation in case of research related injury
- Any additional direct or indirect costs to the subject
- Right to withdraw from the study at any time with NO effect on their medical care

Informed consent procedure was carried out by the PI or the designated site staff. All

the study related screening procedures were carried out only after the Subject & the PI

/Co-PI signed the Informed Consent form. The principal Investigator retained & archived the original subject informed consent form. A copy of the signed consent form was given to the subject.

6.5 Subject Confidentiality

Subjects were not identified on the Case Record Form by name. Appropriate coded identification (e.g., randomization number) and initials were used. The Investigator was responsible for keeping a subject identification code list of all subjects who had signed the informed consent including the subject number, full name, address, and other contact details. However, subject's study related records and health information was made available to personnel working on behalf of Himalaya Wellness Company (HWC) & can be made available to the independent ethics committee members and regulatory authorities as required.

6.6 Insurance Policy

Himalaya Wellness Company (HWC) made provision for insurance coverage for damage arising from the trial and involving the subjects treated with the investigational drug, provided that the investigator(s) and study subjects adhere to the terms and provision of the protocol. The Principal Investigator was provided the details of the insurance coverage (Special Contingency Insurance Policy no 421801/48/2022/ 1060, dated 02/11/2021 to 18/07/2022) which was notified to EC also.

6.7 Data Safety Monitoring Board (DSMB)

Data Safety Monitoring Board was not constituted for this study.

7.0 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Principal investigator	Designation	Institutional Affiliation
Dr Farida Khanum Abbasi, BAMS, MD	Principal Investigator	Healing Earth Multi-speciality Ayurveda hospital #419, sector-5, HSR Ring Road, HSR Layout, Bangalore- 560034

STUDY TEAM

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Sponsor's Signatory (Authorized signatory to the CSR and CSR Amendments)	Dr Rajesh Kumawat, MBBS, MD Head-Medical Services and Clinical Development (R & D) Himalaya Wellness Company
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8.0 BACKGROUND AND INTRODUCTION

8.1 Disease Information

Alcohol hangover is the combination of mental and physical symptoms experienced the day after a single episode of heavy drinking, starting when blood alcohol concentration (BAC) approaches zero.¹ It is the most reported negative consequence of alcohol consumption.² Factors involved in alcohol hangover includes acetaldehyde accumulation, changes in immune system and glucose metabolism, dehydration. Hangover is suggested to be early stage of alcohol withdrawal. Acetaldehyde, a breakdown product of alcohol metabolism, plays a role in producing symptoms. Chemicals formed during alcohol processing and maturation known as congeners increase the frequency and severity of hangover. Congeners may be produced along with ethanol during fermentation, generated during ageing or processing through the degradation of the beverage's organic components, or added to the beverage during production process. They contribute to taste, smell and contribute to the flavour of the alcoholic beverage. Liquors such as brandy, wine, tequila, whiskey and other dark liquors containing congeners tend to produce severe hangover. Whereas the clear liquors such as rum, vodka, gin cause hangover less frequently³. Alcohol dehydrogenase produces acetaldehyde which is toxic which is converted to acetic acid which is later converted to fatty acid and water.

Ethanol has a dehydrating effect by causing increased urine production (diuresis), which could cause thirst, dry mouth, dizziness and may lead to an electrolyte imbalance. Studies suggest the genesis of alcohol hangover and are caused by dehydration effects.⁴ Hyperglycemia has been thought to play an important role in the pathogenesis of hangover. It is due to the inhibition of vasopressin released from posterior pituitary gland. During withdrawal from alcohol vasopressin is released resulting in water retention (antidiuresis).⁵ There are few studies that proposed that dehydration itself is cause of memory impairment. There is significant relationship between immune factor and hangover severity is the most convincing factor studied. Drinking too much alcohol weakens the immune system, making body to much easily encounter a disease.⁶ An imbalance of immune system in particularly the cytokine metabolism has been identified as playing a role in pathophysiology of the hangover state. Especially the

hangover symptoms nausea, headache, and fatigue have been suggested to be mediated by changes in immune system. The concentration of several cytokines has been found to be significantly increased in the blood after alcohol consumption. It includes interleukin 12, interferon gamma and interleukin 10.⁷ It also causes the production of more gastric acid alongside increasing the level of pancreatic and intestinal secretions.⁸

9.0 STUDY OBJECTIVES & ENDPOINTS

9.1 Objectives

- To evaluate the effect of PartySmart Soft Chews on mitigation /prevention of alcohol hangover as evaluated by clinical symptoms, Acute Hangover Scale (AHS) and 1-item overall hangover severity scale.
- To evaluate the safety and compliance of the study product.

9.2 End points

- Changes in the blood alcohol and acetaldehyde levels.
- Clinical assessment of "Alcohol Hangover Symptoms"
- Assessment of Acute Hangover Scale (AHS).
- 1- item Overall Hangover Severity Scale.
- Incidence of adverse effects.

10.0 OVERVIEW OF STUDY DESIGN AND DISCUSSION

After signing the informed consent form (ICF), subjects who fulfill the eligibility criteria were enrolled into the study. This was a double-blind, placebo-controlled, comparative study, followed by an open-label extension clinical study to evaluate the efficacy and safety of PartySmart Soft Chews.

Subjects participated in all the four Periods, i.e., Period I, Period II, Period III and Period IV. Between each period there was a minimum 7 ± 2 days of washout periods.

Period I (Active/Placebo Chews) : Subjects received Active/Placebo PartySmart soft Chews as per the recommended dosage. 40 Subjects of either sex were enrolled to get at least 34

evaluable subjects. Appropriate representation of male and female subjects were enrolled into the study.

Dosage: Active/Placebo Chews – 20 subjects received 2 soft chews with first sip and remaining 20 subjects received 2 soft chews after last sip of alcohol consumption.

Period II (Active/Placebo Chews) [after 7±2 days of Period I]

All the 40 subjects from Period I received Active/Placebo PartySmart soft Chews. Appropriate representation of male and female subjects were enrolled into the study.

Dosage: Active/Placebo Chews – 20 subjects received 2 soft chews with first sip and remaining 20 subjects received 2 soft chews after last sip of alcohol consumption.

Period III (PartySmart Capsule) [after 7±2 days of Period II]

All the 40 subjects from Period II received PartySmart Capsule in this period. Appropriate representation of male and female subjects were enrolled into the study.

Dosage: PartySmart Capsule– 20 Subject received 1 capsule with first sip and remaining 20 subjects received 1 capsule after last sip of alcohol consumption.

Period IV (Cheers® Restore capsule) [after 7±2 days of Period III]

All the 40 subjects from Period III received Cheers® Restore capsule in this period.

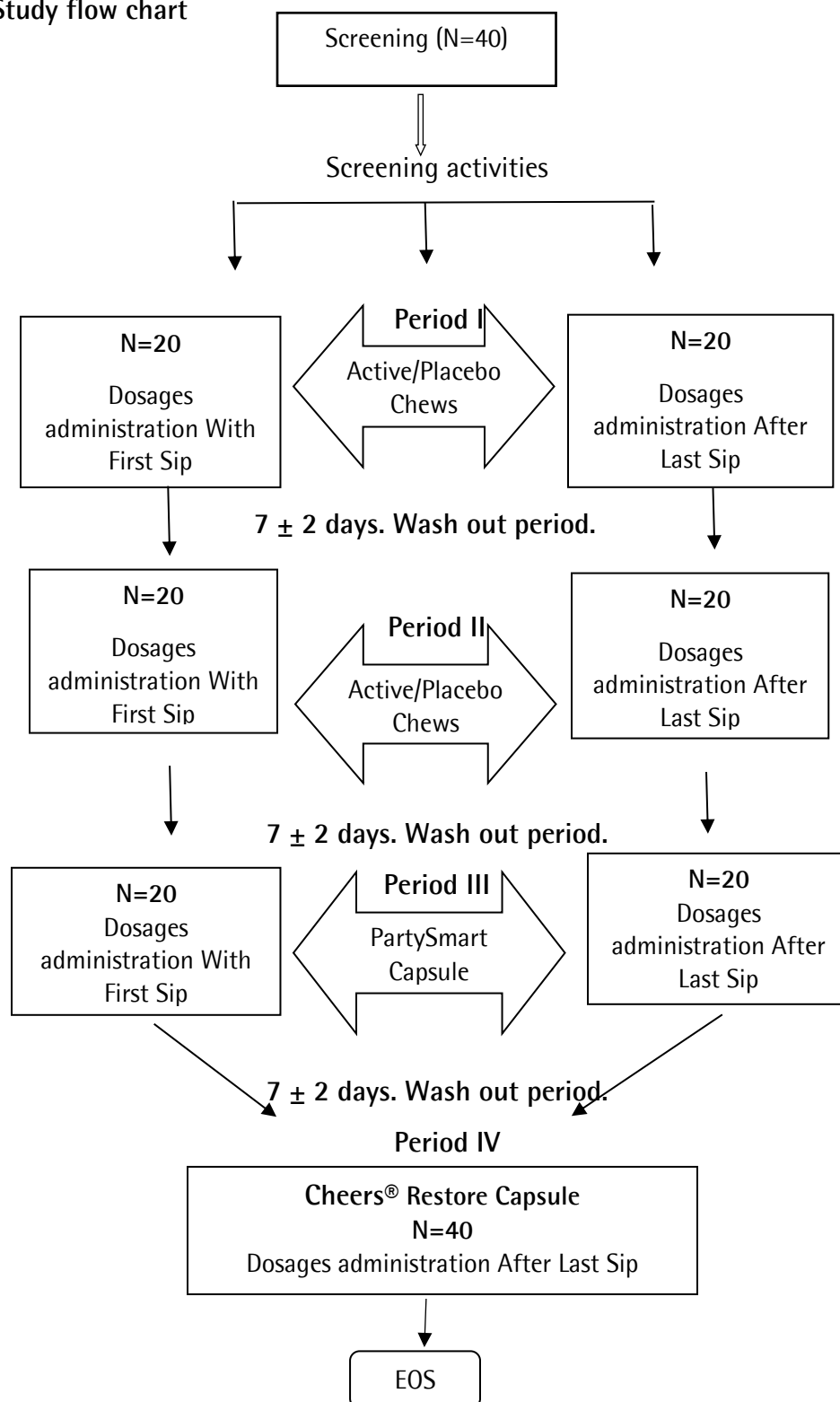
Dosage: Cheers® Restore Capsule– All 40 subjects received 2 capsules after last sip of alcohol consumption.

Assessments:

Subjects were assessed on the following time points in each Period.

- Blood investigations: Estimation of blood alcohol and acetaldehyde levels at, Pre-alcohol consumption (within one hour prior to first sip) (0 hr)
- At 1 hr post last sip
- At 2 hr post last sip
- At 12 hr post last sip

Figure 1: Study flow chart



11.0 STUDY SUBJECTS

11.1 Study population

Healthy adult subjects with previous history of social alcohol consumption were enrolled into the study.

11.2 Number of subjects

A total of 40 subjects were enrolled to get at least 34 evaluable subjects. Appropriate representation of male and female subjects were enrolled into the study.

12.0 SUBJECT ELIGIBILITY

12.1 Inclusion Criteria

1. Male and female subjects aged between 20-50 years, weighing >45 kgs.
2. Subjects who used to drink alcohol regularly (social drink, but not alcohol abuse) and are willing and able to comply with the alcohol consumption, blood withdrawal requirements and overnight stay as per the study requirements.
3. Subjects who were judged by the Investigator to be in general good health based on medical history.
4. Subjects who understood the study procedures and signed the informed consent forms participated in the study.

12.2 Exclusion Criteria

1. Subjects suspected of drug or alcohol abuse.
2. A medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation.
3. Subjective sleep duration of less than 3 hours in the night before every study period.
4. Caffeine, nicotine on the day (from midnight) of every study Period.
5. Alcohol consumption within 7 days of enrollment in the study
6. Use of psycho-active drugs during the past 30 days or any treatment that might interfere with the evaluation of the investigational product.

7. Subjects who were taking any drug known to interact with benzodiazepines and other drugs, e.g., antiepileptics, antihistamines, muscle relaxant drugs, antihypertensive drugs, drugs inhibiting cytochrome P450.
8. Subjects who were suffering from any clinically significant disorder that might interfere with his/her participation in this study and the evaluation of the efficacy or safety of the investigational product (e.g. renal insufficiency, hepatic or metabolic dysfunction, cardiovascular disease, neurological and or psychiatric disorder etc.).
9. Subjects with known hypersensitivity to any of the ingredients of the study product.
10. Subject participation in any other clinical trial within the past 30 days.
11. Pregnant and lactating women.

12.3 Criteria for Withdrawal of Study Subjects

- Subjects were allowed to withdraw from the study if they experience serious discomfort during the study or if they sustained with serious clinical events requiring specific treatment. The reason for withdrawal was recorded in the Case report form (CRF) and monitor / sponsor was informed immediately.
- For all subjects dropping out of the study, efforts were made to ascertain the reason for dropout.
- Subject with severe vomiting or sickness or any other complaints at the discretion of the study investigator.
- Treatment Failure was judged by
 - a) Severe intolerable hangover next day morning
 - b) Treatment intolerance by the subject
- Non-compliance
 - a) Non-compliance was not considered as treatment failure
 - b) Compliance was evaluated at the end of two hours follow up by empty container count of the product.
 - c) Reasons for non-compliance were noted.

12.4 Violation of entry criteria

Adherence to the inclusion and exclusion criteria by the Investigator and by the subject was required and expected. Any queries concerning the inclusion or exclusion criteria was discussed with the medical monitor/designee of HWC prior to subject enrollment.

Waiver was considered to be granted for subjects whose condition are insignificant and would not interfere with the analysis of the study in consultation with designee of HWC. The waiver was documented in the appropriate sections of Source File, CRF and Trial Master File.

If a subject was enrolled in apparent conformity with the protocol eligibility criteria but is later found to be ineligible, it may be possible for the subject to continue participation in the study. In these cases, the decision about participation belongs to HWC in consultation with study Investigator.

13.0 INVESTIGATIONAL PRODUCT MANAGEMENT

13.1 Study Medication & Formulation

PartySmart Capsules

Many treatments are described to prevent hangover, shorten its duration, and reduce the severity of its symptoms, including innumerable folk remedies and recommendations. PartySmart is one such herbal preparation known to have beneficial effect in preventing alcohol-induced hangover.

COMPOSITION:

Table 1: Composition of PartySmart Capsule

Each PartySmart capsule contains:

S. No	Herb name	Botanical Name	Quantity (mg)
1	Kharjura	<i>Phoenix dactylifera</i>	47.0
2	Kasni	<i>Cichorium intybus</i>	47.0
3	Yavatikta	<i>Andrographis paniculata</i>	47.0
4	Bhumyamalaki	<i>Phyllanthus amarus</i>	31.0
5	Draksha	<i>Vitis vinifera</i>	47.0
6	Amalaki	<i>Embolica officinalis</i>	31.0

Pharmacological Actions and Principal Herbs

Phoenix dactylifera, (Dates, Kharjura) ripened fruit pulp is used for its antidote properties against alcohol intoxication.

Cichorium intybus, (Wild chicory, Kasni) roots and seeds contain esculetin which possesses anti-hepatotoxic activity and is useful in hepatitis.

Andrographis paniculata, (Creat, Yavatikta) plant is used medicinally for its bitter principles which are useful as a hepatoprotective. It is effective in treating jaundice.

Phyllanthus amarus, (Bhumyamalaki) plant is very effective against alcohol induced liver damage, hepatitis and possesses antimicrobial and anti-cancer activities.

Vitis vinifera, (Grapes, Draksha) ripe fruit is one of the important plants has antioxidant and anti-stress activities. Traditionally the same is used to prevent alcohol hangover.

Embllica officinalis, (Indian Gooseberry, Amalaki) fruit extracts significantly inhibit hepatocarcinogenesis in a dose dependent manner. It is effective in hepatitis. It has more hepatoprotective action than ascorbic acid.

PartySmart Soft Chews

PartySmart soft chews relieves unpleasant after-effects of alcohol.

The ingredients of PartySmart soft chews are expected to ameliorate effects of alcohol holistically. The ingredients are expected to target following physiological factors contributing to alcohol hangover.

- Gastric irritation & inflammation and delayed gastric emptying caused by alcohol, which is often contributes to abdominal discomfort, nausea and vomiting in alcohol hangover.
- Alcohol metabolites and their effects.
- Oxidative stress induced by alcohol stresses the bodily systems, especially liver.

Table 2: Composition and their functions of PartySmart Soft Chews.

S.No.	Ingredients	Quantity per Chew (mg)	Pharmacological actions
1	<i>Phoenix dactylifera</i> (Date) fruit extract	50	Hepatoprotective, Gastroprotective

S.No.	Ingredients	Quantity per Chew (mg)	Pharmacological actions
2	<i>Curcuma longa</i> (turmeric) rhizome extract	25	Increases Alcohol dehydrogenase (ADH) and Aldehyde dehydrogenase activity (ALDH), Anti-inflammatory
3	<i>Vitis vinifera</i> (grape) fruit extract	20	Gastroprotective, Antioxidant
4	<i>Embllica officinalis</i> (amla) fruit extract	42.5	Hepatoprotective (alcohol induced injury), Antioxidant
5	<i>Zingiber officinale</i> (Ginger) rhizome extract	1.25	Prokinetic, anti-nausea
6	<i>Trigonella foenum greacum</i> (Fenugreek) seed powder	21.25	Supports alcohol metabolism by upregulating metabolizing enzymes Hepatoprotective

13.2 Supply & Packaging

13.2.1 Product stability

The product was stored in a dry place away from direct sunlight for the product to be efficacious until the end of shelf life that is 18 months. The product was found to be stable for the entire shelf life.

13.2.2 Method of packaging

Study medications was packed in an appropriate package deemed to maintain the integrity of the product.

- PartySmart Soft chews active/placebo were individually packed in an aluminum pouch
- PartySmart Capsules were packed in a blister pack containing 5 capsules
- Cheers® Restore capsules were packed in a glass bottle containing 60 capsules

13.3 Labeling

All the study related investigational medicinal products were labelled appropriately and packed as specified in the protocol.

13.4 Product Storage

IPs were stored in a dry place, away from direct sunlight, kept in a secured, restricted and access-controlled area. Temperature was not allowed to exceed 30° Celsius (was not refrigerated).

13.5 Investigational Product Accountability

The study product was kept in a secure place and was supplied to subjects under the responsibility of the Investigator. The Investigator or his designate maintained a complete accountability for all the product supplied by the sponsor. A record was kept of the study product dispensed and returned in the 'Investigational product accountability log'. Any discrepancies between amounts dispensed and returned was explained. Similarly, the sponsor maintained adequate records of dispatch and retrieval of all study medications to and from the study center(s). The investigational product accountability forms were made available to the Principal Investigator/designee for the purpose of accounting for the study product supply at the site. Inspections of the study product supply for inventory purposes and assurance of proper storage was conducted as and when necessary, by the study monitor. Any significant discrepancy was recorded, reported to HWC, and a plan for resolution was documented.

HWC provided additional study products to the Investigator on request through IP request form except at the time of study initiation.

HWC delivered the samples by courier consignments to the Investigator. The medication was given to the Investigator/designee who was responsible for handling the study medication. Investigator or his designate dispensed the study medication to all the study subjects.

The study investigator acknowledged the receipt of the product (through shipment acknowledgement record) indicating total content and condition. Empty containers of damaged supplies if any was returned by the Investigator and was replaced by the sponsor.

The Investigator maintained an accurate record of the number of containers requested, dispensed and number of unused and empty containers returned to the sponsor in the IP accountability form (Site).

Medicines permitted by protocol were supposed to be given under the supervision of the Investigator.

The Investigator ensured to not supply the investigational product to any person not targeted to receive it. Monitors were allowed at intervals and upon request during the study to check unused supplies.

14.0 STUDY ASSESSMENTS

14.1 Safety Evaluation

Study investigator is responsible for monitoring the safety of the study subjects who were enrolled in the study and alerting designee of HWC to any event that seems unusual, even if the event was considered an unanticipated benefit to the subject. Any adverse event occurring during the period of the study was evaluated thoroughly (As per detail in Section 10).

Clinical Assessments

Vital signs measurement

Vital signs (Pulse rate, respiratory rate, systolic and diastolic blood pressure, and temperature) were be measured at all the study visits.

Laboratory Assessment

Urine pregnancy test (UPT) was performed only for childbearing potential women at screening and history of amenorrhea was recorded in rest of periods.

Breath Analysis: Breathe analysis was performed before the alcohol intake (within 1hr) at every period. If the breath analysis result is positive, then the subject was not eligible to participate in the study.

14.2 Efficacy Evaluation

All the subjects were followed-up for efficacy assessments. Efficacy parameters to evaluate the study end points are listed below,

Clinical assessment of "Alcohol Hangover Symptoms": Clinical symptoms like Headache, Nausea, General Energy (Feeling energetic), Mental Energy, Focus, Physical energy, General wellbeing and Daily activity motivation was assessed at 12th hour in every period on a scale of 0 to 4 where (0 [Nil] = About 0%, 1 [Occasionally] = about 25%, 2 [About half of the time] = About 50%, 3 [Mostly] = About 75%, and 4 [Completely] = About 100%).

Blood investigation: Blood alcohol and Blood acetaldehyde levels (2ml of blood was drawn at each time point) was estimated at 4 time points (0hr, 1hr, 2hr and 12hr) in all the four periods.

Acute Hangover Scale (AHS): AHS was used at 12thhr post last sip of alcohol in all the four periods (On a Seven Point Scale) to evaluate the intensity of hangover.

1-item "Overall Hangover Severity Scale" was used to evaluate the intensity of hangover at 12th hour post alcohol consumption in every period.

15.0 STUDY CONDUCT & METHODOLOGY

Overall Plan of Study

All the subjects were consented for the study and informed consent form was signed by the subjects after understanding the study methodology, study benefits and risks involved in the study. Subjects were screened as per inclusion and exclusion criteria. Subjects who fulfilled the eligibility criteria were enrolled into the study.

Study specific method of alcoholic consumption:

Subjects were allowed to drink alcohol [42.8% of alcohol (Whiskey)] and the quantity of the alcohol exceeded or was greater than their normal drinking quantity (drunkenness standardization). The quantity of alcohol intake was maintained uniform across all the periods as far as possible.

- During the washout period throughout the study, subjects was not allowed to drink alcohol.
- Subjects were instructed to avoid heavy/ heavy fat content food at the day of study.
- Subjects were provided with same kind of food on the day of study.

- Study was conducted on different days for male and female subjects

This was a double-blind, placebo-controlled, comparative clinical study followed by an Open-label extension study to evaluate the efficacy and safety of PartySmart Soft Chews.

A total of 40 subjects of either sex were enrolled into the study to get at least 34 evaluable subjects. Total 40 eligible subjects participated in the study and received dosage administration with first sip (N=20) and dosages administration after last sip (N=20). All participants underwent through 4 period i.e., Period I, Period II, Period III and Period IV. Between each period there was a minimum 7 ± 2 days of washout period.

Period I (Active/Placebo Chews)

Subjects received Active/Placebo PartySmart Soft Chews as per the recommended dosage.

40 Subjects of either sex were enrolled to get at least 34 evaluable subjects.

Dosage: Active/Placebo Chews – 20 subjects received 2 Soft chews with first sip and remaining 20 subjects received 2 soft chews after last sip of alcohol consumption.

Period II (Active/Placebo Chews) [after 7 ± 2 days of Period I]

All the 40 subjects from Period I received Active/Placebo PartySmart soft Chews.

Dosage: Active/Placebo Chews – 20 subjects received 2 soft chews with first sip and remaining 20 subjects received 2 soft chews after last sip of alcohol consumption.

Period III (PartySmart Capsule) [after 7 ± 2 days of Period II]

All the 40 subjects from Period II received PartySmart Capsule in this period.

Dosage: PartySmart Capsule– 20 Subject received 1 capsule with first sip and remaining 20 subjects received 1 capsule after last sip of alcohol consumption.

Period IV (Cheers® Restore capsule) [after 7 ± 2 days of Period III]

All the 40 subjects from Period III received Cheers® Restore capsule in this period.

Dosage: Cheers® Restore Capsule– All 40 subjects received 2 to 4 capsules after last sip of alcohol consumption.

Table 3: Schedule of Events

Activities		Period* (Period I/Period II/Period III/Period IV)				Unscheduled Visit
		0 hr (Before alcohol consumption)	At 1 st hr (Post last sip of alcohol consumption)	At 2 nd hr (Post last sip of alcohol consumption)	At 12 th hr (Post last sip of alcohol consumption)	
Informed Consent	X					
Eligibility criteria assessment	X (Assessment & Confirmation)					
Demography	X					
Medical History	X					
Alcohol History	X					
Breathe Analysis ¹		X				
Urine Pregnancy Test ²	X					
Clinical assessment of "Alcohol Hangover Symptoms" ³					X	
Vital signs ⁴	X				X	X
Blood alcohol and Blood acetaldehyde levels ⁵ (Laboratory Investigation)		X	X	X	X	

Activities	Day 1/ Screening/ Baseline	Period* (Period I/Period II/Period III/Period IV)				Unscheduled Visit
		0 hr (Before alcohol consumption)	At 1 st hr (Post last sip of alcohol consumption)	At 2 nd hr (Post last sip of alcohol consumption)	At 12 th hr (Post last sip of alcohol consumption)	
Acute Hangover Scale (AHS) ⁶					X	
1-Item Hangover Severity Scale					X	
Adverse event assessment	X	X	X	X	X	X
Concomitant Medication	X	X	X	X	X	X

***Important Note:** Period II/Period III/ Period IV. Period II after 7 ± 2 days of wash period from Period I, Period III after 7 ± 2 days of wash period from Period II and Period IV after 7 ± 2 days of wash period from Period III. From Period I – Period III, 20 subjects received investigational products with first sip and remaining 20 subjects receive the investigational product after last sip of alcohol consumption; however, in Period IV, all 40 subjects received Cheers® Restore capsule only after the last sip of alcohol consumption.

- Breath Analysis:** Breathe analysis was performed before the alcohol intake (within 1hr) at every period. If the breath analysis result was positive, then the subject was not eligible to participate in the study.
- Urine pregnancy test (UPT)** was performed only for childbearing potential women at screening. and history of amenorrhea was recorded in rest of periods.
- Clinical assessment of "Alcohol Hangover Symptoms"** : Clinical symptoms like Headache, Nausea, General Energy (Feeling energetic), Mental Energy, Focus, Physical energy, General wellbeing and Daily activity motivation was assessed at 12th hour in every period on a scale of 0 to 4 where (0 [Nil] = About 0%, 1 [Occasionally] = about 25%, 2 [About half of the time] = About 50%, 3 [Mostly] = About 75%, and 4 [completely] = About 100%).
- Vitals signs:** Pulse rate, Systolic and Diastolic Blood pressure, Temperature, Respiratory rate.
- Blood investigation:** Blood alcohol and Blood acetaldehyde levels (2ml of blood was drawn at each time point). Blood was drawn at 4 time points (0hr, 1hr, 2hr and 12hr) in all the four periods.
- Acute Hangover Scale (AHS):** AHS was used evaluated at 12th hr post last sip of alcohol in all the four periods (On a Seven Point Scale).

7. 1-item "Overall Hangover Severity Scale" was used to evaluate the intensity of hangover at 12th hr post alcohol consumption in every period.

15.1 Study Visits

Subjects were assessed on the following visit time points in each Period.

Period I (Active/Placebo Chews)/Period II (Active/Placebo Chews) /Period III (PartySmart Capsule)/ Period IV (Cheers® Restore Capsule):

Period I /Day 1:

Screening/ Baseline Period

The following activities were performed

- Informed Consent Document signing activities.
- Eligibility criteria assessment.
- Medical history, alcohol history & subject's demographic data details were recorded.
- Vital signs were recorded.
- UPT was performed for child-bearing potential women
- Concomitant medication assessments
- Adverse event assessment

Dose Regimen: With First Sip (N=20)/After Last Sip (N=20)

0 hour (Before alcohol consumption)

- Concomitant medication assessments
- Blood alcohol and Blood acetaldehyde level assessment
- Breathe analysis was performed.
- Adverse event assessment

At 1st hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments

- Adverse event assessment

At 2nd hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment

At 12th hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment
- Clinical assessment of "Alcohol Hangover Symptoms"
- Vital signs were recorded
- Acute Hangover Scale (AHS) assessment
- 1-Item Hangover Severity Scale assessment

Period II (After 7+2 days of period I):

Dose Regimen: With First Sip (N=20)/After Last Sip (N=20)

0 hour (Before alcohol consumption)

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment
- Breathe analysis was performed
- History of amenorrhea was recorded

At 1st hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment.

At 2nd hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment

- Concomitant medication assessments
- Adverse event assessment

At 12th hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment
- Clinical assessment of "Alcohol Hangover Symptoms"
- Vital signs were recorded
- Acute Hangover Scale (AHS) assessment
- 1-Item Hangover Severity Scale assessment

Period III After 7±2 days of period II):

Dose Regimen: With First Sip (N=20)/After Last Sip (N=20)

0 hour (Before alcohol consumption)

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment
- Breathe analysis was performed
- History of amenorrhea was recorded

At 1st hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment

At 2nd hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment

At 12th hour (Post Last Sip of alcohol consumption [N=40 (20/20)])

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment
- Clinical assessment of "Alcohol Hangover Symptoms"
- Vital signs were recorded
- Acute Hangover Scale (AHS) assessment
- 1-Item Hangover Severity Scale assessment

Period IV (After 7+2 days of period III):

All the 40 subjects from Period-III received Cheers® Restore Capsule (2 capsules) after last sip of alcohol consumption.

0 hour (Before alcohol consumption)

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment
- Breathe analysis was performed.
- History of amenorrhea was recorded

At 1st hour (Post Last Sip of alcohol consumption (N=40))

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment

At 2nd hour (Post Last Sip of alcohol consumption (N=40))

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments
- Adverse event assessment

At 12th hour (Post Last Sip of alcohol consumption (N=40))

- Blood alcohol and Blood acetaldehyde level assessment
- Concomitant medication assessments

- Adverse event assessment
- Clinical assessment of "Alcohol Hangover Symptoms"
- Vital signs were recorded
- Acute Hangover Scale (AHS) assessment
- 1-Item Hangover Severity Scale assessment

At the end of visit, if any AE or any laboratory parameter was abnormal and which was clinically significant, the subject was followed up to satisfactory resolution or stabilization. When a subject discontinues, the end of study visit procedure were completed.

IP compliance & Accountability was checked by asking the subject whether he/she has used the product as per dosage regimen. If the subject is deteriorating in condition (anytime during study period), the subject was allowed to withdraw from the study and assessments for "unscheduled visit" was carried out.

15.2 Unscheduled Visit:

If indicated by the occurrence of a medical emergency or clinically significant abnormality the Investigator/subject planned for additional visit for follow up evaluation during the study period. Extra section in CRF (for unscheduled visit) was recorded accordingly. Following Assessments of the subjects were performed at this visit.

- Vital parameters along with concomitant medications, IP compliance & return, and adverse events recording.

16.0 DATA MANAGEMENT AND STATISTICS

16.1 Data Management

Clinical Database was developed and finalized on the basis of final CRF. Designated investigator site staff entered the data required by the CRF/protocol into the EDC system. Investigator site staff were not given access to the EDC system until they have been trained. Online validation procedures were carried out within the system and check for data discrepancies during and after data entry and showed appropriate error messages if any. As per the error message, Investigator site staff confirmed or corrected the data in the EDC

system. The Investigator approved that the data entered into the electronic Case Report Forms were complete and accurate. After database lock, data analysis activities were stated.

Medical and Surgical Procedure, Adverse Event entered into the database were coded using the medical dictionary for regulatory activities (MedDRA) terminology and Concomitant medications entered into the database were coded using the WHO Drug Medical Dictionary.

16.2 Blinding (In Period I & II)

In Period I & II the study was double-blind one, that is, doctors and subjects were unaware about the study groups. Active/Placebo PartySmart soft Chews was prepared as identical size, shape, colour, texture, and weight. Also, the investigational products had package in such a way that the Active/Placebo PartySmart soft Chews packs were identical in appearance. After the subject enrolment, he or she were provided with the Active/Placebo or PartySmart soft Chews. During data collection, the subjects and the physicians were blinded to the investigational product. The unblinding was allowed only after completion of entire data collection process or in case of serious adverse events (when safety is a concern for the subject).

16.3 Statistical Considerations

This section of the Clinical Trial Protocol is the basis for the Statistical Analysis Plan (SAP) for the study. This plan may be revised during the study to accommodate Clinical Trial Protocol Amendments or to make changes to adapt to unexpected issues in study execution and data that affect planned analysis. These revisions were based on blinded review of the study and data, and a final plan was issued before database lock.

16.4 Sample Size

The Sample size is calculated based on literature data, Severity of Hangover Symptoms by AHS (Acute Hangover Scale) is considered as primary end point for evaluation of sample size.

In a previous study the response within each subject group was normally distributed with standard deviation 1.46. If the true difference in the PartySmart capsule and Placebo means is 1, we need to have 34 evaluable subjects in PartySmart capsule and 34 evaluable subjects in

placebo to be able to reject the null hypothesis that the means of the PartySmart capsule and Placebo groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

Considering a dropout rate of 15%, 40 subjects were enrolled in each group to have at least 34 evaluable subjects in each group.

End Point: Severity of Hangover Symptoms by AHS (Acute Hangover Scale)

Hypothesis: Null hypothesis: Placebo and PartySmart Capsule AHS Score equal at 12 Hrs.

Alternate Hypothesis: Placebo and PartySmart Capsule AHS Score not equal at 12 Hrs.

Formula

$$n = \frac{2s_p^2 [Z_{1-\alpha/2} + Z_{1-\beta}]^2}{\mu_d^2}$$

$$s_p^2 = \frac{s_1^2 + s_2^2}{2}$$

Where,

s_1^2 : Standard deviation in the first group

s_2^2 : Standard deviation in the second group

μ_d^2 : Mean difference between the samples

α : Significance level

$1 - \beta$: Power

Assumption for sample size estimation:

α (Type I error) = 5%

power = 80%

δ (difference in means) = 1.00

*** σ (standard deviation)** = 1.46

m (ratio)= 1:1

*Sd (Variability) from other study Article:

Articles	Value
J. C. Verster	1.6
J. C. Verster	1.9
Rohsenow et al.	0.9
Average	1.46

Sample size for each group was:

$n1 = n2 = 34 + \text{dropout (15\%)} = 40$

In a previous study the response within each subject group was normally distributed with standard deviation 1.46. If the true difference in the PartySmart capsule and Placebo means is 1, we need to 34 evaluable subjects in PartySmart capsule and 34 evaluable subjects in placebo to be able to reject the null hypothesis that the means of the PartySmart capsule and Placebo groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

Considering a dropout rate of 15%, 40 subjects were enrolled in each group to have at least 34 evaluable subjects in each group.

Software: nMaster 2.0

16.5 Statistical Analysis

The principal analysis for the Primary endpoint was employing the mITT analysis set and the per-protocol approach was considered supportive. Safety analyses were performed using the safety analysis set. Continuous variables was summarized using mean, median, standard deviations, 95%CI, min, and max. Categorical variables were summarized using number and percentages. All statistical tests and confidence intervals are two-sided unless otherwise stated. Statistical analysis was made using GraphPad Prism Software Version 6.07 for Windows, GraphPad Software, San Diego, California, USA.

16.5.1 Subject Disposition

A detailed description of subject disposition was provided. It include:

- Subjects enrolled in the trial
- A summary of data on subject discontinuation
- An account of all identified protocol deviation/violation

All subjects entered in the study was accounted for in the summation. The number of subjects who do not qualify for analysis (non-evaluable) and subject, who discontinue the study before starting treatment was also be specified.

16.5.2 Demographic and Baseline Characteristics

Summary statistics were provided by treatment group for demographics (e.g., age, sex, race, and weight, height) and for baseline characteristics including medical history.

16.5.3 Safety Analysis

- The safety was assessed on ITT basis. Safety data was summarized in the Safety analysis set. Safety analysis was evaluated based on vital signs, adverse events, and laboratory data. Individual safety data was tabulated and summarized for vital signs (body temperature, blood pressure, respiratory rate, and pulse rate). Descriptive statistics was provided for vital signs. All concomitant medications were detailed in the subject data listings.

- Incidence rates for AE was recorded by highest severity grade for each system organ class (SOC) for all subjects. The incidence of AEs and ADRs were compared across the treatment groups using Fisher's exact test. SAE was listed separately.

All AEs were coded using the Medical Dictionary for Regulatory Authorities (MedDRA). Treatment-emergent AEs are those with an onset after the first dose of study product or any event already present that worsens in either intensity or frequency following exposure to the study treatment. The incidence of treatment-emergent AEs, SAEs were summarized by system organ class and AE preferred term in each treatment group. A summary of treatment-emergent AEs by preferred term and severity, using the worst reported severity grade for each event for a given subject, was presented.

- SAEs, ADRs and AEs leading to discontinuation were summarized and listed. Proportion of the subjects withdrawing from trial because of adverse events (tolerability) were tabulated appropriately.

Clinical Laboratory

Descriptive statistics for laboratory parameter values, and for values of changes from baseline, by treatment group and visit, were provided. The occurrence of significantly abnormal changes in laboratory values from baseline were summarized by treatment group.

16.5.4 Efficacy Analysis

Efficacy was analyzed in both mITT and PP populations. Appropriate imputation or exclusion methods were used to deal with missing data for mITT analysis.

16.5.4.1 Primary Efficacy Endpoint

- Assessment of Acute Hangover Scale (AHS) & 1- item Overall Hangover Severity Scale, assessed at 12 hrs. in each Period, was summarized in Mean (Sd), Shapiro-Wilk test was used to check the normality of data. If the data is normally distributed, One Way-ANOVA followed by Post hoc test was performed to find out statistical difference between group. If the data is not normally distributed, Kruskal-Wallis' test was used to find out statistical difference between group.

- Clinical assessment of "Alcohol Hangover Symptoms" was summarized using number and percentages.
- Blood alcohol and acetaldehyde levels, assessed at 0,1,2 & 12 hrs. in each Period, was summarized in Mean (Sd), Shapiro-Wilk test was used to check the normality of data. If the data is normally distributed, RM One Way ANOVA followed by Post hoc test was performed. If the data is not normally distributed, Friedman's test was used.
- Compliance of the subject to the study medication. Overall percent compliance to study product, was calculated and summarized by treatment period.

17.0 EFFICACY EVALUATION

17.1 Subject Disposition

A total of 40 subjects were screened and enrolled in the study. Subjects were allowed to participate in four Periods, i.e., Period I, Period II, Period III and Period IV. 40 subjects participated in period I, 37 participated in period II and III and 36 subjects participated in period IV. Overall 04 subjects discontinued from the study.

Table 4: Subject disposition

Description	N (%)
Screened subjects	40
Screening fail subject	0
Enrolled subjects	40
Completed subjects in Placebo Chews (Period I)	40
Completed subjects in PartySmart Chews (Period II)	37
Completed subjects in PartySmart Capsule (Period III)	37
Completed subjects in Cheers® Restore Capsule (Period IV)	36
Discontinued subjects/ withdrawal	4
Reason for Discontinued /withdrawal	Lost to Follow up

17.2 Demographic Characteristics

In this study, total 40 subjects were screened with an average age, height and weight of 29.18 years, 161.5 cm and 61.41 Kgs respectively. Among 40 subjects, 23 were male and 17 were female subjects.

Table 5: Baseline Demographic Characteristics (N=40)

Baseline Demographic Characteristics (N=40)		
Age (Years)	Mean \pm Sd	29.18 \pm 10.25
	Median	26
	Min, Max	19, 68
Gender	Male, n (%)	23 (57.50%)
	Female, n (%)	17 (42.50%)
Height (cm)	Mean	161.5 \pm 9.25
	Median	163.5
	Min, Max	145, 178
Weight (Kgs)	Mean	61.41 \pm 14.17
	Median	57.5
	Min, Max	39, 98
BMI kg/m ²	Mean	23.51 \pm 4.99
	Median	22.93
	Min, Max	16.66, 37.39
Sd: Std. Deviation, Min: Minimum, Max: Maximum, Number of Subjects		

In the present study, subjects were allowed to participate in 4 different period. All the subjects who completed the study were considered for statistical evaluation. Below are the assessments related to the endpoint analysis specific to the present study.

A. Assessment of Acute Hangover Scale (AHS)

B. 1- item Overall Hangover Severity Scale

- C. Blood alcohol and acetaldehyde levels
- D. Clinical assessment of "Alcohol Hangover Symptoms"
- E. Incidence of adverse effects

A. Assessment on Acute Hangover Symptom Scale Post Alcohol Consumption

The details of AHS at 12 hrs. post alcohol Consumption in total subjects have been elicited in table 6 and graphically represented in figure 2.

Interpretation:

The mean scores for total hangover score was significantly lower in PartySmart chews when compared placebo chews whereas the mean scores for other symptoms showed no significant difference. The mean score of PartySmart chews was also comparable to PartySmart Capsule and Cheers® Restore Capsule.

Table 6 : AHS at 12 Hrs. post alcohol Consumption (Individual Parameters & Total Score)

Parameters		Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
Hangover	Mean \pm Sd	0.73 \pm 1.11	0.03 \pm 0.16	0.03 \pm 0.16	0.08 \pm 0.28
	Min, Max	0, 5	0, 1	0, 1	0, 1
	Median	0	0	0	0
	IQR	1	0	0	0
	Mean Rank	99.38	65.47	65.47	69.58
	p value		a: p<0.0001	a: p<0.0001	a: p<0.0001
Thirsty	Mean \pm Sd	0.18 \pm 0.68	0 \pm 0	0.03 \pm 0.16	0 \pm 0
	Min, Max	0, 4	0, 0	0, 1	0, 0
	Median	0	0	0	0
	IQR	0	0	0	0

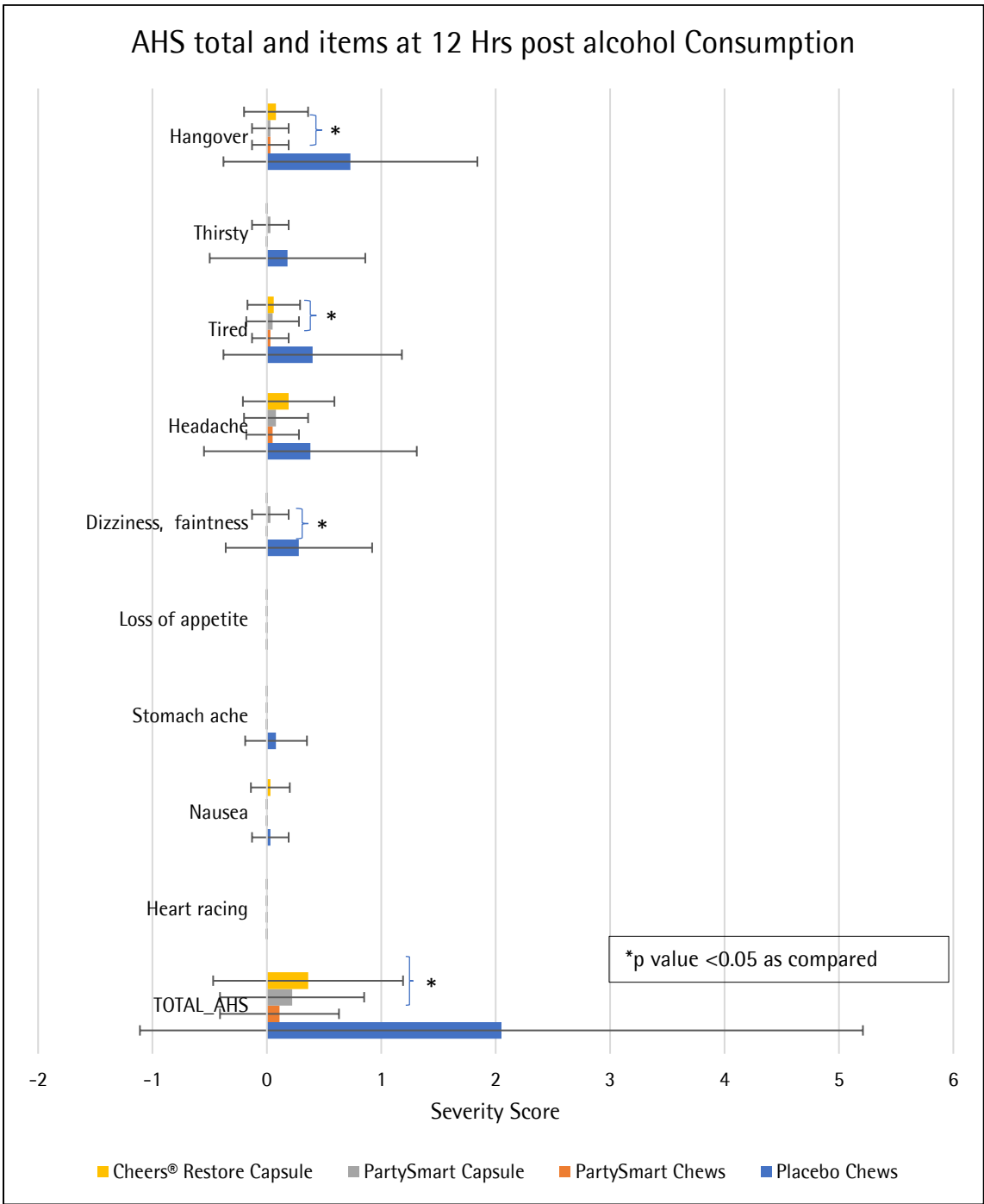
Parameters		Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
	Mean Rank	80.51	73	75.01	73
	p value		ns	ns	ns
Tired	Mean \pm Sd	0.4 \pm 0.78	0.03 \pm 0.16	0.05 \pm 0.23	0.06 \pm 0.23
	Min, Max	0, 4	0, 1	0, 1	0, 1
	Median	0	0	0	0
	IQR	1	0	0	0
	Mean Rank	89.63	69	71	71.11
	p value		a: p<0.0009	a: p<0.0038	a: p<0.0044
Headache	Mean \pm Sd	0.38 \pm 0.93	0.05 \pm 0.23	0.08 \pm 0.28	0.19 \pm 0.4
	Min, Max	0, 5	0, 1	0, 1	0, 1
	Median	0	0	0	0
	IQR	0	0	0	0
	Mean Rank	82.33	68.97	70.96	79.29
	p value		ns	ns	ns
Dizziness, faintness	Mean \pm Sd	0.28 \pm 0.64	0 \pm 0	0.03 \pm 0.16	0 \pm 0
	Min, Max	0, 3	0, 0	0, 1	0, 0
	Median	0	0	0	0
	IQR	0	0	0	0
	Mean Rank	86.03	71	73	71
	p value		a: p<0.0014	a: p<0.0084	a: p<0.0015
Loss of appetite	Mean \pm Sd	0 \pm 0	0 \pm 0	0 \pm 0	0 \pm 0
	Min, Max	0, 0	0, 0	0, 0	0, 0
	Median	0	0	0	0

Parameters		Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
	IQR	0	0	0	0
	Mean Rank	75.5	75.5	75.5	75.5
	p value		ns	ns	ns
Stomach-ache	Mean \pm Sd	0.08 \pm 0.27	0 \pm 0	0 \pm 0	0 \pm 0
	Min, Max	0, 1	0, 0	0, 0	0, 0
	Median	0	0	0	0
	IQR	0	0	0	0
	Mean Rank	79.63	74	74	74
	p value		ns	ns	ns
Nausea	Mean \pm Sd	0.03 \pm 0.16	0 \pm 0	0 \pm 0	0.03 \pm 0.17
	Min, Max	0, 1	0, 0	0, 0	0, 1
	Median	0	0	0	0
	IQR	0	0	0	0
	Mean Rank	76.38	74.5	74.5	76.58
	p value		ns	ns	ns
Heart racing	Mean \pm Sd	0 \pm 0	0 \pm 0	0 \pm 0	0 \pm 0
	Min, Max	0, 0	0, 0	0, 0	0, 0
	Median	0	0	0	0
	IQR	0	0	0	0
	Mean Rank	75.5	75.5	75.5	75.5
	p value		ns	ns	ns
TOTAL_AHS	Mean \pm Sd	2.05 \pm 3.16	0.11 \pm 0.52	0.22 \pm 0.63	0.36 \pm 0.83
	Min, Max	0, 14	0, 3	0, 3	0, 3

Parameters		Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
	Median	0.5	0	0	0
	IQR	3	0	0	0
	Mean Rank	98.01	62.36	67.62	72.08
	p value		a: p<0.0001	a: p<0.0002	a: p<0.0023
<p>Statistical Test: Kruskal-Wallis test followed by Post Hoc Dunn's multiple comparisons test using a Bonferroni -adjusted alpha level of 0.008 (0.05/6) were used to compare all pairs of groups. There is significant difference were all comparator group compared to placebo. None of other comparisons were significant.</p> <p>a: as compared to Placebo. Acute Hangover Scale (AHS) parameters Assessed on scale of 0 to 7, 0=None, 1=Mild, 2,3,4=Moderate , and 5,6,7=Incapacitating</p> <p>There was a statistically significant difference between Placebo compared to PartySmart chews, PartySmart Capsule and Cheers® Restore Capsule, Total AHS score in different groups (p<0.005) with the mean rank of 98.01 for Placebo, 62.36 for PartySmart Chews, 67.62 for PartySmart Capsule, 72.08 for Cheers® Restore Capsule.</p>					



Figure 2: Graphical representation of Acute Hangover Scale Assessment



Percentage of Subjects free from Symptoms based on AHS in all groups

Percentage of Subjects free from Symptoms based on AHS in all groups have been elicited in table 7 and graphically represented in figure 3.

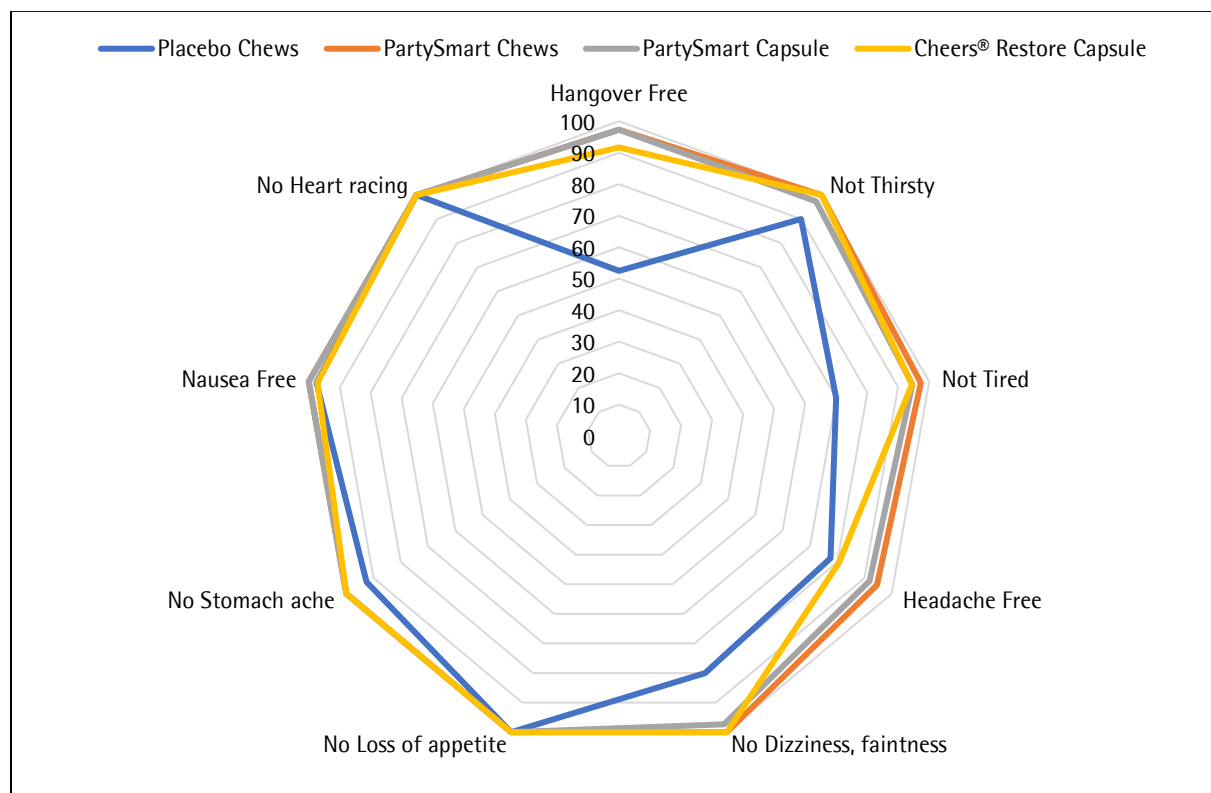
Interpretation:

Percentage of Subjects free from below given symptoms were more in PartySmart Chews and PartySmart Capsule when compared to Cheers® Restore Capsule and Placebo Chews.

Table 7 : Percentage of Subjects free from Symptoms based on AHS in all groups

	Hang over Free	Not Thirsty	Not Tired	Headache Free	No Dizziness, faintness	No Loss of appetite	No Stomach-ache	Nausea Free	No Heart racing
Placebo Chews	52.5	90	70	77.5	80	100	92.5	97.5	100
PartySmart Chews	97.3	100	97.3	94.59	100	100	100	100	100
PartySmart Capsule	97.3	97.3	94.59	91.89	97.3	100	100	100	100
Cheers® Restore Capsule	91.67	100	94.44	80.56	100	100	100	97.22	100

Figure 3 : Percentage of Subjects free from Symptoms based on AHS in all groups



B. 1- item Overall Hangover Severity Scale

The details of Overall Hangover Severity have been elicited in table 8 and graphically represented in figure 4.

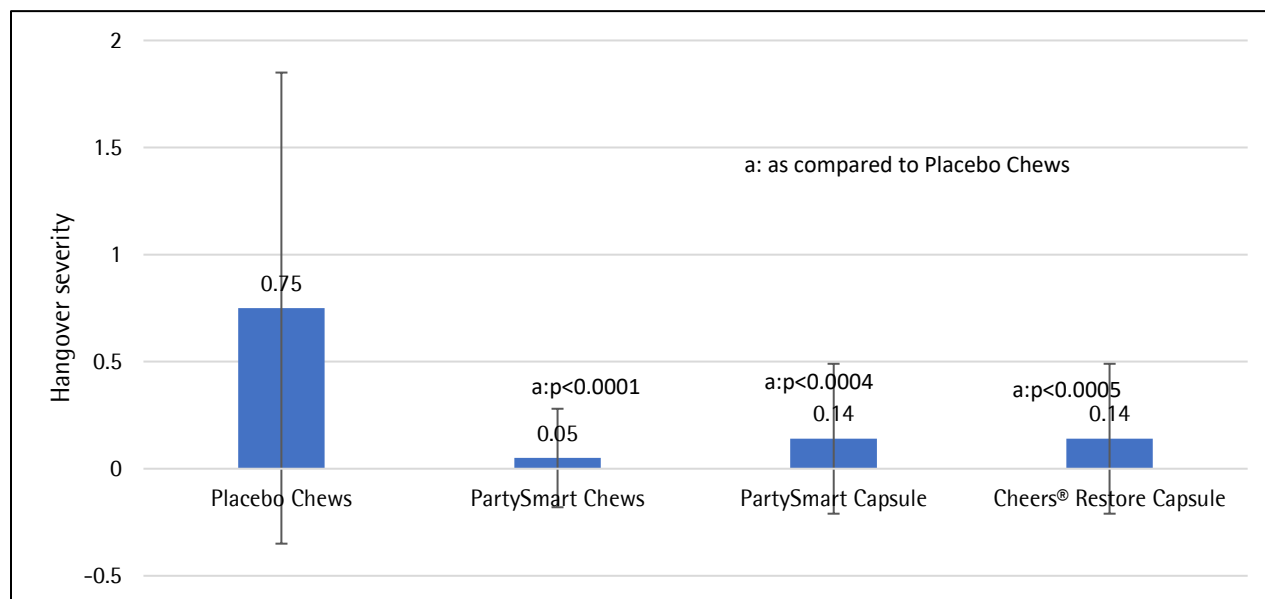
Interpretation:

There was a statistically significant difference between Placebo compared to PartySmart chews, PartySmart Capsule and Cheers® Restore Capsule. Total AHS score in different groups ($p < 0.005$) with the mean rank of 97.6 for Placebo, 63.45 for PartySmart Chews, 69.36 for PartySmart Capsule, 69.64 for Cheers® Restore Capsule. The overall Hangover Severity in Party Smart Chews is less compared to other groups.

Table 8 : 1-item scale assessing "Overall Hangover Severity"

	Placebo Chews	Party Smart Chews	Party Smart Capsule	Cheers® Restore Capsule
N	40	37	37	36
Mean	0.75 ± 1.1	0.05 ± 0.23	0.14 ± 0.35	0.14 ± 0.35
Min, Max	0, 5	0, 1	0, 1	0, 1
Median	0.5	0	0	0
IQR	1	0	0	0
Mean ranks	97.6	63.45	69.36	69.64
		a: p<0.0001	a: p<0.0004	a: p<0.0005
<p>Statistical Test: Kruskal-Wallis test followed by Post Hoc Dunn's multiple comparisons test using a Bonferroni -adjusted alpha level of 0.008 (0.05/6) were used to compare all pairs of groups. There is significant difference were all comparator group compared to placebo. None of other comparisons were significant.</p> <p>Assessment: Severity scoring of items, 0 (absent) to 10 (extreme)</p> <p>There was a statistically significant difference between Placebo compared to PartySmart chews, PartySmart Capsule and Cheers® Restore Capsule, Total AHS score in different groups (p<0.005) with the mean rank of 97.6 for Placebo, 63.45 for PartySmart Chews, 69.36 for PartySmart Capsule, 69.64 for Cheers® Restore Capsule.</p>				

Figure 4 : 1-item scale assessing "Overall Hangover Severity"



1- item Hangover Severity Scale at 12th hour

The details of Hangover Severity at 12th hour have been elicited in table 9 and graphically represented in figure 5.

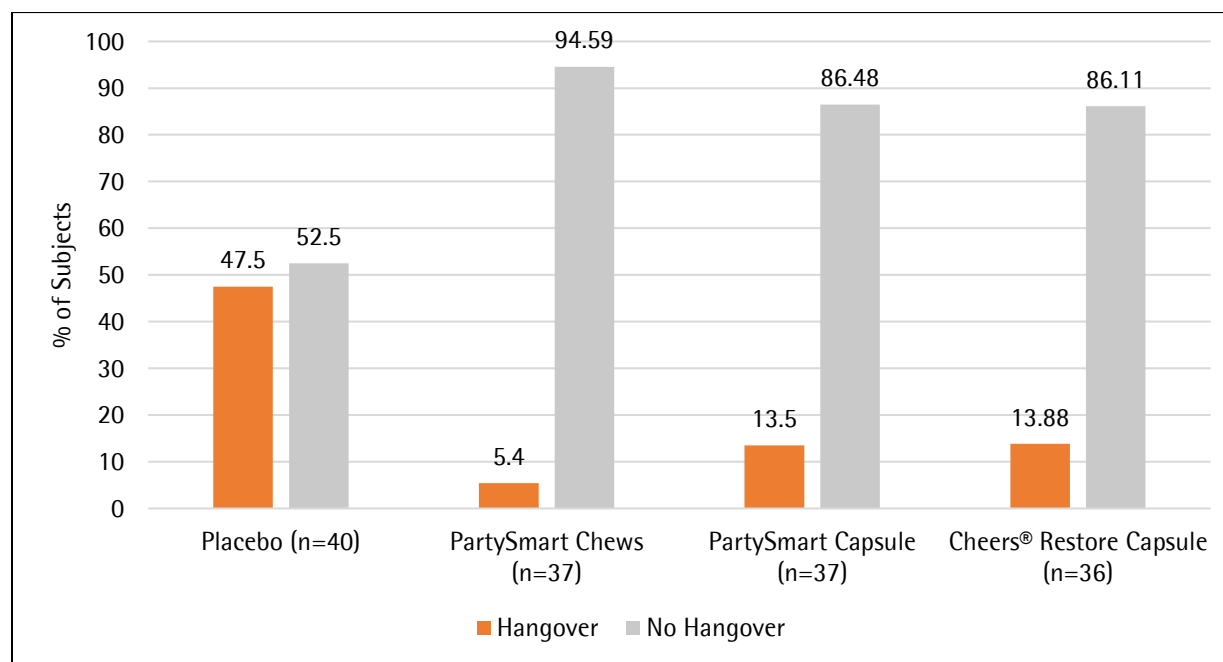
Interpretation:

At 12th hr. only 5.40% of subjects shows hangover in PartySmart Chews whereas 47.5% of subjects shows hangover in Placebo group. 13.50% and 13.88% subjects show hangover in PartySmart Capsule and Cheers® Restore Capsule whereas 50% of subjects shows hangover in both the Placebo groups. Therefore, Party Smart chews shows less hangover at 12th hour compared to other groups.

Table 9 : % of subjects Experienced Hangover on 1 item Score at 12th hr

Groups	Hangover	No Hangover	p value
Placebo (n=40)	19 (47.5%)	21 (52.5%)	p<0.0001
PartySmart Chews (n=37)	2 (5.40%)	35 (94.59%)	
Placebo (n=40)	20 (50%)	20 (50%)	p<0.0006
PartySmart Capsule (n=37)	5 (13.50%)	32 (86.48%)	
Placebo (n=40)	20 (50%)	20 (50%)	p<0.0008
Cheers® Restore Capsule (n=36)	5 (13.88%)	31 (86.11%)	
Analysed by Chi-square test, level of significance was fixed at 0.05.			

Figure 5 : % of subjects Experienced Hangover on 1 item Score at 12th hr



C. Assessment of Blood Alcohol and Acetaldehyde Levels in 12hrs

Assessment of Blood Alcohol Concentration in 12hrs Post Alcohol Intake

The details of Assessment of Blood Alcohol Concentration in all the subjects of the four periods in 12hrs Post Alcohol Intake have been elicited in table 10 and graphically represented in figure 6.

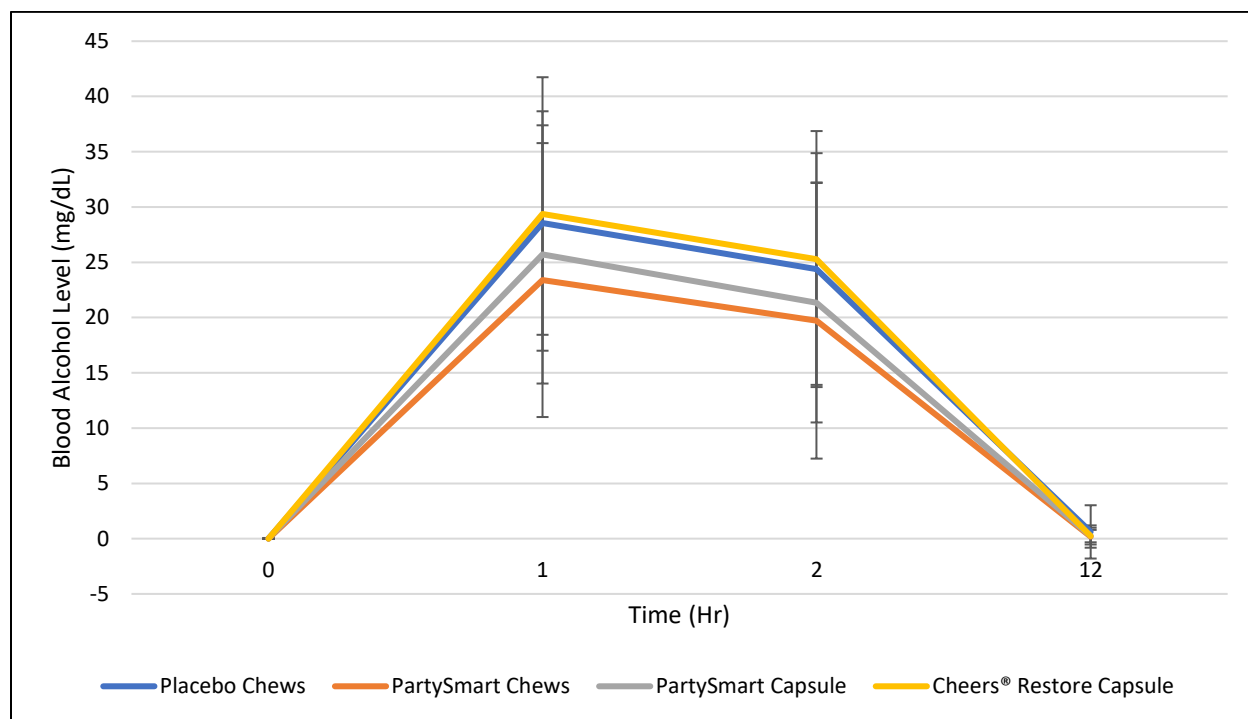
Interpretation

Alcohol concentration in blood at each hour (0hr, 1hr, 2hr, 12hr) were lower in PartySmart soft chews group in comparison with the placebo, PartySmart Capsule and Cheers® Restore Capsule.

Table 10 : Assessment of Blood Alcohol Concentration in 12hrs Post Alcohol Intake

Time Point		Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
At 0 Hr	Mean \pm Sd	0 \pm 0.02	0 \pm 0.02	0.02 \pm 0.04	0 \pm 0
	Min, Max	0, 0.08	0, 0.14	0, 0.18	0, 0
	p value		ns	ns	ns
At 1 hr	Mean \pm Sd	28.55 \pm 10.11	23.39 \pm 12.39	25.71 \pm 11.68	29.37 \pm 12.37
	Min, Max	11.64, 50.83	1.36, 46.71	0, 54.78	8.71, 55.49
	p value		ns	ns	ns
At 2 Hr	Mean \pm Sd	24.39 \pm 10.48	19.73 \pm 12.49	21.34 \pm 10.83	25.29 \pm 11.58
	Min, Max	3.69, 44.75	0.65, 45.33	0.13, 47.43	5.53, 48.72
	p value		ns	ns	ns
At 12 Hr	Mean \pm Sd	0.61 \pm 2.41	0.19 \pm 1.01	0.23 \pm 0.76	0.23 \pm 0.56
	Min, Max	0, 13.87	0, 6.12	0, 4.23	0, 2.36
	p value		ns	ns	ns
Statistical test: ANOVA followed by Tukey's multiple comparisons test, a: as compared to Placebo Chews.					

Figure 6 : Assessment of Blood Alcohol Concentration in 12hrs Post Alcohol Intake



Assessment of Blood Acetaldehyde Levels in 12hrs Post Alcohol Intake

The details of Assessment of Blood Acetaldehyde Concentration in all the subjects of the four periods in 12th Post Alcohol Intake have been elicited in table 11 and graphically represented in figure 7.

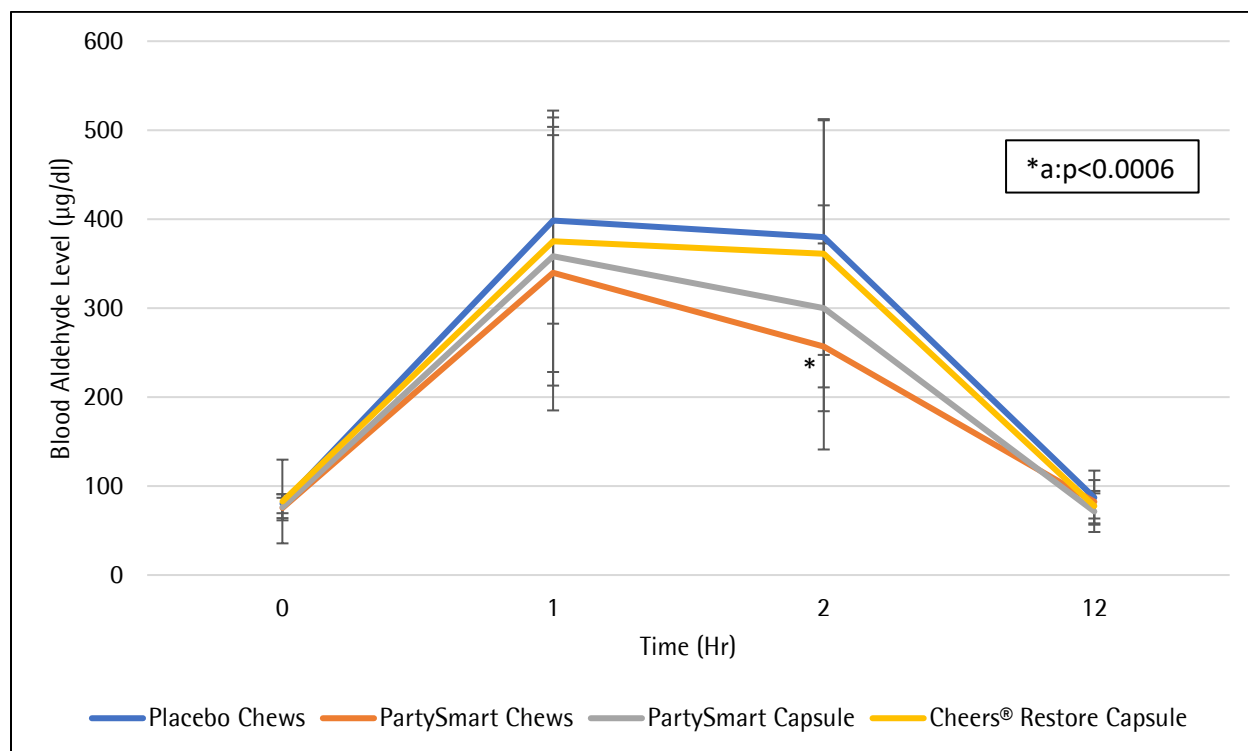
Interpretation

The blood acetaldehyde concentration level at 2nd hour was significantly lower in PartySmart soft chews group in comparison with the placebo. There was no significant difference between the other groups in this parameter.

Table 11 : Assessment of Blood Acetaldehyde Levels in 12hrs Post Alcohol Intake

Time Point		Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
At 0 Hr	Mean \pm Sd	80.21 \pm 10.73	75.39 \pm 11.4	76.09 \pm 14.63	82.65 \pm 47.04
	Min, Max	55.64, 100.6	46.4, 101.9	51.56, 120.3	37.64, 349.3
	p value		ns	ns	ns
At 1 hr	Mean \pm Sd	398.4 \pm 115.9	339.7 \pm 154.7	358.3 \pm 145.4	375.1 \pm 146.9
	Min, Max	194.5, 623.4	73.79, 653.7	0, 704.3	147.9, 759.2
	p value		ns	ns	ns
At 2 Hr	Mean \pm Sd	379.9 \pm 132.5	256.9 \pm 115.8	299.8 \pm 115.7	361 \pm 150.1
	Min, Max	119.3, 628.3	66.67, 485	70.08, 530.5	120.4, 822.6
	p value		a: p<0.0006	ns	ns
At 12 Hr	Mean \pm Sd	86.98 \pm 30.39	82.4 \pm 24.32	71.42 \pm 23.07	77.66 \pm 14.13
	Min, Max	41.74, 250	27.55, 190.9	5.56, 117.5	56.02, 113
	p value		ns	ns	ns
Statistical test: ANOVA followed by Tukey's multiple comparisons test, a: as compared to Placebo Chews.					

Figure 7 : Assessment of Blood Acetaldehyde Levels in 12hrs Post Alcohol Intake



D. Clinical Assessment of Alcohol Hangover Symptoms

The details of assessment made by clinical examination of Alcohol Hangover Symptoms in all the subjects of the four periods at 12hrs have been elicited in table 12,13 and graphically represented in figure 8.

Interpretation

Based on the assessment made by clinical examination, the percentage of subjects who experienced hangover symptoms were lower in the period II, III and IV when compared to period I. These results are represented here in table 12, 13 & figure 7. Also, there was no significant difference in the severity of symptoms in subjects taking PartySmart soft chews after the first sip versus those taking it after the last sip. The results are represented in table 14.

Table 12 : Clinical Assessment of Alcohol Hangover Symptoms

Period I (Placebo)								
Scale	Headache	Nausea	General Energy	Mental Energy	Focus	Physical energy	General wellbeing	Daily activity motivation
0 [Nil] = About 0%,	31 (77.5 %)	39 (97.5 %)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1 [Occasionally] = about 25%,	5 (12.5 %)	1 (2.5%)	1 (2.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2 [About half of the time] = About 50%	4 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3 [Mostly] = About 75%,	0 (0%)	0 (0%)	18 (45%)	14 (35%)	8 (20%)	7 (17.5%)	8 (20%)	7 (17.5%)
4 [completely] = About 100%.	0 (0%)	0 (0%)	21 (52.5%)	26 (65%)	32 (80%)	33 (82.5%)	32 (80%)	33 (82.5%)
Total	40 (100%)	40 (100%)	40 (100%)	40 (100%)	40 (100%)	40 (100%)	40 (100%)	40 (100%)

Period II (PartySmart Chews)								
Scale	Headache	Nausea	General Energy	Mental Energy	Focus	Physical energy	General wellbeing	Daily activity motivation
0 [Nil] = About 0%,	35 (94.59%)	37 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1 [Occasionally] = about 25%,	2 (5.41%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2 [About half of the time] = About 50%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3 [Mostly] = About 75%,	0 (0%)	0 (0%)	3 (8.11%)	1 (2.7%)	1 (2.7%)	0 (0%)	1 (2.7%)	1 (2.7%)
4 [completely] = About 100%.	0 (0%)	0 (0%)	34 (91.89%)	36 (97.3%)	36 (97.3%)	37 (100%)	36 (97.3%)	36 (97.3%)
Total	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)

Period III (PartySmart Capsule)								
Scale	Headache	Nausea	General Energy	Mental Energy	Focus	Physical energy	General wellbeing	Daily activity motivation
0 [Nil] = About 0%,	34 (91.89%)	37 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1 [Occasionally] = about 25%,	3 (8.11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2 [About half of the time] = About 50%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3 [Mostly] = About 75%,	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
4 [completely] = About 100%.	0 (0%)	0 (0%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)
Total	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	37 (100%)

Period IV (Cheers® Restore Capsule)								
Scale	Headache	Nausea	General Energy	Mental Energy	Focus	Physical energy	General wellbeing	Daily activity motivation
0 [Nil] = About 0%,	29 (80.56%)	35 (97.22%)	0 (0%)	0 (0%)	0 (0%)	1 (2.78%)	0 (0%)	0 (0%)
1 [Occasionally] = about 25%,	7 (19.44%)	1 (2.78%)	1 (2.78%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2 [About half of the time] = About 50%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3 [Mostly] = About 75%,	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
4 [completely] = About 100%.	0 (0%)	0 (0%)	35 (97.22%)	36 (100%)	36 (100%)	35 (97.22%)	36 (100%)	36 (100%)
Total	36 (100%)	36 (100%)	36 (100%)	36 (100%)	36 (100%)	36 (100%)	36 (100%)	36 (100%)

Table 13 : Summarization of Alcohol Hangover Symptoms in % subjects at 12 hrs in 4 periods

	Headache Free	Nausea Free	General Energy	Mental Energy	Focus	Physical energy	General well being	Daily activity motivation
Placebo Chews (N=40)	78	98	53	65	80	83	80	83
PartySmart Chews (N=37)	95	100	92	97	97	100	97	97
PartySmart Capsule (N=37)	92	100	100	100	100	100	100	100
Cheers® Restore Capsule (N=36)	81	97	97	100	100	97	100	100

Figure 8 : Alcohol Hangover Symptoms in % subjects at 12 hrs in 4 periods

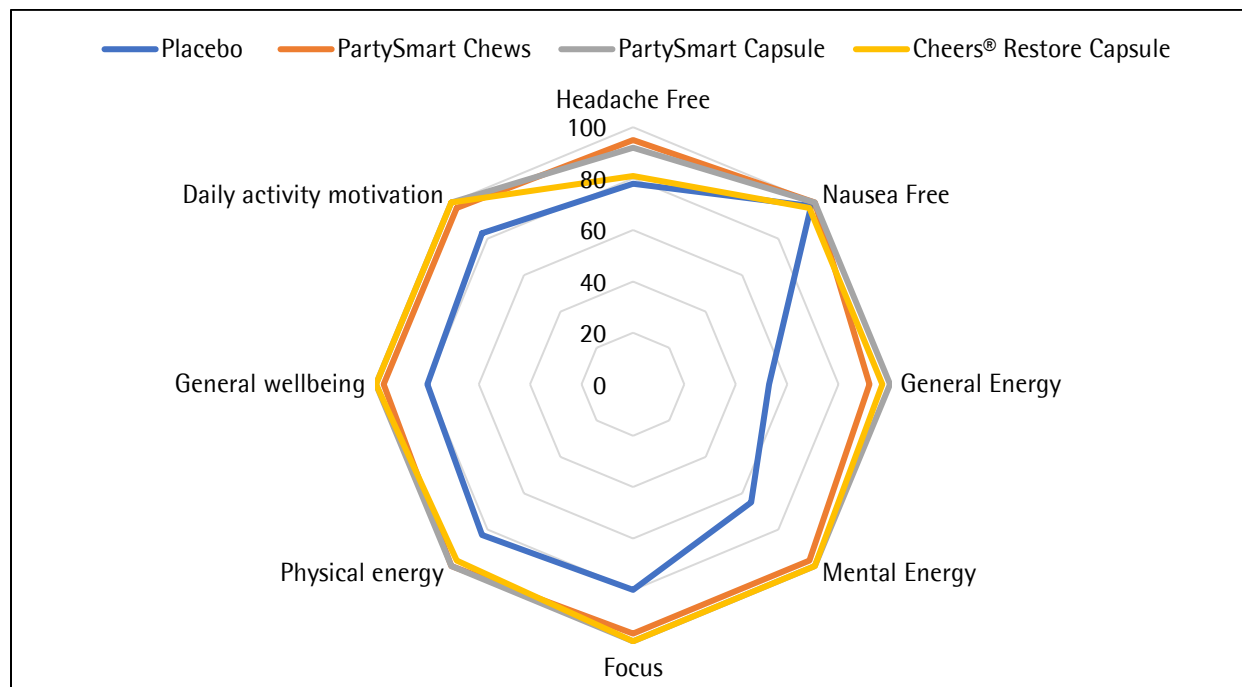


Table 14 : Comparative Assessment of Alcohol Hangover Symptom (Total Mean score) at 12 Hrs [Before & After Alcohol Consumption]

IP Intake		Placebo Chews (N=40) Before 1st Sip: n=20 After Last Sip: n=20)	PartySmart Chews (N=37) Before 1st Sip: n=20 After Last Sip: n=17	PartySmart Capsule (N=37) Before 1st Sip: n=20 After Last Sip: n=17
Before 1st Sip	Mean	2.7	0.2	0.25
	Std. Deviation	3.03	0.7	0.55
After Last Sip	Mean	1.4	0	0.18
	Std. Deviation	3.24	0	0.73
	p value	b: p<0.03	ns (0.49)	ns (0.35)
Statistically Test: Mann Whitney test, Level of Significance was fixed at >0.05, b: as compared to Before 1st Sip In PartySmart Chews and Capsule: There is no Statistical difference either subjects taking IP before or after Alcohol Consumption				

E. Incidence of Adverse Events

The incidence of adverse events in all the four periods have been elicited in table 15.

Interpretation

The incidence of adverse events was more in subjects who received placebo chews compared to other groups.

Out of 37 subjects only 4 subjects showed adverse events in PartySmart chews.

The results suggests that PartySmart soft chews have a good safety profile as they have a lower incidence of adverse – events.

Table 15: Incidence of Adverse Events

Adverse Events (AE)				
	Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
Number of Subjects with AE	9	3	6	3
Number of AEs (Events)	9	4	6	3
Events Details				
Vomit	9	3	6	6
Breathlessness	-	1	-	-

Table 16 : Baseline Characteristics (Alcohol) of all 40 participants

Parameters	Description	Value
History of taking Whiskey, n	Yes	40
	No	0
Since how many years/months subject has been consuming whiskey, Years	Mean \pm Sd	4.2 \pm 3.95
	Median	3
	Min, Max	0.5, 15

Frequency of Alcohol Intake, n (%)	Daily	1 (2.5)
	Weekly	11 (27.5)
	Monthly	9 (22.5)
	Quarterly	14 (35)
	Every 6 months	3 (7.5)
	Once in 6 months	2 (5)
Usual quantity (ml)	Mean \pm Sd	128.5 \pm 87.75
	Median	90
	Min, Max	30, 500
Maximum quantity (ml)	Mean \pm Sd	219.3 \pm 193.6
	Median	150
	Min, Max	30, 750
Quantity at which subject experienced hang over (ml)	Mean \pm Sd	214.5 \pm 195.4
	Median	150
	Min, Max	30, 750
Last hangover	Yes	40
	No	0
Previous hangover duration (Hours)	Mean \pm Sd	5.13 \pm 3.56
	Median	5
	Min, Max	0.5, 12

Table 17: Overall Assessment on the Amount of Alcohol Consumption

	Placebo Chews (N=40)	PartySmart Chews (N=37)	PartySmart Capsule (N=37)	Cheers® Restore Capsule (N=36)
N	40	37	37	36
Mean	176.3	166.8	169.7	171.4
Std. Deviation	58.4	57.2	54.6	54.4
Median	175	150	150	160
Minimum	60	60	60	60
Maximum	270	270	270	270
p value	ns	ns	ns	ns
There is no significant deference between group in alcohol intake quantity				

18.0 SAFETY EVALUATION

18.1 Vital Signs, Physical Findings and Other Observations Related to Safety

All the vitals were within the normal range, and there were no abnormal physical findings recorded neither during the study nor at the end of the study.

18.2 Adverse Events

The findings suggests that PartySmart soft chews have a good safety profile as they have a lower incidence of adverse effects compared to other groups.

19.0 DISCUSSION

To assess the hangover symptoms in this study, AHS was chosen as the primary end point. The Alcohol Hangover Research Group has given a consensus statement that the best practice in alcohol hangover research should use AHS as the scoring scale in acute experimental administration studies [9]. The AHS is a reliable and valid instrument for assessing acute hangover symptoms in experimental investigations of residual alcohol effects [10].

The mean score and each item scores of AHS are significantly affected by the type of beverage but not by the demographics or typical drinking behaviors, supporting validity. However, solely relying on hangover symptom scales like AHS may yield false positives in subjects who report not having a hangover [11]. Since many of the somatic and psychological symptoms of hangover such as headache may also be experienced in the absence of a hangover, non-hangover subjects may be categorized as having hangover. Therefore, a 1-item overall hangover severity scale is also considered to accurately assess overall hangover severity [11]. Hence, both these scales were used in this study. The study results showed that PartySmart soft chews reduce the intensity of hangover symptoms as assessed by both two scales.

An earlier recommendation had suggested cutoff blood alcohol concentration (BAC) of 0.11% as a toxicological threshold to indicate that sufficient alcohol has been consumed to develop a hangover [12]. However, recent research has shown that subjective intoxication (the level of severity of reported drunkenness) is the most important determinant of hangover severity instead of the BAC level [12]. Despite having lower BACs, many participants in these studies reported having a hangover especially when their subjective intoxication levels were high. This

was probably the case when alcohol consumption on the drinking occasion that resulted in a hangover significantly exceeded their "normal" drinking level [12]. Thus, the consumption of an alcoholic beverage in a quantity that exceeded a subject's normal drinking level was taken as the criteria to ensure that the subjects were induced with alcohol hangover during the study. For this purpose, each individual subject's alcohol consumption history and the quantity consumed on the experimental day were also noted.

When ethanol is converted to acetaldehyde by CYP2E1, it leads to the formation of reactive oxygen species (ROS) or free oxygen radicals. Like hydroxyethyl, superoxide anions and hydroxyl radicals [12,14]. Acetaldehyde is further oxidised by aldehyde dehydrogenase-2 (ALDH2) in mitochondria to ultimately create acetate.[13,15,16] Acetaldehyde can also directly induce the formation of ROS by the activation of NADPH oxidase NOX2 which results in cell membrane damage that induces apoptosis. [17]. PartySmart chews may have benefitted in reducing the hangover symptoms by lowering the acetaldehyde levels in the study.

Besides lowering the acetaldehyde levels, the beneficial effects may also be attributed to the other targeted actions of the ingredients. The various ingredients of the soft chew include Phoenix dactylifera (Date) fruit extract, Curcuma longa (turmeric) rhizome extract, Vitis vinifera (grape) fruit extract, Emblica officinalis (amla) fruit extract, Zingiber officinale (Ginger) rhizome extract and Trigonella foenum greacum (Fenugreek) seed powder. These ingredients have hepatoprotective [18], gastroprotective[19], antioxidant[10], prokinetic and anti nausea effects[20-26]. Thus, this study result suggests that drugs acting by different mechanisms than those that aim to only enhance the alcohol and acetaldehyde dehydrogenase enzymes are effective in reducing hangover symptoms. This is an important insight into the Pathophysiology of hangover which is not yet completely understood. There was no significant difference in the severity of symptoms (AHS score) in those subjects who consumed PartySmart soft chews after the first sip versus those who took it after the last sip. Thus, it is equally effective when taken at any time.

Since men and women have different rates of alcohol metabolism, there may be a difference in the presence and severity of hangover symptoms [27]. The subjects enrolled in this study included both men and women to eliminate this confounding factor.

The study has measured 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 since all the subjects were housed in the same center during the study under the same conditions and were provided with the same food and alcoholic beverage for hangover induction.

There are a few limitations of this study. Ethnic and interracial variations in hangover severity have not been studied even though the study design eliminates the inter-subject variability. The emotional hangover symptoms such as embarrassment, misery and guilt might not appear as in normal settings. The severity of symptoms due to the congeners present in different beverages has not been studied because a common beverage was given to all subjects. With respect to the mechanism of action, the immune function after alcohol consumption was not assessed. Whether PartySmart benefits by acting via this mechanism could not be examined.

In future studies, several aspects of hangover prevention may be addressed. Since there is an interracial variation in alcohol metabolism due to differences in key enzymes involved, there may be a resultant in difference in patterns, frequency, and severity of alcohol hangover amongst the different ethnic groups [28]. An effective hangover preventive or treatment strategy in one ethnic group might not have the same efficacy in another due to these variations [28]. Therefore, subjects of different ethnicities should be studied. Even if a substance is proven to be effective for one type of alcoholic beverage it is difficult to generalize the result for other types [28]. Thus, the drug effect due to hangover caused by different drinks may be studied.

It is known that sleeping in a new (and especially clinical) environment may require adaptation [29]. Future studies may include a sleep rehearsal night during screening to identify any possibilities of 'first-night effects' or other sleep disturbances that may influence the study results.

Administration of one standard type of alcoholic drink to all the subjects in this study has helped in overcoming the confounding factors but it does not reflect the usual drinking behavior of the participants. In naturalistic studies, consumer satisfaction ratings have shown to be more reliable when obtained in a real-life setting [30] like drinking alcohol in a bar or at home. Research has also shown that consumer satisfaction of food products and beverages rated in controlled laboratory settings are generally underestimated in terms of product acceptance when compared to real-life testing [31]. A study which reflects the naturalistic behavior can be conducted.

It is important to include biomarkers of immune function such as IL-10 and IL-6 levels in future RCTs to assess the effect of the soft chew. Extract of the fruit of *Hovenia dulcis* has shown to act by this mechanism [24]. Assessment of saliva and urine parameters to examine the possible mechanism of action of this new hangover cure can also be incorporated. Cognitive and psychometric tests to determine effects in reducing hangover-related performance on skills and abilities essential in daily activities such as driving a car or on-the-job performance may be fruitful [32].

The study suggests that PartySmart soft chews have a good safety profile as they have a lower incidence of adverse effects.

Alcohol consumption has many negative consequences reported with it. The most common among them is the experience of a hangover. Hangover symptoms have huge economic consequences due to decreased productivity of employees. Therefore, there is an increasing need to find remedies that significantly reduce these symptoms. The purpose of this study was to evaluate the safety and efficacy of a polyherbal formulation marketed as PartySmart Soft chews. It was a double blinded, placebo controlled, comparative study conducted in four periods. Period one included 40 subjects who were given two placebo soft chews. After a washout period of 7+/-2 days, the subjects were enrolled in period two. In period two, 37 of the 40 subjects continued to participate. The same methodology was followed but active PartySmart soft chews were administered instead of placebo. Both these periods were double blinded. After the next washout periods, periods three and four were conducted with

PartySmart capsules (other polyherbal formulation) and the Cheers® Restore Capsule respectively in an open labeled manner. Parameters assessed were blood alcohol and acetaldehyde levels at 4 time points (within 1 hour prior to alcohol consumption, at 1 hour, 2 hours and 12 hours post the last sip). The Acute Hangover Scale (AHS) and the 1 item overall Hangover Severity Scale (HSS) scores at the 12th hour post last sip was assessed. Clinical assessments of the hangover symptoms at 12th hour, the incidence of adverse effects and compliance were also performed. The study revealed that the mean AHS score and the mean 1 item HSS scores were significantly lower after PartySmart soft chew consumption when compared to a placebo and that PartySmart soft chew is comparable to PartySmart capsules and the Cheers® Restore Capsule. The percentage of subjects who were symptom free was also recorded highest in Period 2. The blood alcohol and acetaldehyde levels at various timepoints were not significantly different among groups.

20.0 CONCLUSION

Alcohol intoxication has become one of the most commonly found clinical condition in the present days. Correction of the systemic impact with the administration of polyherbal formulation in the form of PartySmart Soft Chews as compared to placebo, and PartySmart Capsule and Cheers® Restore Capsule has been the point of focus in this present study. The ingredients present in the formulation can protect and restore the hepatic function by potentially eliminating the acetaldehyde from the system and thereby reduce the toxic systemic impact post alcohol consumption.

Based on the results of the present study, it was clearly observed that PartySmart chews brings a significant change in blood alcohol and acetaldehyde levels in all the subjects who had protocol specified amount of alcohol. Significant symptomatic improvement was observed in those who received PartySmart Soft Chews as compared to those who received Placebo with significant overall reduction in the alcohol hangover scores (AHS Scores).

The results of the present study might be possibly due to the synergistic potential of the potent hepatoprotective herbs present in both the formulation facilitating the elimination of hepatotoxic acetaldehyde from the blood and thereby reduce the hepatocellular damage due

to alcohol consumption. So, based on the current study results, it can be concluded that PartySmart soft chews is safe and effective in reducing the symptoms of hangover.

20.0 Reference

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