Original Article

Clinical validation of efficacy and safety of herbal cough formulation "Honitus syrup" for symptomatic relief of acute non-productive cough and throat irritation

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Abstract

Background: Acute cough represents the most common illness evaluated in the outpatient settings. Available remedies for its management are generally allopathic combinations of antihistamines and decongestants that achieve antitussive activity, but often with unpleasant side effects prompting the need to explore safer and effective options. Honitus is an Ayurvedic proprietary herbal cough syrup with benefits of honey, intended to provide relief in acute nonproductive cough and throat irritation without causing drowsiness. This study investigated the safety and efficacy of Honitus in reducing acute nonproductive cough and throat irritation in comparison to a standard marketed allopathic cough syrup intended for use in similar conditions. **Materials and Methods:** This was a randomized double-blind study conducted in 105 individuals who received orally 2 tsp (10 ml) of either Honitus or marketed cough syrup (MCS) four times a day for 3 days. Response to treatment was evaluated from baseline to the end of treatment period on the basis of changes in day and night frequencies of cough, throat irritation and development of adverse events (AEs). **Results:** Honitus was found safe and effective in reducing symptoms of acute nonproductive cough, throat irritation, and comparable to MCS in reducing day and night frequencies of cough, the time to relief from cough and throat irritation and the Physician's Global Assessment of cough. Honitus showed comparably better results than MCS on throat irritation, the duration of relief from cough and throat irritation without causing drowsiness. No AEs related to study or study products were reported. **Conclusion:** Honitus Syrup is safe and effective in reducing the symptoms of acute nonproductive cough and throat irritation without causing drowsiness.

Keywords: Acute nonproductive cough, herbal, Honitus, throat irritation

Introduction

Acute cough represents the most common acute illness evaluated in the outpatient setting.[1] Self-medication with the available cough and cold remedies often forms the first line of treatment for acute cough. These remedies are generally combinations of antihistamines and decongestants that achieve antitussive activity, but often with undesirable side effects such as sedation, constipation and dryness of mouth.[2,3] As such, there is a need to explore a reliable, long-acting formula that can safely and consistently deliver relief from cough for extended periods, particularly at night.

Cough and its management have been described extensively in Ayurvedic classics under the chapter on *Kasa*.[4] Ayurvedic Materia Medica mentions a number of herbs that are beneficial in alleviating cough and its symptoms. Honitus Cough Syrup (Mfd by Dabur India Limited) is a proprietary honey-based Ayurvedic herbal, cough syrup formula comprising goodness of herbs such as *Tulsi* (*Ocimum sanctum* Linn.),[5] *Mulethi* (*Glycyrrhiza glabra* Linn),[6] *Banaphsa* (*Viola odorata* Linn),[7] *Shunthi* (*Zingiber officinale* Roscoe),[8] *Vasaka* (*Adhatoda vasica* Nees)[9] and *Pippali* (*Piper longum* Linn.)[10] which has been reported to provide effective relief

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in cough without causing adverse effects like those associated with the use of antihistamines. Its contents such as *Ocimum* and *Zingiber* are also reported to possess anticholinesterase-like and antihistaminic activities.[11-13] Combination of these herbs with honey is intended to provide additive benefit in relieving symptoms of acute nonproductive cough.[14,15]

The current clinical study investigated the safety and efficacy of Honitus Cough Syrup in reducing acute nonproductive cough and throat irritation in comparison to an established marketed brand of allopathic cough syrup (MCS) intended for use in similar conditions. Results were evaluated on the basis of changes in day and night frequencies of cough, throat irritation, the time taken for relief from cough and throat irritation, and the duration of relief of symptoms for all the first morning doses of study products. Safety was assessed based on the development of adverse events (AEs) during the course of treatment.

Materials and Methods

Study product

Honitus Cough Syrup (Mfd by Dabur India Limited) is an Ayurvedic proprietary formulation comprising extracts of herbal ingredients such as *Tulsi* (*O. sanctum*, Lf.), *Yashti* (*G. glabra*, Rt.), *Kantakari* (*Solanum xanthocarpum*, Pl.), *Banaphsa* (*V. odorata,* Aerial.), *Shunthi* (*Z. officinale*, Rz.), *Pippali* (*P. longum*, Fr.), *Vasa* (*A. vasica*, Lf.), *Shati* (*Hedychium spicatum*, Rz.) and honey. Batch: BD0344 of Honitus was used in the present study.

MCS contained diphenhydramine, ammonium chloride and sodium citrate as active ingredients.

Study design

This was a randomized, double-blind; two-armed, parallel group clinical study conducted across three sites in Maharashtra (Nalini Clinic, C/o Dr. Umesh Deshpande, Ghatkopar (E). Mumbai - 400 075; Dr. Kulkarni's Clinic, Koliwada, Mumbai - 400 003; and Dr. Jaideep Joshi's Clinic, Pokhran Road, Thane - 400 606). The study was conducted with prior approvals from an independent ethics committee (Clinical Ethics Forum [CEF] ref no. CEF/10–11/102, Dated March 16th, 2011) and applicable regulatory guidelines. The study was registered with the Clinical Trials Registry of India vide Ref. no. CTRI/2011/05/001768.

Blinding

Investigator, study-site personnel and participants were blinded with respect to the allocation of the treatment. Medications were packed and labeled such that the product could not be identified by study investigators or the participants. The blind was supposed to be broken in an emergency where it would be essential to know which treatment a participant received in order to give the appropriate medical care. Investigator was asked to contact the sponsor/contract research organization prior to breaking the blind and document the reason for breaking the code and sign and date the appropriate document.

Eligibility criteria

Participants who fulfilled all the inclusion criteria and none of the exclusion criteria and were willing and able to provide signed informed consent form (ICF) prior to the study initiation were included.

Inclusion criteria

Males and females between 18 and 65 years of age with a history of acute nonproductive cough due to any cause except those listed in exclusion criteria and throat irritation for <1 week duration, who were able to comply with the study requirements, had a cough score of 0, 1 or 2 during day time (as per Day Time Cough Scale described under end points), and were willing and able to provide signed ICF prior to any study-related procedures were included in the study.

Exclusion criteria

Participants with a history of acute lower respiratory tract infections such as pneumonia, bronchitis whooping cough, chronic obstructive pulmonary disease/asthma, tuberculosis, systemic bacterial infections for which specific drug therapy will be required; any underlying lung pathology such as lung abscess or cystic fibrosis, individuals with a history of myocardial infarction within 4 weeks prior to enrollment; individuals with known hypersensitivity to ingredients of study products; individuals with immediate life-threatening diseases such as preexisting cardiovascular, liver, or neoplastic diseases or who received any immunosuppressant, sedative, hypnotic or tranquilizer within 14 days prior to enrollment; hypertensive patients on angiotensin-converting enzyme inhibitors; individuals or who had received any of the:-anti-histamines, cough suppressants, mucolytics, expectorants, or antibiotics 3 days prior to enrollment that may act as confounding factor; individuals with a history of Parkinson's disease and who were on monoamine oxidase inhibitors; individuals with any psychiatric illness which may impair the ability to provide written ICF; individuals participating in any other clinical trial; pregnant or lactating females; and those who were under study treatment or any other condition due to which individuals were deemed unsuitable by the investigator for reason(s) not specifically stated in the exclusion criteria were excluded. Alcohol, smoke, and drug abusers were excluded though occasional users of cigarettes and alcohol were included on investigator's discretion with instructions to restrict the use of cigarettes/ alcohol during study participation.

Methodology

Screening/baseline procedures included medical history, physical examination and recording of vitals. Participants fulfilling the selection criteria were randomized according to SAS 9.1 (SAS Institute (India) Pvt Ltd., Mumbai) -generated randomization list to receive either Honitus Syrup or MCS at doses of 2 teaspoons (10 ml) q.i.d orally for 3 days. Participants were advised to take the assigned study products with or without food and shake the bottle well before use. Concomitant

medications allowed during the study period were antipyretics and non-steroidal anti-inflammatory drugs.

The expected duration of individual's participation was 4 days (including 1 day of screening). Assessment of clinical signs and symptoms, vitals and AEs was done at follow-up visits on days 2, 3 and 4 (visits 2, 3 and 4) and post treatment. Response to treatment was assessed on the basis of changes in the frequency of cough and throat irritation from the baseline to the end of 3rd day treatment in both the treatment arms.

End points

Primary end points analyzed were changes in day/night time cough scales and throat irritation evaluated over a period of 3 days from baseline on verbal category descriptive (VCD) scale scores [Table 1].[2,16,17]

Secondary end points analyzed were time to relief from cough and throat irritation for all the first morning doses, duration of relief from symptoms for all first morning doses of Honitus and MCS, drowsiness, and Physician's Global Assessment of efficacy evaluated at visit 4 in both the treatment groups on VCD scales [Table 2]. Development of AEs was observed throughout the course of treatment.

Criteria for evaluation

Efficacy

Changes from baseline for each scale at visits 2, 3 and 4 and the number and proportion of participants showing improvement in each of the above scale at visits 3 and 4 were used to assess efficacy.

Safety

AEs were evaluated according to incidence, severity and relationship of AEs to treatment throughout the study.

Statistical methods

Analysis of covariance (ANCOVA) was used to compare the subjective measures of day and night frequencies of cough between the study treatment and reference comparator product at visits 2, 3 and 4. Statistical comparisons were made on (1) cough scoring during daytime, (2) cough scoring during night time and (3) throat irritation. A secondary analysis was also conducted for (1) time to relief of cough and throat irritation, (2) duration of relief from symptoms, (3) Drowsiness scale, and (4) Physician Global Assessment Scale. Within treatment, improvement from baseline was tested using the same model as described above at the 5% significance level. Ninety-five percentage (95%) confidence intervals were also constructed. Appropriate nonparametric methods were used in cases where normal distribution assumptions were not met for ANCOVA. Summary statistics were provided for measure of drowsiness, Physicians' Global Assessment of efficacy, and all other items by treatment groups at baseline and at visits 2, 3 and 4.

Table 1: Primary end points

End point	Scale for evaluation
Day-time cough scale: Changes in day frequencies of cough from baseline (cough scoring during >08:00 up to 22:00 h)	Evaluated on a 6-point scale as 5 = no cough during the day 4 = cough for one or two short periods 3 = cough for more than two short periods 2 = frequent coughing, which did not interfere with usual day-time activities 1 = frequent coughing, which interferes/ interrupts with usual day-time activities 0 = distressing coughs most of the day
Night-time cough scale Changes in night frequencies of cough from baseline (cough scoring during >22:00 up to 08:00 h)	Evaluated on a 6-point scale as 5 = no cough during the night 4 = cough on waking only 3 = waking once or early due to cough 2 = frequent waking due to cough activities 1 = frequent coughs most of the night 0 = distressing coughs preventing any sleep
Change in throat irritation	Evaluated on a 5-point scale as 4 = 76%-100% decrease 3 = 51%-75% decrease 2 = 26%-50% decrease 1 = 0%-25% decrease 0 = 0% decrease

Table 2: Secondary end points

Secondary end points	Scale for evaluation
Time to relief from cough and throat irritation for all first morning doses of Honitus and MCS	Evaluated on a 5-point scale as 4 = relief within 0-15 min 3 = relief within 16-30 min 2 = relief within 31-60 min 1 = relief >61 min 0 = no relief
Duration of relief from symptoms for all first morning doses of Honitus and MCS	Evaluated on a 5-point scale as 4 = relief up to 4 h 3 = up to 3 h 2 = up to 2 h 1 = up to 1 h 0 = no effect
Drowsiness scale: Drowsiness was measured from baseline to the end of study in both treatments	Evaluated on a 2-point scale as 1 = drowsy 2 = alert
Global Assessment Scale: physician's global assessment of efficacy evaluated at visit 4 in both the treatment groups	Evaluated on a 5-point scale as 4 = excellent 3 = Very good 2 = good 1 = fair 0 = poor

MCS: Marketed cough syrup

Results

Both Honitus and MCS showed improvement in symptoms related to acute nonproductive cough. Honitus was effective in reducing day- and night-time frequencies of cough in all the participants comparable to MCS [Tables 3 and 4]. Throat irritation was decreased significantly by Honitus ($P < 0.01$) at the end of study [Table 5] and the effect was statistically significant ($P < 0.004$) than MCS. Honitus showed improvement in time to relief from cough and throat irritation similar to that in MCS group. Significantly higher number of

Table 3: Changes in frequencies of cough during day

Cough scoring for day time	Cough scoring during day time Mean±SD (percentage improvement)							
	Visit 1		Visit 2		Visit 3		Visit 4	
	Honitus	MCS	Honitus	MCS	Honitus	MCS	Honitus	MCS
Distressing cough most of the day (0)	0	0	0	0	0	0	0	0
Frequent coughing, which interferes/ interrupts usual day-time activities (1)	5 (9.43)	6 (11.54)	0	23 (85)	0	2 (3.85)	1 (1.89)	0
Frequent coughing, which did not interfere with usual day-time activities (2)	48 (90.57)	46 (88.46)	26 (49.06)	23 (44.23)	3 (5.66)	5 (9.62)	0	2 (3.85)
Cough for more than two short periods (3)	0	0	27 (50.94)	24 (46.15)	46 (86.79)	39 (75.00)	20 (37.74)	20 (38.46)
Cough for one or two short periods (4)	0	0	0	3 (5.77)	47.55)	6 (11.54)	30 (56.60)	29 (55.77)
No cough during the day (5)	0	0	0	0	0	0	2 (3.77)	1 (1.92)
Mean±SD	1.91±0.30	1.88±0.32	2.51±0.50	2.54±0.67	3.02±0.37	2.94±0.61	3.6±0.66	3.56±0.61
Median	2	2	3	3	3	3	4	4

Since normality was satisfied, ANCOVA was fit, 95% CI for median and *P* values were calculated. MCS: Marketed cough syrup, ANCOVA: Analysis of covariance, SD: Standard deviation, CI: Confidence interval

Table 4: Changes in frequencies of cough at night

Cough scoring for night time	Cough scoring during night time							
	Visit 1		Visit 2		Visit 3		Visit 4	
	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)
Distressing cough preventing any sleep (0)	0	1 (1.92)	0	0	0	0	0	0
Frequent cough most of the night (1)	10 (18.87)	14 (26.92)	1 (1.89)	3 (5.77)	1 (1.89)	1 (1.92)	0	0
Frequent waking due to cough (2)	43 (81.13)	37 (71.15)	12 (22.64)	10 (19.23)	1 (1.89)	4 (7.69)	1 (1.89)	0
Waking once or early due to cough (3)	0	0	39 (73.58)	35 (67.31)	31 (58.49)	29 (55.77)	17 (32.08)	20 (38.46)
Cough on waking only (4)	0	0	1 (1.89)	2 (3.85)	19 (35.85)	16 (30.77)	18 (33.96)	24 (46.15)
No cough during the night (5)	0	0	0	2 (3.85)	1 (1.89)	2 (3.85)	17 (32.08)	8 (15.38)
Mean±SD	1.81±0.39	1.69±0.51	2.75±0.52	2.81±0.77	3.34±0.65	3.27±0.74	3.96±0.85	3.77±0.70
Median	2	2	3	3	3	3	4	4

Since normality was satisfied, ANCOVA was fit, 95% CI for median and *P* values were calculated. MCS: Marketed cough syrup, ANCOVA: Analysis of covariance, SD: Standard deviation, CI: Confidence interval

Table 5: Change in throat irritation changes in throat irritation

Throat irritation score (percentage decrease)	Visit 2		Visit 3		Visit 4	
	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)
0	0	0	0	0	0	1 (1.92)
0-25	1 (1.89)	0	0	0	0	0
26-50	45 (84.91)	4076.92)	17 (32.08)	17 (32.69)	1 (1.89)	2 (3.85)
51-75	7 (13.21)	10 (19.23)	32 (60.38)	31 (59.62)	32 (60.38)	42 (80.77)
76-100	0	2 (3.85)	4 (7.55)	4 (7.69)	20 (37.74)	7 (13.46)
P	–	0.2507#	–	1.0000#	–	0.0095#
Mean±SD	2.11±0.38	2.27±0.53	2.75±0.59	2.75±0.59	3.36±0.52	3.04±0.59
Median	2.00	2.00	3.00	3.00	3.00	3.00
95% CI for median	2.00-2.00	2.00-2.00	3.00-3.00	3.00-3.00	3.00-4.00	3.00-3.00
P	–	0.1507*	–	0.9552*	–	0.0035*

#*P* value was obtained using Fisher's exact *t*-test; **P* value was obtained using two-tailed, Wilcoxon Mann-Whitney U-test. MCS: Marketed cough syrup, SD: Standard deviation, CI: Confidence interval

participants ($P = 0.023$) in Honitus group got relief of >4 h duration from symptoms as compared to MCS [Table 6]. Honitus was better than MCS ($P < 0.03$) in producing relief from acute nonproductive cough without causing drowsiness [Table 7]. Overall, Honitus was found to be excellent in more participants than MCS in providing effective symptomatic relief from acute

nonproductive cough and throat irritation [Table 8]. Only one participant from MCS group had mild AE of abdominal pain which was not related to the study/study products.

Discussion

This study evaluated the safety and efficacy of Honitus, an Ayurvedic proprietary herbal cough syrup formula, in controlling acute nonproductive cough and its associated symptoms. A standard allopathic MCS intended for use in similar conditions was used as reference comparator. Response to treatment was evaluated on the basis of changes in the frequency of cough and throat irritation from baseline to the end of 3rd day treatment period in both the arms. Safety was assessed on the basis of development of AEs during the course

Table 6: Time to relief from cough and throat irritation score (verbal category descriptive score)

Time to relief from cough and throat irritation score	Visit 2		Visit 3		Visit 4	
	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)
No relief (0)	0	0	0	0	1 (1.89)	0
Relief >61 min (1)	0	0	0	0	0	0
Relief within 31-60 min (2)	39 (73.58)	36 (69.23)	18 (33.96)	22 (42.31)	5 (9.43)	3 (5.77)
Relief within 16-30 min (3)	14 (26.42)	16 (30.77)	34 (64.15)	30 (57.69)	40 (75.475)	45 (86.54)
Relief within 0-15 min (4)	0	0	1 (1.89)	0	7 (13.21)	4 (7.69)
P	-	0.6697†		0.4838†	-	0.4646†
Mean±SD	2.26±0.45	2.31±0.47	2.68±0.51	2.58±0.50	2.98±0.64	3.02±0.37
Median	2.00	2.00	3.00	3.00	3.00	3.00
95% CI for median	2.00-2.00	2.00-2.00	3.00-3.00	2.00-3.00	3.00-4.00	3.00-3.00
P		0.6260††		0.3274††		1.0000†††

†*P* value was obtained using Fisher's exact *t*-test, ††*P* value was obtained using two-tailed, Wilcoxon Mann-Whitney U-test. MCS: Marketed cough syrup, SD: Standard deviation, CI: Confidence interval

Table 7: Duration of relief of symptoms for all first morning doses

Duration of Relief of Symptoms for all first morning doses (VCD Scores)						
Duration of relief scores	Score	Visit 2		Visit 3		Visit 4	
		Honitus	MCS	Honitus	MCS	Honitus	MCS
No relief	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.89%)	0 (0.0%)
Up to 1 h	1	2 (3.77%)	0 (0.0%)	2 (3.77%)	0 (0.0%)	0 (0.0%)	00.0%)
Up to 2 h	2	42 (79.25%)	37 (71.15%)	18 (33.96%)	24 (46.15%)	1 (1.89%)	47.69%)
Up to 3 h	3	9 (16.98%)	15 (28.85%)	31 (58.49%)	28 (53.85%)	35 (66.04%)	42 (80.77%)
>/Up to 4 h	4	0 (0.0%)	0 (0.0%)	2 (3.77%)	0 (0.0%)	16 (30.19%)	6 (11.54%)
Mean		-	0.1525*	-	0.1484*	-	0.0229*
		2.13	2.29	2.62	2.54	3.23	3.04
±SD		±0.44	±0.46	±0.63	±0.50	±0.67	±0.44
Median		2.00	2.00	3.00	3.00	3.00	3.00
95% CI for Median		(2.00, 2.00)	(2.00, 2.00)	(2.00, 4.00)	(2.00, 4.00)	(3.00, 3.00)	(3.00, 3.00)
		-	0.0873**	-	0.3792**	-	0.0191**

**P* was obtained using Fishers exact *t*-test; ***P* was obtained using Wilcoxon Mann-Whitney U test

Table 8: Measure of drowsiness (verbal category descriptive scores)

Drowsiness score	Visit 2		Visit 3		Visit 4	
	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)	Honitus (%)	MCS (%)
Drowsy	9 (16.98)	15 (28.85)	8 (15.09)	13 (25.00)	1 (15.09)	17 (32.69)
Alert	44 (83.02)	37 (71.15)	45 (84.91)	39 (75.0)	45 (84.91)	35 (67.31)
P	-	0.1477*	-	0.2045*	-	0.0343*
Mean±SD	1.83±0.38	1.71±0.46	1.85±0.36	1.75±0.44	1.85±0.36	1.67±0.47
Median	2.00	2.00	2.00	2.00	2.00	2.00
95% CI for median	2.00-2.00	2.00-2.00	2.00-2.00	2.00-2.00	2.00-2.00	2.00-2.00
P	-	0.1509**	-	0.2084**	-	0.0355**

**P* value was obtained using Chi-square test, ***P* value was obtained using Wilcoxon Mann-Whitney U-test. SD: Standard deviation, CI: Confidence interval, MCS: Marketed cough syrup

of treatment.

A total of 105 individuals were recruited, of which 53 were randomized into Honitus group and 52 to MCS group. Across the study groups, males were more in number (73.58% and 76.92%, respectively) in both Honitus and MCS Groups. Mean age in both groups was approximately comparable (34 ± 14 for Honitus group and 33 ± 12 for MCS group). Body weight across the study groups was almost similar.

The study participants were males and females between 18 and 65 years of age with a history of acute nonproductive cough of any cause except for those listed in exclusion criteria and those with throat irritation for <1 week duration were included in the study. These patients presented with frequent coughing not interfering/interfering with usual daytime activities or distressing coughs most of the day. About 5% of adults self-reported an episode of acute cough each year and up to 90% of them had sought medical advice. Viruses appear to be the main causative factor for acute nonproductive cough in otherwise healthy adults.[18]

Changes in frequencies of cough in day time

Changes in day frequencies of cough were assessed on the basis of day time cough scale. Both Honitus and MCS showed improvement in symptoms related to nonproductive cough in all the enrolled participants. Across the study groups, most of the participants who were having frequent cough initially improved to cough for one or two short episodes only toward the end of study. A few participants also had no cough during day [Table 3]. Both mean and median cough scores during day were similar across the groups. Overall, Honitus was effective in reducing day-time symptoms of cough in participants with acute nonproductive cough and the effect was comparable to MCS.

Changes in frequencies of cough in night time

Changes in night frequencies of cough were assessed on the basis of night-time cough scale. Participants who were waking frequently due to cough initially showed improvement toward the end of study, with cough on waking only or no cough during night time in both the treatment arms. Though the effect of Honitus could be considered better because participants with no cough during night were more in number (32.08%) in Honitus group than in MCS group (15.38%), statistically, Honitus and MCS groups showed comparable improvement in reducing night-time frequencies of cough in all the participants of acute nonproductive cough [Table 4].

Change in throat irritation

Changes in throat irritation were evaluated on the basis of changes in throat irritation score. Overall, there was a decrease in throat irritation across the study groups from visit 2 onward to the end of study and most of the participants in both study groups showed about 75% decrease in throat irritation. In some patients, total relief from throat irritation was also seen. Throat irritation was decreased significantly by Honitus ($P < 0.01$) at the end of study [Table 5]. Statistically, Honitus showed significant improvement ($P < 0.004$) than MCS on throat irritation related to acute nonproductive cough.

Time to relief from cough and throat irritation

Relief from cough and throat irritation for all the first morning doses of Honitus and MCS was evaluated on the basis of VCD scores. Toward the end of the study, most of the participants showed up to 75% relief from cough and throat irritation within 30 min in both the groups. In Honitus group, a greater number of participants, though statistically not significant, also got relief from cough and throat irritation within 0–15 min than in MCS group. Overall, Honitus showed improvement in time to relief from cough and throat irritation similar to that in MCS group [Table 6 and Figure 1].

Duration of relief of symptoms

Maximum participants got relief from symptoms for up to 3 h at the end of study. Both mean and median cough scores of duration of relief were similar across the study groups at all visits. Significantly higher number of participants in Honitus group got relief of >4 h from symptoms than participants in MCS group. Statistically, Honitus showed better improvement in duration of relief to acute nonproductive cough in most of the participants than that in MCS group [Table 7 and Figure 2].

Measure of drowsiness

Drowsiness is one of the most annoying adverse effects of allopathic cough syrups. In the present study, maximum participants across the study groups showed improvement from drowsiness to alertness from visit 2 to visit 3. However, at visit 4, a significantly higher numbers of participants in Honitus group were feeling alert than those in MCS group. Statistically, Honitus was better than MCS in producing relief from acute nonproductive cough without causing drowsiness [Table 8].

Physician's Global assessment of efficacy

Physician's Global Assessment of efficacy was evaluated on Global assessment scale. Overall, Honitus was found to be excellent in more participants than MCS in providing effective symptomatic relief from acute nonproductive cough and throat irritation. However, almost an equal number of participants in both the groups also showed very good efficacy [Table 9].

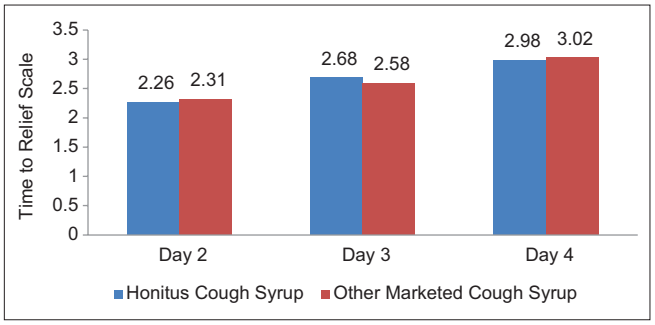

Figure 1: Mean time to relief of cough and throat irritation. Higher score reflects quicker relief (Time to relief scale: 4= Relief within 0 to 15 min; 3=Relief within 16 to 30 min; 2=Relief within 31 to 60 min; 1 = Relief >61 min; 0 = No relief)

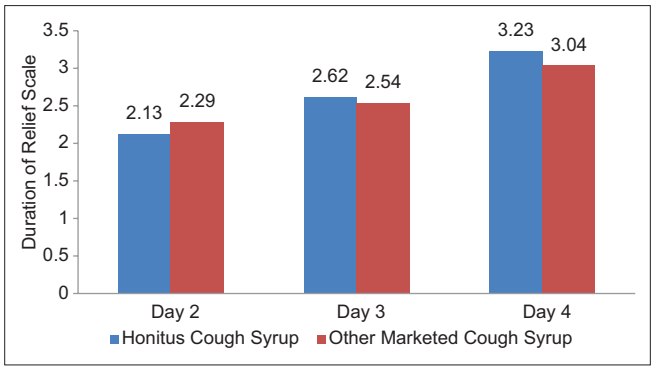

Figure 2: Mean duration of relief of cough and throat irritation. Higher score reflects quicker relief. (Duration of relief scale: 4=>/up to 4 h; 3 =up to 3 h; 2 = up to 2 h; 1 = Up to 1 h; 0 = no effect)

Table 9: Physician's global assessment of efficacy

Physician's global assessment	Honitus (%)	MCS (%)
Excellent (4)	8 (15.09)	1 (1.92)
Very good (3)	31 (58.49)	33 (63.46)
Good (2)	13 (24.53)	17 (32.69)
Fair (1)	0	1 (1.92)
Poor (0)	1 (1.89)	0
P	-	0.0536*

**P* value was obtained using Fisher's exact *t*-test. MCS: Marketed cough syrup

Safety evaluation

Safety evaluation was carried out in all the enrolled participants who received at least one dose of the study products. All the enrolled participants completed the study and were considered for safety evaluation. Only one participant from MCS group had mild AE of abdominal pain which was not related to the study/study products.

Honitus syrup comprises goodness of ayurvedic herbs such as *Tulsi* (*O. sanctum* Linn.),[5] *Mulethi* (*G. glabra* Linn),[6] *Banaphsa* (*V. odorata* Linn),[7] *Shunthi* (*Z. officinale* Roscoe),[8] *Vasaka* (*A. vasica* Nees)[9] and *Pippali* (*P. longum* Linn.),[10] which have been used traditionally for their benefits in respiratory health.

O. sanctum is useful in cough, dyspnea/asthma, and coryza.[19,20] Antitussive effects and immunomodulatory effects of *O. sanctum* have been reported.[5,21] *Z. officinale* is hot in potency. It is beneficial in cough/bronchitis, asthma/dyspnea, coryza and hoarseness of voice.[8,22] As per published literature, *Z. officinale* has been reported to exhibit antibacterial properties and exerts anti-inflammatory and relaxant effects on airway lumen.[8]

G. glabra is useful in management of cough, hoarseness of voice and phthisis. Anti-inflammatory and immunomodulatory effects of *G. glabra* have been reported in published literature.[23,24] As per published clinical studies, *G. glabra* gargling was found to reduce the incidence of postoperative sore throat and coughing.[24] *S. xanthocarpum* is reported to be anti-inflammatory and beneficial for throat. It is useful in treating cough, asthma/dyspnea, hoarseness of voice and rhinitis.[25]

As per published literature, *S. xanthocarpum* has been found effective in decreasing rhonchi, cough, breathlessness, and sputum associated with mild-to-moderate bronchial asthma and improving the peak expiratory flow rate indicating bronchodilatory and anti-inflammatory effects.[26] *P. longum* is considered to be a rejuvenator and beneficial in conditions such as cough, asthma/dyspnea and phthisis.[27] Beneficial effects of *P. longum* in respiratory conditions such as cough, bronchitis, and asthma have been reported.[28]

V. odorata is documented to be an expectorant and useful in coryza.[29] As per published clinical studies, *V. odorata* was found to alleviate cough in children with intermittent asthma.[7] *A. vasica* is found to be beneficial in respiratory conditions such as asthma/dyspnea, cough, phthisis, and hoarseness of voice.[30] Antitussive effects of *A. vasica* extract have been reported similar to codeine in mechanically and electrically induced coughing in rabbits and guinea-pigs on oral administration.[9] *H. spicatum* is documented to be beneficial in conditions such as asthma/dyspnea and cough.[30] *Mentha* sp. is considered to be mucolytic and analgesic.[31] Honey is attributed with mucolytic/expectorant properties and is useful in cough, asthma/dyspnea, and phthisis.[32] Honey acts as a *Yogavahi* or "a carrier of herbs," thereby potentiating absorption of various herbs.[33] As per a published clinical study, honey was rated favorably for symptomatic relief of nocturnal cough and sleep difficulty due to upper respiratory tract infection in children.[14] These therapeutic properties of contents of Honitus syrup appear to have contributed to its antitussive and throat irritation-relieving effects without causing drowsiness.

Conclusion

Honitus has been found to be significantly better than MCS reduction of drawsiness and comparatively better in throat irritation, the duration of relief from symptoms of cough and throat irritation and drowsiness.

Hontius was found to comparable to MCS in reducing day and night-time cough, the time to relief from cough and throat irritation, and Physician's Global Assessment of cough and throat irritation. Overall Honitus and MCS found to be safe during the study duration.

Results concluded that Honitus cough syrup is safe and effective in reducing symptoms related to acute nonproductive cough and throat irritation without causing drowsiness.

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Conflicts of interest

Some of the authors of the research article are currently employed with the sponsor, Dabur India Limited, which is also marketing this product.

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हिन्दी सारांश

तीव्र शुष्क कास और गले की ख़राश में नियंत्रण के लिए एक मानक कास सिरप तथा एक वानस्पतिक कासहर योग "हनिटस सिरप" का नैदानिक परीक्षण

अरुण गुप्ता, वैजयंती गायकवाड़, सत्येंद्र कुमार, रुचि श्रीवास्तव, जे. एल. एन. शास्त्री

तीव्र कास बहिरंग स्तर पर पाई जाने वाली एक आम बीमारी का प्रतिनिधित्व करता है । इसके प्रबंधन में एन्टीहिस्टामिन और डी-कंजेस्टंट्स एलोपैथिक उपचार बार बार प्रयोग करने पर अवांछनीय दुष्प्रभाव दर्शाते हैं जो सुरक्षित और कारगर विकल्प को खोजने की ओर प्रवृत कर रहे हैं। ""हनिटस सिरप" तीव्र शुष्क कास और गले के ख़राश में राहत के लिए शहद के लाभ से युक्त एक आयुर्वेदिक प्रोपाएटरी वानस्पतिक कासहर कल्प है। प्रस्तुत अध्ययन में उपरोक्त परिस्थितियों में उपयोग के लिए मानक विक्रय एलोपैथिक कास की सिरप की तुलना में तीव्र शुष्क कास और गले की ख़राश को कम करने में " हनिटस सिरप" की सुरक्षा और प्रभावकारिता की जांच का तुलनात्मक अध्ययन किया गया। कास और गले में खराश का दिन और रात में आवृत्तियों और प्रतिकूल प्रभाव में परिवर्तन के आधार पर मूल्यांकन किया गया। इस प्रकार यह परिणाम पाया गया कि हनिटस सिरप तीव्र शुष्क कास और गले में ख़राश और इन लक्षणों से राहत के लिए लगे समय पर तथा कास की दिन और रात की आवृत्तियों में परिवर्तन पर, विक्रय एलोपैथिक कास सिरप की तुलना में सुरक्षित और प्रभावी पाया गया और फिजीशियन ग्लोबल असेसमेंट ऑफ कफ में भी विक्रय एलोपैथिक सिरप तुलनात्मक पाया गया। अध्ययन हेतु औषधि के कोई अवांछित परिणाम नही पाये गए । इससे यह निष्कर्ष निकलता है कि हनिटस सिरप से कास और गले में ख़राश से राहत की अवधि पर और विपरीत प्रभावों के तुलनात्मक बेहतर परिणाम पाए गए।