



EVALUATION OF ANTITUSSIVE ACTIVITY OF VASU COUGH SYRUP IN SULPHUR DIOXIDE (SO₂) INDUCED COUGH MODEL IN MICE

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ABSTRACT

Cough is the most common symptom of respiratory diseases. When cough becomes serious, opioid drugs are effective, but they have side effects like sedation, delirium, constipation etc.. Therefore, there is a need to search out effective anti-tussive agents that are free from previously mentioned side effects. The present study was carried out to evaluate acute oral toxicity study and anti-tussive activity of Vasu Cough Syrup in sulphur dioxide (SO₂)-induced cough model in mice. Albino mice of either sex, weighing 25-30 g were divided into four groups (n = 6). Group I served as Disease control, Group II received standard drug i.e. Codeine phosphate (10 mg/kg), p.o., group III to IV were given Vasu Cough Syrup 0.25mL/kg and 0.5mL/kg body wt. p.o., dose. After 30 minutes, the mice were exposed to Sulphur dioxide for 30 sec. The mice were then placed in an observation chamber for counting of cough bouts for five minutes. Vasu Cough Syrup showed 63.91% and 70.64% inhibition in frequency of cough at 0.25mL/kg and 0.5mL/kg dose level respectively. It proves significant anti-tussive activity of Vasu Cough Syrup in Sulphur dioxide induced cough model. Thus, Vasu Cough Syrup can be useful as an alternative medicine for cough.

Keywords: Anti tussive activity, Vasu Cough Syrup, Sulphur dioxide, Codeine phosphate.

INTRODUCTION

A cough is a sudden and forceful expiration of air from the lungs caused by an involuntary contraction of the muscles controlling the process of breathing. It is a protective reflex that removes foreign material and secretions from the bronchi and bronchioles. The cough reflex consists of four phases: Inhalation, Compression of air against a closed glottis, Expression, Relaxation.¹ It can be inappropriately stimulated by inflammation of the respiratory tract or by neoplasia. In these cases, anti-tussive or cough suppressant drugs are used.² For uncontrolled cough, opioidergic central cough suppressants are used. Among opioids, codeine, pholcodeine, noscapine, dextromethorphan are effective, but they have certain inherent side effects like sedation, constipation, and also some addiction liability.³ Therefore, there is need to have effective anti-tussive drug which can successfully alleviate chronic cough without any contraindication & side effects.

Vasu Cough Syrup is one such Ayurvedic formulation containing herbal ingredients like Extract of *Glycyrrhiza glabra* (Yashtimadhu)^{1,4,5}, *Ocimum sanctum* (Tulsi)⁶, *Terminalia bellerica* (Bibhitaki)⁷, *Adhatoda vasica* (Vasa)^{1,8}, *Solanum xanthocarpum* (Kantakari)⁹, *Zingiber officinale* (Shunthi)¹⁰, *Curcuma longa* (Haridra)^{11,12}, Trikatu¹³. Literature search for each of these ingredients have showed promising anti-tussive activity but no scientific evidence was available for overall anti-tussive action of combination of such herbs. Hence, the present study was aimed to evaluate anti-tussive activity of Vasu Cough Syrup in sulphur dioxide (SO₂) induced cough model in mice along with acute oral toxicity.

MATERIALS AND METHODS

Drugs and chemicals

Solvents and chemicals required for the investigations are Vasu Cough Syrup, distilled water, codeine phosphate, sodium hydrogen sulfite (NaHSO₃), sulphuric acid (H₂SO₄).

All chemicals were of analytical grade. Vasu Cough Syrup was procured from Vasu Healthcare Pvt Ltd Vadodara, India.

Experimental animals

The experiments were performed on male albino mice weighing between 25–30 g. Mice were grouped and housed in polyacrylic cages (38x23x10 cm) with not more than six animals per cage and maintained under standard laboratory conditions with natural dark and light cycle. They were allowed free access to standard dry rodent diet (Golden Feeds, India) and tap water *ad libitum*. Food and water were withheld only during experimentation. After acclimatization, mice were randomly divided into four groups. Each group comprised of 6 animals. All experimental procedures described were reviewed and approved by the Institutional Animal Ethics Committee. All the experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC), Sigma Institute of Pharmacy (SIP/IAEC/02/2012-13). All the experiments and the care of the laboratory animals were according to current ethical guidelines by the Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA), Ministry of Environment and Forests, Government of India, New Delhi.

Acute oral toxicity study

The acute toxicity study was carried out as per the guidelines set by Organization for Economic Co-operation and Development (OECD), revised draft guidelines no. 423, received from Committee for the purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Govt. of India.¹⁴

Evaluation of anti-tussive activity of polyherbal formulation in Sulphur dioxide (SO₂) induced cough model in mice¹⁵

For evaluation of anti-tussive activity method of Miyagoshi et al., 1986 was modified and simplified to use. Briefly, a vial

containing 2 mL of 500mg/mL solution of sodium hydrogen sulfite (NaHSO₃) in double distilled water was placed at the base of a dessicator and covered with wire gauze to serve as a platform for placement of mice. To the NaHSO₃ solution, 0.2 mL of sulphuric acid (H₂SO₄), was added using a pipette. The reaction involved is as follows:



After 15 seconds, the mice were placed on the platform in the dessicator and exposed to SO₂ for 30 seconds. The mice were then removed from the dessicator and placed in an observation chamber for counting of bouts of cough for five minutes thereafter.

Scoring of bouts of cough

To avoid the observer bias, cough bouts were independently counted by two observers using digital counters and stopwatches. If for any reading the difference in count among

observers was more than 10%, the experiment was discarded. Readings are mean of these two observations.

Grouping & Drug treatment

All drugs were administered orally. The mice were divided into four groups of six animals each. Group-I served as Disease control and was not administered anything. Group-II received standard drug i.e. Codeine phosphate (10 mg/kg), p.o., Group-III to IV were given Vasu Cough Syrup 0.25mL/kg and 0.5mL/kg dose respectively. Each animal served as its own control and was exposed to Sulphur dioxide twice i.e. Before and 30 minutes after drug treatment. Grouping and drug treatment detail was tabulated in Table 1.

Statistical Analysis: The results are expressed as mean values \pm S.E.M. (standard error of mean). The significance was evaluated by one way ANOVA, followed by Tukey's multiple comparison test. The results were considered statistically significant when $P < 0.05$.

Table 1: Grouping & Drug treatment

Groups	Number of Animals	Treatment to be given
I	6	Disease control (only vehicle)
II	6	Codeine phosphate (10mg/kg, p.o)
III	6	Vasu Cough Syrup (0.25mL/kg, p.o)
IV	6	Vasu Cough Syrup (0.5mL/kg, p.o)

Table 2 Effect of Vasu Cough Syrup on the body weight of mice

Product	Dose	Mean body weight(g)		
		0 day	7 th day	14 th day
Vasu Cough Syrup	2000 mg/kg	27.98 \pm 0.73	28.28 \pm 0.36	28.86 \pm 0.72

Table 3: Percentage inhibition in frequency of cough

Experimental group	No. of Animals	Frequency of cough	% Inhibition in frequency of cough
Disease control	6	75.00 \pm 3.67	---
Codeine phosphate (10mg/kg)	6	15.83 \pm 0.60*	79.35%
Vasu Cough Syrup (0.25mL/kg)	6	27.66 \pm 1.17*	63.91%
Vasu Cough Syrup (0.5mL/kg)	6	22.50 \pm 0.88*	70.64%

All value represented as Mean \pm S.E.M, where n=6. *P<0.05 as compared with Disease control

RESULTS & DISCUSSION

Acute oral toxicity study of Vasu Cough Syrup

During the acute oral toxicity study, the animals did not show any signs of toxicity and mortality at 2000 mg/kg single dose administration of Vasu Cough Syrup. The body weight was not significantly increased or decreased (Table 2).

Evaluation of anti-tussive activity of Vasu Cough Syrup in Sulphur dioxide (SO₂) induced cough model in mice

In Disease controls, there was no significant change in the number of cough bouts, between the two exposures. The effect of the Vasu Cough Syrup on SO₂ gas induced cough in experimental animals showed significant cough suppressant effects at both the dose levels in comparison to disease control. Vasu Cough Syrup showed 63.91% and 70.64% inhibition in frequency of cough at 0.25mL/kg and 0.5mL/kg dose level respectively. The Codeine phosphate used as a standard drug for suppression of cough showed 79.35% inhibition in frequency of cough at a dose of 10 mg/kg. Vasu Cough Syrup at 0.5mL/kg dose level showed comparative effect like standard drug, Codeine phosphate (Table 3).

CONCLUSION

It can be concluded that the anti-tussive products exerted significant ($p < 0.05$) anti-tussive effect in experimentally induced cough reflex in mice comparable to the standard drug

codeine phosphate and it provides pharmacological evidence in support of Vasu Cough Syrup as anti-tussive agent. Based on available results, it can be conclude that Vasu Cough Syrup is a safe and effective Ayurvedic formulation having significant anti-tussive activity

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All Authors' contribution:

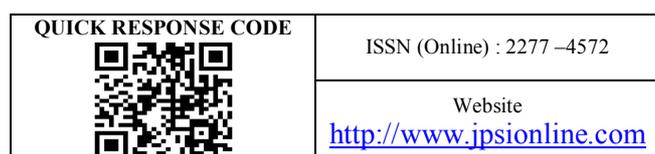
Soni Hardik ^{2*}, Patel Prateek ²: These authors are from Vasu Healthcare Pvt Ltd. The sample studied on was provided by Vasu Healthcare and the guidance for the study was also provided by the authors from Vasu Patel Hirenjal ¹, Upadhyay Umesh ¹, Upadhyay Siddhi ¹: These authors are from Sigma Institute of Pharmacy. Hirenjal carried out the study at Sigma under the guidance of her twoguides Upadhyay Umesh and Upadhyay Siddhi

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