

**Review article****Acute oral toxicity and anti tussive effect of kashloff syrup (poly herbal formulation) on so₂ induced cough model****Nilesh Patel¹, Janmejy Patel², Achal Patel³, Upendra U Zala^{4*}**

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ABSTRACT

The herbal drugs mentioned in classics for treatment of airway infections are better than modern drugs like anti-tussive, expectorants, mucolytic, as they have no any side effect. To evaluate acute oral toxicity on Swiss albino mice and anti tussive effect in So₂ induced cough model of kashloff Syrup (Anti-tussive poly-herbal formulation). The present study was conducted according to OECD guideline AOT-425 to know single dose toxicity of Kashloff Syrup on Swiss albino mice. IAEC No. for the study is SKPCPER/IAEC/2016-02/02. The study was conducted using 5 Swiss albino mice. The male and female animals were selected for study of 8 - 12 weeks old with weight range of within ± 20 % of mean body weight at the time of randomization. A limit dose of 2000 mg/kg of extract was used involving five mice. Each mouse was treated with a single oral dose of 2000 mg/kg of extract in sequence at 48 h intervals. There were no physical and behavioral changes observed in Swiss albino mice during 14 days. Body weight of all animals did not reveal any significant change as compared to vehicle control group. So No Observed Adverse Effect Level (NOAEL) of Kashloff Syrup is 2000 mg/kg. The significant decrease in cough bouts proves potential anti tussive activity of Kashloff Syrup.

INTRODUCTION

Medicinal herbs have always been used as traditional primary healthcare agents, especially in Asian countries. Over the last 20 years, rapid changes have been observed in the popular use of natural products from plant sources for maintenance of health and for alternative therapy, in Western countries [1]. The general public, patients and consumers are primarily interested in fast access to safe and efficient drugs, as well as in animal welfare. Based on their long-term use by humans one might expect plants used in traditional medicine to have low toxicity [2,3]. Therefore, it should be emphasized that the traditional use of any plant for medicinal purposes, by no means, guarantees the safety of such plant. This raises concern about the potential toxic effects resulting from the short-term and long-term use of such medicinal plants [4].

There is frequent and the rapid expulsion of the air from the lungs clear mucus and secretions from the lungs that known as a tussis. Cough is a comorbid sign of various pathological instances and hence it needs to be suppressed by the suppressing agent. Antitussive agents are commonly used to treat cough and it protects from dry and painful cough. Traditional treatment of cough is cost effective and free from unwanted effects too. Nowadays usage of herbal drug is increasing tremendously.

However, while voluminous pharmacological studies have been conducted to ascertain the subjective traditional uses of various medicinal plants, very few plants have been thoroughly evaluated for their detrimental effect. Reports of efficacy are, very far, more numerous than those on toxicity [5,6]. There is, therefore, a

need to further the investigation of herbal remedies and phytochemicals to incorporate the observations of short and long-term toxicity manifestations and to ensure effectual open communication of such findings.

The present study has been conducted to test the acute oral toxicity) on Swiss albino mice to develop the NOEL for the same and anti tussive effect in SO₂ induced cough model of Kashloff syrup (poly herbal formulation).

AIM AND OBJECTIVES

- To evaluate acute oral toxicity of Kashloff Syrup (Antitussive Poly-herbal formulation) on Swiss Albino Mice.
- To evaluate anti tussive effect of Kashloff Syrup (Anti-tussive Poly-herbal formulation) in SO₂ induced cough in Mice.

MATERIALS AND METHODS

Test Material

The test drug (Kashloff Syrup) was manufactured at Petlad Mahal Arogya Mandal Pharmacy, PO, Pipalata, Kheda, Gujarat, India. All the GMP standards were followed during manufacturing. The detail of Kashloff Syrup is mentioned below;

Table 1: Ingredients of Kashloff Syrup (Each 5 ml contains)

Name of ingredient	Quantity
Ext. Adhatoda vasica	100mg
Ext. Glycyrrhiza glabra	100mg
Ext. Terminalia belerica	100mg
Ext. Ocimum sanctum	75mg
Ext. Zingiber officinale	25mg
Hordeum vulgare	25mg
Mentha salvestris	3mg
Shuddha Tankan	25mg
Aqueous Base	Q.S.
Colour PONCEU 4 R	Q.S.

Method

The present study was performed after obtained permission from IAEC (SKPCPER/IAEC/2016-02/02) as per the CPCSEA, Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India.

(A) Acute oral toxicity

It was conducted according to OECD guideline AOT-425 to know single dose toxicity of test drug on Swiss albino mice. All the Animals were kept in proper cages with proper diet and acclimatized prior to dosing. They were divided in different groups. Each mouse was treated with a limit single oral dose of 2000 mg/kg of extract in sequence at 48 h intervals. The dosing detail is mentioned below.

Table 2: Individual animal dosing record

Expt. Day	Animal No.	Gender	Volume dose(ml)
1 st day	H	M	1
3 rd day	B	M	1
5 th day	T	M	1
7 th day	HT	F	1
9 th day	UM	F	1

Expt.: Experiment, *Conc.:* Concentration, *H:* Head, *B:* Body, *T:* Tail, *HT:* Head & Tail, *UM:* Unmarked, *M:* Male, *F:* Female

Observations

The animals were observed continuously for behavioural changes, autonomic profiles and other signs of toxicity or mortality up to a period of 14 days. The body weight, food intake and water intake were also observed on 1st, 7th and 14th day.

The acute toxicity profile of Kashloff Syrup (Anti-tussive Polyherbal formulation) is not available till date. This study can consider as a pioneer step for the establishment of safety profile

of Kashloff Syrup (Anti-tussive poly herbal formulation). It also reveals a safe use of this formulation as an effective Polyherbal cough syrup.

Table 3: Showing individual animal weekly body weight record, dose and mortality

Animal	Sex	Dose mg/kg	Experiment Day & Date Unit : gram			Mortality
			1 st	7 th	14 th	
H	M	2000	28	28	29	Nil
B	M	2000	29	30	30	Nil
T	M	2000	25	26	27	Nil
HT	F	2000	29	30	31	Nil
UM	F	2000	28	29	30	Nil

H: Head, *B:* Body, *T:* Tail, *HT:* Head & Tail, *UM:* Unmarked, *M:* Male, *F:* Female

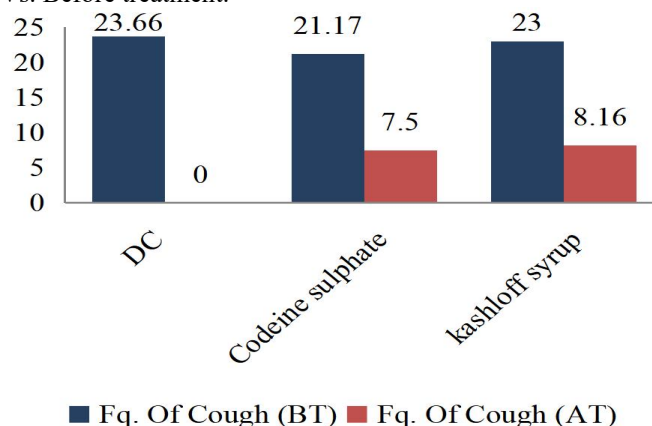
(B) Anti-tussive effect

Table 4: Effect of Kashloff syrup on frequency of cough bouts in SO₂ induced cough model in mice (Value of cough bouts are expressed as mean ± S.E.M. (n=6).

Group	Treatment & Dose (mg/kg)	Frequency of cough before treatment	Frequency of cough after treatment	% inhibition of cough
I	Disease control	23.66	-	-
II	Codeine sulphate (10 p.o)	21.17 ± 0.94	7.5 ± 0.67	64.55***
III	Kashloff syrup (360 p.o)	23.00 ± 1.5	8.16 ± 1.13	64.43***

*** $P < 0.001$ Vs Before treatment.

Figure 1: Value of cough bouts are expressed as mean ± S.E.M. (n=6). ### $P < 0.001$ Vs Normal Control, *** $P < 0.001$ Vs. Before treatment.



DISCUSSION

This formulation contains ingredients as mentioned in (Table01). *Adhatoda vasica* is used in cough, asthma, cold, bronchitis and tuberculosis⁷. *Glycyrrhiza glabra* used in cough and tuberculosis management⁸. *Terminalia bellerica* is rejeunative and cures cough disorder and beneficial for throat⁹. *Ocimum Sanctum* is the herb used for common cold, cough and have anti-inflammatory activity¹⁰.

Zingiber officinale is useful in respiratory tract infections¹¹. *Hordeum vulgare* is used in conditions like bronchitis and inflammations¹². *menthesal vestris* highly effective in treating headache, rhinitis, cough, sore throat, and colic, vomiting¹³. *Shuddha tankan* used in management of chest congestion, cough, bronchitis and wheezing¹⁴.

Oral route of drug administration is perhaps the most appealing route for the delivery of drugs. The syrup is advantageous dosage form among the various dosage forms administered orally because of having more flexibility in achieving the proper dosage of the medicines and helping in faster absorption.

The anti tussive activity of test drug was performed in Sulphur dioxide (SO₂) induced cough model. The test drug treated group shows significant decrease in cough bouts and greater % inhabitation of cough bouts (Table 4) which favors its potential anti tussive effect as compared to DC and Standard drug treated groups. Kashloff syrup showed positive effect to reduce cough, which might be due to reduction of the bronchial

irritation and also by suppressing the cough center in medulla.

CONCLUSION

This study reveals that Kashloff Syrup (Antitussive poly-herbal formulation) does not have any toxic effect at dose of 2000 mg/kg. So No-Observed-Adverse-Effect-Level (NOAEL) of Kashloff Syrup is 2000 mg/kg. The significant decrease in cough bouts proves potential anti tussive activity of Kashloff Syrup (Antitussive poly-herbal formulation).

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REFERENCES

1. Wills RB, Bone K, Morgan M, 2000. Herbal products: Active constituents, modes of action and quality control. *Nutrition Research Reviews*. 13(1), Pages 47-57. Doi: 10.1079/095442200108729007.
2. Ertekin V, Selimo glu MA, Altinkaynak S, 2005. A combination of unusual presentations of *Datura stramonium* intoxication in a child: rhabdomyolysis and fulminant hepatitis, *Journal of Emergency Medicine*. 28(2), Pages- 227–228. Doi: 10.1016/j.jemermed.2004.11.006.
3. S Koduru, Grierson DS, Afolayan AJ, 2006. Anti-microbial activity of *Solanum aculeastrum*. *Pharmaceutical Biology*. 44(4),

Pages – 283 – 286. Doi: 10.1080/13880200600714145.

4. Ukwuani AN, Abubakar MG, Hassan SW, et al, 2012. Toxicological studies of hydro Methanolic leaves extract of *Grewiacrenata*. International Journal of Pharmaceutical Science and Drug Research. 4, Pages-245–249.
5. Ekor M, 2014. The Growing Use of Herbal Medicines: Issues Relating to Adverse Reactions and Challenges in Monitoring Safety. *Frontiers in Pharmacology*. 4, Pages-177-184. Doi: 10.3389/fphar.2013.00177.
6. Chalut DS, 1999. Toxicological risks of herbal remedies. *Pediatric Child Health*, 4, Pages-536–538.