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ACUTE ORAL TOXICITY AND ANTI TUSSIVE EFFECT OF K SYRUP (POLY HERBAL FORMULATION) ON SO_2 INDUCED COUGH MODEL

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ABSTRACT

Introduction- The herbal drugs mentioned in classics for treatment of airway infections are better than modern drugs like anti-tussive, expectorants, mucolytics etc., as they have no side effect. **Aim:** To evaluate acute oral toxicity of K Syrup on Swiss Albino Mice and to evaluate anti tussive effect of K Syrup in SO_2 induced cough in Mice. **Method:** The present study was conducted according to OECD guideline AOT-425 to know single dose toxicity of K-Syrup. The IAEC no of study is SKPCPER/IAEC/2016-02/02. 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. Animals were observed individually at least once during the first 30 min after dosing, periodically during the first 24 h, and daily thereafter, for a total of 14 days for any clinical signs of toxicity or mortality. Body weight of all animals was recorded once in a week. The anti tussive effect was evaluated in SO_2 induced cough model in mice by method as describe by Miyagoshi et al., 1986 with modified and simplified. **Results:** 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. Mortality was not observed in any animal of a group. The test drug treated group shows significant decrease in cough bouts and greater % inhabitation of cough bouts which favors its potential anti tussive effect as compared to DC and Standard drug treated groups. **Conclusion:** This study reveals that K Syrup (Anti tussive polyherbal formulation) does not have any toxic effect at dose of 2000 mg/kg. So No-Observed-Adverse-Effect-Level (NOAEL) of K Syrup is 2000 mg/kg. The significant decrease in cough bouts proves potential anti tussive activity of K Syrup (Anti tussive polyherbal formulation).

KEYWORDS: Anti tussive, Acute oral toxicity, K Syrup, Mortality, NOEL.

INTRODUCTION

Pharmacological evaluation of medicinal plants has recently witnessed a growing interest amongst researchers worldwide. Research on the therapeutic potential of plants has surged over the years, with volumes of scientifically documented information showing considerable potential for medicinal plants to be used in the treatment of several diseases.[1] However, there is little information or evidence available concerning the possible toxicity that medicinal plants may cause to the consumers.[2] Acute oral toxicity refers to those adverse effects occurring following oral administration of a single dose of a substance, or multiple doses given within 24 hours.[3] 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. So, it should be emphasized that the 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 use of such medicinal plants. The data of the acute toxicity studies on medicinal plants or preparations derived from them should be obtained in order to increase the confidence in their safety to humans, particularly for use in the development of pharmaceuticals.[4],[5] Therefore, it is a need to further the investigation of herbal remedies to incorporate the observations of toxicity manifestations.

The present study has been conducted to test the acute oral toxicity of K syrup on swiss albino mice to develop its NOEL.

AIM AND OBJECTIVES

- To evaluate acute oral toxicity of K Syrup on Swiss Albino Mice.
- To evaluate anti tussive effect of K Syrup in SO_2 induced cough in Mice.

MATERIALS AND METHODS

Test Material: The test drug (K-Syrup) was manufactured at Petalad Mahal Arogya Mandal Pharmacy, At. po. Pipalata, Dist. Kheda, Gujarat, India. All the GMP standards were followed during manufacturing. The detail of K Syrup is mentioned below;

Table 1: Ingredients of K Syrup (Each 10 ml contains).

Sl. No.	Name of ingredient	Quantity
1	Ext. Solanum xanthocarpum	600mg
2	Ext. Terminalia belerica	125mg
3	Ext. Adhatoda vasica	60mg
4	Ext.Terminalia chebula	60mg
5	Ext. Glycyrrhiza glabra	40mg
6	Ext. Cleodendrum serratum	40mg
7	Ext. Trikatu	20mg
8	Ext. Chaturjat	30mg
9	Ext. Pistacia chinesis	10mg
10	Ext. Bambusa arundinacea	5mg
11	Yavakshara	5mg
12	Menthol	3mg
13	Camphor bhimseni	2mg

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 (MoFCC), 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)
1st day	H	M	1
3rd day	B	M	1
5th day	T	M	1
7th day	HT	F	1
9th 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.

Table 3: Showing individual animal weekly body weight record dose and Mortality.

Animal No.	Sex	Dose mg/kg	Experiment Day & Date, Unit : gm			Mortality
			1st	7th	14th	
H	M	2000	23	24	25	Nil
B	M	2000	24	25	26	Nil
T	M	2000	25	25	27	Nil
HT	F	2000	26	27	28	Nil
UM	F	2000	29	30	31	Nil

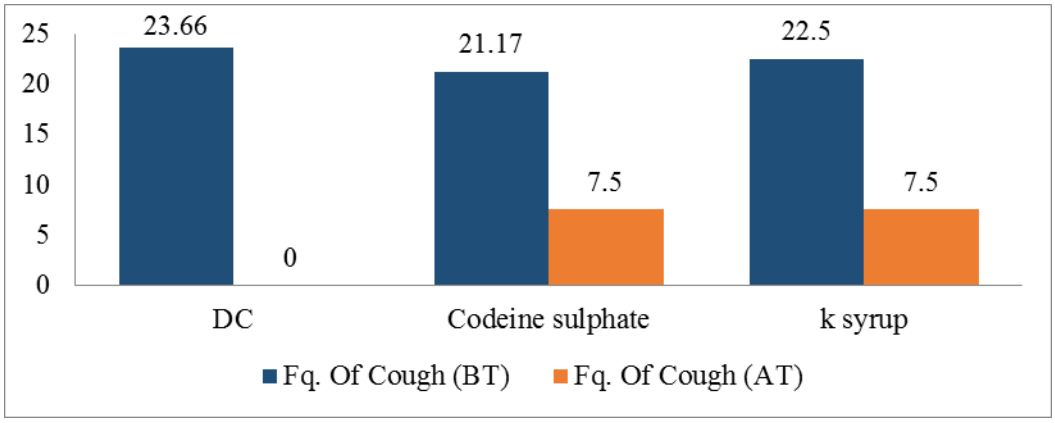
H: Head , B: Body , T: Tail , HT: Head & Tail, UM: Unmarked, M: Male , F: Female

(B) Anti-tussive effect

Table 4: Effect of K-syrup on frequency of cough bouts in SO_2 induced cough model in mice (Value of cough bouts are expressed as mean ± S.E.M. (n=6).

Group No.	Treatment & Dose (mg/kg)	Frequency of cough bouts before treatment mean ± SEM	Frequency of cough bouts after treatment mean ± SEM	% inhibition of cough bouts
I	Disease control	23.66	-	-
II	Codeine sulphate (10 p.o)	21.17 ± 0.94	7.5 ± 0.67	64.55***
III	K-syrup (775 p.o)	22.50 ± 0.99	7.5 ± 0.42	66.66***

***P<0.001 Vs Before treatment.



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

The acute toxicity profile of K Syrup is not available till date. This study can consider as a pioneer step for the establishment of safety profile of K-Syrup. It also reveals a safe use of this formulation as an effective polyherbal anti tussive.

The K-Syrup contains ingredients like, *Solanum xanthocarpum* is used in treatment for bronchial asthma and bronchitis and chronic cough.[6] *Terminalia belerica* cures cough disorder and beneficial for throat.[7] *Adhatoda vasica* is used in cough, asthma, cold, bronchitis and tuberculosis.[8] *Terminalia chebula* prevents cough and cold, acts as rejuvenator and boosts immunity.[9] *Glycyrrhiza glabra* used in cough and tuberculosis management.[10] *Cleodendrum serratum* is also called as *Kasaghni* hence used to cure common cold, cough, tuberculosis, rhinitis, asthma and chronic respiratory disorder.[11] *Trikatu* is used in running nose, allergic rhinitis and also relieves anorexia.[12] *Chaturjata* used for all *Kaphaj* disorders.[13] *Pistacia chinesis* is used for its analgesic, antitussive and sedative effect.[14] *Bambusa arundinacea* is used to cure cough, asthma and inflammations.[15] *Yavakshara* is used in management of cough, blotting and in throat obstruction.[16] Camphor bhimseni is used in cough syrup, tablets or throat drops as it is good for respiratory problems.[17]

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 screening of the toxicity of drug was essential to assure the safety and effectiveness of the drug. This study was done on Swiss Albino Mice of both the sex for 14 days to rule out any toxic effect of K Syrup at the dose of 2000 mg/kg. Individual animal weekly body weight was recorded and found to be increasing during the observation period. Animal daily observation was recorded and found to be same and the mortality rate was Nil. There were no physical and behavioral changes observed in animals during the observation period. This study reveals that K Syrup has no oral toxicity effect on Swiss albino mice. Hence, this can be used safely for therapeutic purposes.

The anti tussive activity of test drug was performed in Sulphur dioxide (SO_2) 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.

CONCLUSION

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

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