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EVALUATION OF ANTI- TUSSIVE ACTIVITY OF LEAVES OF *CAESALPINIA BONDUCELLA* F. IN EXPERIMENTALLY INDUCED COUGH IN MICE

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ABSTRACT

Cough is a natural reflex expulsive defense mechanism of the body, for clearing excess secretions, mucous, inhaled irritants, toxins or foreign substance in the respiratory tract. It is the most common symptom of respiratory disease. When cough becomes serious, opioids are effective, but they have side effects like sedation, constipation, some addiction liability and also compromise the respiratory function. Therefore, there is a need to have effective anti-tussive agent which do not have respiratory suppressant activity. The present study was carried out to evaluate anti-tussive activity of leaves of *Caesalpinia bonducella* in ammonium hydroxide induced cough model in mice.

INTRODUCTION: Coughing protects the respiratory system by clearing or cleaning it voluntarily or involuntarily. As long as cough is helpful in getting rid of infectious material with the help of mucous from the airway, it should not be stopped. Cough usually manifests in common cold, but it may be the initial manifestation of serious illness such as pulmonary hypertension, pneumonia, tuberculosis or asthma. It can be in various situations inappropriately stimulated; for example, by inflammation in the respiratory tract or neoplasia. In these cases, cough has a pathological character and it is necessary to use cough-suppressing agents. Anti-tussive agents are used mainly to suppress dry and painful coughs [1].

Hydration of respiratory tract by steam inhalation, demulscents, etc. are effective in reducing symptoms in majority of cases but, for uncontrolled cough, opioidergic central cough suppressants are used. Among opioids, codeine, pholcodeine, noscapine, dextromethorphan, etc. are effective, but they have certain inherent side effects like sedation, constipation, and also some addiction liability. Furthermore, their use in severe cough conditions like asthma is contraindicated, as they are known to further compromise the respiratory function. Therefore, there is need to have effective anti-tussive which can successfully alleviate chronic cough without side effects.

Cough suppressant and antiasthmatic activities have been claimed for many medicinal plants [2]**.** In traditional Chinese medicine, coughing and expectoration were tightly related with lung disease such as lung infections, heat and dryness. Some medicinal plants, which had the function of removing heat from the lungs or moistening the lung, were specialized as drugs for resolving phlegm, relieving cough and asthma. One such plant is *Caesalpinia bonducella* belonging to family *Caesalpiniaceae.*

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The juice of tender leaves is used in the treatment of bronchitis and cough [3]. On clinical application, the leaves are decocted with water for antitussive and anti-bronchitis activity. Since there is no scientific evidence to support the antitussive activity of *Caesalpinia bonducella* the objective of the present study was to ascertain the scientific basis for the use of this plant in the treatment of cough.

Caesalpinia bonducella is mainly found in Himalaya and also occurs wild throughout the plains of India and particularly along the seacoast throughout the hotter parts of India, Burma and Sri Lanka [4, 5].

The leaves contain pinitol (4.1%), glucose and minerals like calcium (2%) and phosphorous (0.3%). Brazillin and bonducin have been isolated from leaf 15, 60. A waxy material and an amorphous bitter principle ($C_{20}H_{32}O_8$, m. p. 119.12, yield 0.35%) have also been isolated from the leaves. The waxy material on saponification yields mysteric acid and an alcohol [3].

MATERIALS AND METHODS:

Collection and authentification of Plant Material: *Caesalpinia bonducela Linn* leaves were collected from botanical garden, Indore (M.P) and identified and authenticated at Department of Botany, Govt. Agriculture College, Indore. A voucher specimen has been kept in the herbarium of our department for future references**.**

Preparation of Extracts: The shade dried and powdered leaves were subjected to cold maceration using distilled water as the solvent. The aqueous extract obtained was filtered, concentrated on water bath, dried in vacuum and stored in refrigerator for subsequent experiments.

Experimental Animals: Swiss albino mice of either sex (20-30g) were used in the study. The animals were housed in polypropylene cages under standard conditions (12 h light; 12 h dark cycle; 25± 5^{o}C; 35-60% humidity). They were fed with standard pellet diet (Pranav Agro Ltd, Dehradun) and water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethical Committee of our institute. (IAEC/SCOPE/11-12/68)

Pharmacological Study:

Ammonium hydroxide induced Cough: Swiss albino mice were divided into four groups, each group containing six mice. The control group was treated with distilled water orally, and the positive control was treated with dextramethorphan. The remaining groups were treated with the aqueous extract at doses of 250 and 500 mg/Kg body weight respectively.

Anti-tussive activity was investigated on a classical mouse cough model induced by ammonia liquor. Each mouse was placed in a 300 ml special glass chamber and exposed to 40µl 25% NH_4OH. The cough frequency produced during 2 min exposure period was counted. The cough frequency and latent period of cough were also recorded. [6]

The percentage frequency of cough reflex was calculated by the formula

$$\% \text{ Frequency of Cough Reflex} = (1 - T / C) \times 100$$

Where T= Cough reflex in tested drug treated in mice; C= Cough reflex in control group treated mice.

RESULTS AND DISCUSION: All experimental data were expressed as mean ± SEM. Statistical analysis was carried out by using one way ANOVA followed by Dunnett's test.

TABLE 1: EFFECT OF AQUEOUS EXTRACT OF *CAESALPINIA BONDUCELLA* ON COUGH FREQUENCY IN AMMONIUM HYDROXIDE INDUCED COUGH MICE

S. No.	Treatment (n=6)	Dose	Cough Frequency (Minutes)				
			0	30	60	90	120
1	Control	-	105.25±1.80	97.00±1.43	95.30±1.3	86.75±1.40	85.75±1.57
2	Standard (dextramethorphane)	10mg/kg	102.00±0.80	52.77±0.40*	39.25±0.40*	25.00±0.70*	18.00±1.20*
3	*C. bonducella* (aq.)	250mg/kg	110.25±.2.50	60.75±.2.20	40.00±.76	28.25±1.53	20.75±1.17
4	*C. bonducella* (aq.)	500mg/kg	99.25±3.00	64.00±1.50	44.5±2.40	33.00±3.01	24.50±1.50

Values are mean ± SEM, n= No. of animals in each group. ** $p < 0.01$ Significance versus control

TABLE 2: EFFECT OF AQUEOUS EXTRACT OF *CAESALPINIA BONDUCELLA* ON % INHIBITION OF COUGH REFLEX IN AMMONIUM HYDROXIDE INDUCED COUGH MICE

S. No.	Treatment (n=6)	Dose	% Inhibition of Cough Reflex			
			30 Min.	60 Min.	90 Min.	120 Min
1	Standard(dextramethorphane)	**10ml/kg**	74.30	59.00	71.20	79.10
2	*C. bonducella* (aq.)	**250mg/kg**	38.20	58.10	58.10	75.90
3	*C. bonducella* (aq.)	**500mg/kg**	30.50	62.00	62.00	71.50

DISCUSSION: The aim of the present study was to investigate the anti-tussive activity of aqueous extract of leaves of *Caesalpinia bonducella* in experimental animal model.

Cough is a protective reflex for the expulsion of respiratory secretions or foreign particles from air passages and is a symptom of respiratory illness that prevents talking and cause chest and thorax pain. It occurs due to stimulation of mechano or chemo receptors in the throat, respiratory passages or stretch receptors in the lungs [7]**.** Coughing is a normal physiological response to an irritation of the laryngo-tracheo-bronchial system caused by mechanical or chemical stimulation. It may be painful and fatiguing and require suppression by antitussive drugs [8]**.**

Anti-tussive agents or cough suppressants are used mainly to suppress dry and painful cough. They act to reduce the urge to cough. The larynx and extrapulmonary airways are richly supplied with non myelinated C- fibres and rapidly adapting receptors having myelinated Aδ- fibres. These are involved in the cough mechanism [9]. Vagal afferent nerve provide inputs to brainstem nuclei, primarily the nucleus of the solitary tract (nTS) that receive inputs from airway cough evoking afferents and generate cough reflex in body [10].

Centrally acting antitussives such as codeine and dextromethorphan act within the central nervous system (CNS) at the level of the brain stem by depolarization or a dulling of the vagus nerve, the nerve leading from the brain stem and serving the chest area. Peripheral antitussive drugs act outside the CNS to inhibit cough by suppressing the responsiveness of one or more vagal sensory receptors that produce cough [10].

The *in vivo* antitussive activity of the aqueous extracts of leaves of *Caesalpinia bonducella* was investigated on a cough model induced by ammonium hydroxide in mice. In animals, coughing has been elicited by mechanical or chemical irritation and by electrical stimulation of tracheal mucosa or by nerve stimulation.

Ammonium hydroxide well-described inducers of bronchoconstriction in individuals and are chemically related and, therefore, may share a common mechanism of action.

Acute exposure of ammonium hydroxide causes dryness of nose and throat and a measureable increase in resistance to bronchial air flow.

Many medicinal plants like *Withania somnifera***,** *Trichodesma indicum***,** *Adhatoda vasica***,** *Glycyrrhiza glabra*, *Ocimum sanctum* etc. have shown significant antitussive activity.

In this study, aqueous extract of *Caesalpinia bonducella* orally administered at the dose levels of 250mg/kg b.w. and 500mg/kg b.w. showed maximum inhibition of cough by 75.9% and 71.5% respectively.

The standard anti-tussive drug dextromethorphan (10mg/kg b.w.) showed maximum inhibition of cough by 79.1%.

The results obtained support the traditional claims of the plant and provide a scientific approach towards their use in modern medicine.

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