Chapter-10

Anti-tussive Evaluation of *Eupatorium adenophorum* Spreng. Leaf extract against sulphur dioxide-induced cough in mice.

9.1 Introduction

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10.1. Introduction

Coughing is the body’s way of removing foreign material or mucous from the lungs and throat. The general classifications of cough are productive coughs (producing mucous from the lungs) and nonproductive coughs (dry and not producing any mucous).

Coughs are also divided into acute and chronic. Acute cough lasts for 3 weeks or less. The most frequent cause is the common cold but occasionally, acute cough can be due to a more serious illness such as pneumonia or congestive heart failure. Chronic cough lasts for 3 weeks or more. It is sometimes caused by more than one condition (most commonly in nonsmokers by postnasal drip syndrome (PNDS), asthma and is very frequent in tobacco smokers whose “smoker’s cough” can mask a second, more serious cause of cough.

Acute cough and chronic cough are symptoms of conditions that may require medical attention. Hundreds of conditions can cause cough and about a dozen conditions are the most frequent causes. In case of chronic cough, more than one cause may simultaneously be at work. A full medical examination and laboratory tests may be necessary to arrive at a correct diagnosis and effective treatment. Post Nasal Drip Syndrome is the most frequent cause of both acute and chronic cough. In addition to cough, complaints associated with PNDS are a) A feeling of something dripping into the throat, b) A need to constantly clear the throat, c) Nasal congestion or discharge, and d) hoarseness.

The person with PNDS usually suffers from allergic rhinitis or suffers from acute or chronic sinusitis. Treatment of cough due to PNDS is determined by the diagnosis, including diagnosis of underlying conditions such as sinusitis.

Asthma is a common cause of chronic cough in both children and adults. In some persons, chronic cough is the only symptoms of asthma. In other persons, symptoms in addition to cough include wheezing, shortness of breath and a feeling of tightness in the chest. Asthma is a serious medical condition that requires monitoring and treatment with carefully selected drugs. When cough is due to asthma, the cough usually goes away when the asthma is effectively treated.
Chronic Bronchitis is a frequent cause of chronic cough, especially in smokers. Tobacco smoke causes airway inflammation, excessive mucus secretion and impairment of normal clearance of mucus. Effective cough is important for the smoker, as it helps clear excessive mucus from the airways. Smoking cessation is the only fully effective treatment for chronic cough due to chronic bronchitis in a smoker. Because smokers often “expect to cough”, they may not seek medical attention for a cough that persist. Smokers should be aware, however, that cough is also an important symptom of lung cancer, which is primarily a disease of smokers.

There are medicines to stop coughing (antitussive) and others to help coughing more effectively (protussives). Angiotensin-converting enzyme (ACE) inhibitors are blood pressure-lowering drugs that cause chronic cough as a side effect in about 10% of persons who take the drugs. The cough is typically dry and hacking. Discontinuance of the drug causes the cough to improve or resolve within a month. Anti-tussive agent like codeine phosphate, which exerts action in CNS to elevate the threshold of coughing.

The local people of Sikkim use the juice of this plant for sinusities and in cough. To substantiate the claim, the present study was undertaken to evaluate its antitussive potential using the plant extract in an experimental animal model using sulphur dioxide gas as an agent to cough in mice (Miyagoshi et al., 2000).

10.2. Experimental

10.2.1. Plant material

The dried methanol extract of *Eupatorium adenophorum* leaves as explained in chapter-3 was used in this experiment. The extract was suspended in 2%\text{v/v} aqueous tween 80 solution for the present study. 2%\text{v/v} aqueous tween 80 solution was used as control vehicle.

10.2.2. Animals Used
Swiss albino mice of either sex weighing between 25-30g obtained from M/S B.N Ghosh & Co., Kolkata were used for this experiment. The animals were housed in standard metal cages and provided with food and water *ad libitum.*

**10.2.3. Antitussive evaluation** (Miyagoshi *et al.* 1986)

The antitussive effect was examined by the method described by the experimental model shown in Figure-11 where A is a 500ml 3-necked flask containing aqueous saturated sodium hydrogen sulfite solution. By opening the stopcock of a burette B, concentrated sulphuric acid was introduced to generate sulphur dioxide gas. Sulphur dioxide gas filled previously in A and C (the gas reservoir) and by opening cocks c and b, pressure in the gas reservoir C is elevated, which is recorded by the water manometer D. The chemical reaction occurring in flask A is

$$2\text{NaHSO}_3 + \text{H}_2\text{SO}_4 \rightleftharpoons 2\text{SO}_2 + \text{Na}_2\text{SO}_4 + 2\text{H}_2\text{O}$$

Then the stopcock b is closed and the stopcock d is opened slightly until pressure in D (11mm i.d.) reaches to 75 mm water, when the cock is closed. These procedures were operated in a draft. Each treatment was then orally administered to mice.

The animals were divided into four groups each containing 10 mice. The first group served as control group, which received 2 %v/v aqueous tween 80 solution (10ml/kg). The second group received codeine phosphate, a standard antitussive agent (10 mg /kg) whereas the third and fourth groups received methanol extract of *Eupatorium adenophorum* at doses of 200mg/kg and 400mg/kg p.o respectively. Initially the cough response of all the groups was observed by placing the animals in desiccator E. The cocks c, f and e were opened in order and when the pressure in D became 0 mm of H$_2$O, all the cocks were closed immediately. A certain amount of sulphur dioxide gas was introduced into the desiccator in this way. After a minute of introducing the gas, the mice were taken out of the desiccator and frequency of cough was observed for 3 min in an open-ended filter funnel with a stethoscope at the tip in which the mouse was confined. In the same fashion the frequency of cough was observed for the methanol extract (200 and 400mg/kg. p.o.) and Codeine phosphate (10mg/kg, p.o.) treated groups of animals, at 3h after administration.
10.3. Results

The effect exerted by the methanol extract of *Eupatorium adenophorum* leaves on sulphur dioxide induced cough on experimental basis, has been shown in Table: 26. The extract at the dose of 400mg/kg showed significant activity in inhibiting the cough when compared with that of 2% v/v aqueous tween 80 solution treated animals as control. Significant suppression of the cough was produced at 400mg/kg dose at the end of 3h. Codeine phosphate, also produced significant inhibition. The extract at 200 mg/kg (p.o.) and 400mg/kg gave a maximum inhibitions of cough 36% and 40% respectively at 3h after administration. Codeine phosphate gave 58.5% inhibition at the end of 3h after its administration. The extract showed significant inhibition of cough, like the standard drug (codeine phosphate).

Table 26 Effect of methanol extract of *Eupatorium adenophorum* Spreng. Leaves on the cough induced by sulphur dioxide gas in mice

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>Frequency of cough after 3h (Mean ± SEM)</th>
<th>Inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10ml/kg</td>
<td>70 ± 2.6</td>
<td>Nil</td>
</tr>
<tr>
<td>Codeine phosphate</td>
<td>10mg/kg</td>
<td>32 ± 2.1*</td>
<td>58.5</td>
</tr>
<tr>
<td>MEEAL</td>
<td>200mg/kg</td>
<td>46 ± 2.1*</td>
<td>36.0</td>
</tr>
<tr>
<td>MEEAL</td>
<td>400mg/kg</td>
<td>44 ± 1.9*</td>
<td>40.0</td>
</tr>
</tbody>
</table>

The frequency of cough was counted for 3 min. after SO$_2$ gas challenge; ( n=10). *P < 0.001 compared with control by student’s t-test; MEEAL ; Methanol Extract of *Eupatorium adenophorum* Leaves.

10.4. Discussion
So it can be concluded that this leaf extract has significant anti-cough effect in experimentally induced cough reflex in mice like the standard drug (codeine phosphate). Thus it could be assumed that the extract might be acting via the central nervous system. Further studies regarding the mechanism of action of the antitussive activity as well as the isolation and characterization of the active constituents are under way in our laboratory. The present activity supports the traditional use of this plant in asthma and severe bronchitis.

10.5. Publication