Antitussive effect of *Cuminum cyminum* Linn. in guinea pigs

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Abstract

Several therapeutic effects including the effect on asthma and dyspnoea have been described for the seeds of cumin, *Cuminum cyminum* Linn. In the present study the antitussive effect of this plant was evaluated. The antitussive effects of aerosols of two different concentrations of aqueous and macerated extracts, Codeine and saline were tested on guinea pigs by counting the number of coughs produced due to aerosol of citric acid 10 minutes after exposing animal to aerosols of different solutions (n=5 for each solution). The results showed significant reduction of cough number in the presence of both concentrations of aqueous and macerated extracts and Codeine (P<0.01 to P<0.001). The cough number observed in the presence of higher concentrations of aqueous and macerated extracts were not significantly different than those of lower concentrations. In addition, there was no significant difference between cough numbers observed in the presence of both concentrations of extracts with that of Codeine. These results indicated an antitussive effect of cumin which was comparable to that of Codeine.

Keywords: *Cuminum cyminum*, Cumin, Antitussive, Citric acid, Codeine.

IPC code; Int. cl.7 — A61K 35/78, A61P 11/14

Introduction

*Cuminum cyminum* Linn. (Family — Apiaceae) commonly known as cumin grows in Egypt, Saudi Arabia, Iran, Mediterranean areas and some other parts of the world. The plant bears white or pink flowers and small green seeds. The seeds contain cuminol, cymine, hellandren, carvone and cuminique alcohol1-3. Several therapeutic effects including therapeutic effect on gastrointestinal, gynaecological and respiratory (asthma and dyspnoea) disorders have been described for the seeds in Iranian ancient medical books4.

Different pharmacological activities have been reported for the extracts and essential oil from cumin plant including antimicrobial5 6, anti-diabetic7, lowering effect on hyperlipidemia8, anti-inflammatory9 and anti-carcinogenic10. In addition, there is evidence of the relaxant effects of the volatile oil from this plant on smooth muscle preparations11. With regard to the relaxant effect of the plant on smooth muscle and its anti-inflammatory property which could affect cough, in the present study the antitussive effects of different extracts from this plant were evaluated.

Materials and Methods

Plant and extract: The plant was identified by botanists in the herbarium of Ferdowsi University of Mashhad and the extracts were prepared as follows: for macerated extract, 50 g of the chopped, dried plant was macerated with 300 ml distilled water and shaken (on a shaker) for 48 hours; for aqueous extract same amount of the plant was extracted with 300 ml distilled water by soxhlet apparatus. The solvent of both extracts were then removed under reduced pressure and distilled water was added so that the plant ingredient concentration in the final extracts was 10% w/v in all extracts.

Protocols: Dunkin-Hartley guinea pigs of both sexes were used in the study (body wt 500-600g). The method followed was described earlier by other authors12.

Un-anaesthetized unrestrained animals were placed individually in a transparent perspex chamber, dimensions 30 × 20 × 20 cm and exposed to a nebulized aqueous solution of 0.1 g/ml citric acid for 7 minutes. The aerosol was produced by an air flow of 8 l/min through a Wright nebulizer. The aerosol particles had a mass median aerodynamic diameter...
of 0.9 µm as determined by laser light scattering (Malvern Instruments 2600 HSD analyzer, Malvern, U.K.). The output of nebulizer was 0.65±0.04 ml solution per minute. The same nebulizer was used throughout the experiment. During the last 5 minutes of the exposure, a trained observer continuously watched the animals and the number of coughs were determined. Coughs could easily be distinguished from sneeze, since there is a clear difference in sound as well as in behaviour of the animals.

The above protocol was performed 10 minutes after exposing animals to aerosols of various solutions for a period of 7 minutes (n=5 for each solution): normal saline (baseline measurements), Codeine solution (0.03 g/ml, positive control), macerated extract (2.5% w/v), macerated extract (5% w/v), aqueous extract (2.5% w/v) and aqueous extract (5% w/v).

All experiments were performed randomly with 2 hours resting period between each of the two experiments.

**Statistical analysis:** Data were expressed as mean ± SEM. Comparison of baseline data with number of coughs obtained in the presence of plant extracts and Codeine was made using ANOVA with Tukey-Kramer post hoc test. Comparison of data obtained in the presence of two different concentrations of aqueous and macerated extracts were made using paired “t” test. Significance was accepted at P<0.05.

### Results

Both concentrations of aqueous and macerated extracts and Codeine caused significant reduction in cough numbers compared to baseline value (P<0.01 to P<0.001), (Table 1, Fig. 1). However, the antitussive effects of both concentrations of aqueous and macerated extracts were not significantly different from that of Codeine (Table 1, Fig. 1).

### Table 1: Comparison of number of coughs observed in the presence of cumin plant extracts with those obtained in the presence of saline (baseline) and Codeine (for each experimental design, n=5)

<table>
<thead>
<tr>
<th>Experimental design</th>
<th>Number of coughs</th>
<th>St. Dif. vs Baseline</th>
<th>St. Dif. vs Codeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>12.0±0.71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aqueous extract 2.5 w/v</td>
<td>5.8±1.20</td>
<td>P&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td>Aqueous extract 5.0 w/v</td>
<td>5.6±1.72</td>
<td>P&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td>Macerated extract 2.5 w/v</td>
<td>3.2±0.97</td>
<td>P&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Macerated extract 5.0 w/v</td>
<td>3.0±1.14</td>
<td>P&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Codeine 0.03 g/ml</td>
<td>2.6±0.68</td>
<td>P&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean ± SEM; St. Dif. — statistical difference; NS — non-significant difference.

**Fig 1: Cough numbers observed in the presence of lower concentration (2.5 w/v; medium filled bars) and higher concentration (5.0 w/v; fine filled bars) of aqueous and macerated extracts from *C. cyminum* and those obtained in the presence of saline (baseline) and Codeine.**

**NS=Non-significant; cough numbers observed in the presence of low compared to high concentration of each extract**
Although, the antitussive effect of both the concentrations of aqueous extracts was lower than those of macerated extracts, the differences between the effects of two extracts (macerated and aqueous) were not statistically significant. In addition, the antitussive effects of higher concentration of aqueous and macerated extracts were not significantly different than those of lower concentrations.

Discussion

In the present study the antitussive effects of extracts from cumin plant were evaluated using a standard method used previously by several investigators. The result of the present study demonstrated a relatively potent antitussive effect for both extracts. However, the effect of the higher concentration of each extract was not significantly different with the lower concentration. The antitussive effects of both extracts were comparable with the effect of Codeine at concentration used.

Although the antitussive effects of different extracts were similar to that of Codeine, the mechanism(s) of antitussive effect of this plant cannot be concluded from the results of the present study.

In another study, we demonstrated a relative potent relaxant effect of aqueous and macerated extracts. Therefore, the bronchodilatory effect of extracts of this plant may be responsible for its antitussive property as stated by Karlsson et al.

Opioids, such as Morphine and Codeine, are generally considered to be the most potent and effective antitussive drugs available and are believed to inhibit coughs through suppression of a cough center in the central nervous system. Morphine was recently shown to reduce a vaguely mediated bronchoconstriction produced by inhaled distilled water in asthmatics. The bronchoconstriction to inhaled capsaicin was attenuated by nebulized Codeine and Morphine. A partial antagonism of a noncholinergic neurogenic bronchoconstriction in the guinea pig by opioid agonists has also been reported. Karlsson et al. also reported that nebulized Codeine and Morphine could inhibit bronchoconstriction and coughs induced by citric acid using a method similar to that of the present study. Therefore, the similar antitussive effect of cumin plant extracts and Codeine may indicate that the antitussive effect of this plant is due to its bronchodilatory property.

Advenier et al. observed that the tachykinin receptor antagonists also have antitussive effect. In addition one possible mechanism responsible for bronchodilatory effect of this plant is inhibition of stimulatory nonadrenergic noncholinergic nervous system (NANC). Therefore, the antitussive effect of cumin might be due to its possible tachykinin inhibitor substance(s) content mediating both bronchodilatory and antitussive effect. Thus, the antitussive effect of this plant may be due to its anti-inflammatory effect. However, the mechanism(s) of antitussive effect of cumin should be investigated in further studies.

Misawa and Kizawa also evaluated the antitussive effect of several volatile oils by inhalation and i.p. injection. The antitussive effect of volatile oils in their study was smaller than that of Codeine.

The higher antitussive effect of macerated extract compared to aqueous extract may suggest that the effective antitussive substance(s) of two extracts are different. This is due to variation in method of extraction of two different extracts. The non-significant difference in antitussive effect between two concentrations of extract may indicate that in lower concentration of extracts (2.5% w/v) the maximum effect is achieved.

In conclusion the results of the present study indicated antitussive effect of cumin plant which is comparable to that of Codeine at concentration used but the exact mechanism of this effect need to be investigated in further studies.

Acknowledgement

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