Anti-inflammatory Effects of Erynagium Caucasicum Trautv extract in Carrageenan Model of Inflammation in Rat

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Abstract

Background: Eryngium caucasicum, in the family of Umbelliferae (Apiaceae) 117 cultivated species excluding ornamentals have been recorded. Many pharmacological activities have been reported in Umbelliferae family. The aim of present study was to investigate anti-inflammatory activity of Eryngium caucasicum Trautv inflorescence.

Materials and Methods: 30 rats were put in 3 treatment groups and 2 observed groups, were injected 200,400,800, mg/kg dosage of erungium and as positive control group injected with celecoxib, 100 mg/kg and for negative control groups normal saline 0.9% was injected peritoneally. 1 hour after extract injection, carrageenan as an inflammation producing agent, was injected on subcutaneous of feet. The rate of inflammation producing 3 hours later were studied by measuring the change produced in the volume of foot using a plethysmometer apparatus and analyzed with ANOVA (p<0.001).

Results: The data showed that Eryngium caucasicum was good anti-inflammatory activity in 200 and 400 mg/kg dosages and that was dose-independent after 400 mg/kg.

Conclusion: According to this study we can introduce Eryngium caucasicum as potential anti-inflammatory medicinal herb which can be used in co-treatments of inflammatory episodes.

Keywords: Eryngium caucasicum, Inflammatory, Rat, Carrageenan

Introduction

Inflammations and pain is a problem which involve almost all of people in the world. Although in mild conditions there is not necessary for cure but in severe conditions it is needed for pharmacotherapy. As high consumption drugs are non-steroidal anti-inflammatory drugs, glucocorticoids and more severe drugs as tramadol and narcotics analgesics as morphine [1].

Among difficulties of these drugs, some adverse effect can be considered. So the interest for discovering the products with little or no adverse effect is favorite. Some natural products have these propensities [1,2]. Amblifera (Apiacea family) are at least 117 species which mainly known as herbal medicine (41%), vegetables and salad plants (23.1%), Seasoning and spices (19.7%), Forage plants (11.1%), Plants with essential and organic use (4.3%) [3]. By reviewing of published articles, mainly anti-inflammatory and analgesic effect of Eryngium species has been emphasized [4]. Eryngium species have been used also for some therapeutic aims as, sweetenering, diuretic, anti-inflammatory of bladder, anti-kidney stones, multiplier of sexual potency, expectorant and anti-helminthic [5,6].

There are few studies about this herb, Anti-oxidant activity of this plant has been reported in flowering season [7-11]. Moreover, the flowered branches and leaves of this plant have good anti-oxidant activity [12] which someone correlate this subject to phenol and flavonoids components in this herb [13].

As the studies for anti-inflammatory properties of this herb are limited and according to importance of this herb in traditional medicine [14,15]. This study has been aimed to assay anti-inflammatory properties of this plant comparing with COX-2 specific inhibitor, Celecoxib and also to determine the Saponin contents of the herb.

Material and Methods

This project was an experimental study which the samples have been assayed in control and treatment groups (receiving variant concentration of Eryngium extract. E.caucasicum

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Trautv has been accumulated around Kootena village as suburbs of Gaemshahr city, Iran. Plant air organs have been dried with air at dark and then cheeped to particles [16].

In this study, male Wistar rats weighing 190-230 gm were provided form lab animal center of Mazandaran University of Medical Sciences and kept at 25 ± 1 °C, with no limitation for food and water. All experiments have been done between 10 AM to 2 PM. Carrageenan, as inflammatory product was provided from Sigma Co (Germany). All procedures on animals were based on ethics protocols for lab animals of Mazandaran University of Medical Sciences with project and ethics code of:1415.

**Herbal Extraction**

400 gm of herbal powder has been used with 100 ml ethylacetate for extraction, the extraction has been done with percolator twice and the solvent has been blown out with rotary and dried under the laminar hood and finally, 12gm extract has been obtained [16].

**Saponin content assay**

For determining saponin contents of the herb we used Nya, et al. method [17], first we weighted 5gm of total dried herb and suspended in 50 cc of ethanol 20% in 55° C and transferred to decanter and extraction has been done for 90 minutes; this process has been repeated, then the mixture has been transferred through filter and decanted three times with di-ethyl ether and then di-ethyl ether removed and decanted again with butyl normal and saved and then decanted with sodium chloride 5% and butyl phase removed and dried under the hood in free air and total saponin determined with following equation:

\[
\% \text{Total saponin} = \left( \frac{\text{Weight of precipitate / Weight of dried herbal powder}}{100} \right)
\]

**Drug treatment**

Three different dose of 200, 400 and 600 mg/kg of the extract dissolved in DMSO 10% have been injected intraperitoneally to Rats in group’s pf 6 as maximum volume of 0.5 ml [18-22]. Carrageenan solution 1% in normal saline 0.9% has been injected to metatarsus of rat in 0.05 ml as inflammatory material 1hr after drug treatments and one group received carrageenan alone as positive control and normal saline 0.9% injected as negative control to 6 mice. Also Celecoxib (100 mg/kg) has been administered to one group as positive control of treatment.

**Anti-inflammatory test**

1 hr before and 3 hrs after carrageenan injection, the foot volumes of animal have been determined by Plethysmometer Apparatus (Ugo Basile,Italy) b/a ratio has been defined as anti-inflammatory index, [b=foot volume after injection, a=foot volume before injection] [18-20]. As standard scores, the ratio, equal or less than 1.5 was significant [21].

### Statistical Analysis

Statistical analysis has been done with SPSS 22 software with variance analysis (ANOVA) and subsequently by student Newman Keuls test, and P<0.05 was significant.

### Results

According to results of this project the saponin content of the extract has been determined by Nyam etal method as 5.4 which was almost high outcome. The results of Karaginan inflammatory test have been shown in table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>(a) Before Carrageenan injection Mean±std</th>
<th>(b) 3 hours after Carrageenan injection Mean±std</th>
<th>b/a ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Saline</td>
<td>1.41 ± 0.08</td>
<td>2.21 ± 0.09</td>
<td>1.51</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>1.2 ± 0.06</td>
<td>1.3 ± 0.12†</td>
<td>1.08**</td>
</tr>
<tr>
<td>Extract Dose: 200 mg/kg</td>
<td>1.37 ± 0.05</td>
<td>1.5 ± 0.21***</td>
<td>1.09***</td>
</tr>
<tr>
<td>Extract Dose: 400 mg/kg</td>
<td>1.33 ± 0.07</td>
<td>1.41 ± 0.15***</td>
<td>1.06***</td>
</tr>
<tr>
<td>Extract Dose: 800 mg/kg</td>
<td>1.39 ± 0.05</td>
<td>1.55 ± 0.09***</td>
<td>1.11***</td>
</tr>
</tbody>
</table>

The results of each group has been shown as mean ± std (a) The volume of two feet before Carrageenan injection, cm³ (b) The volume 3hrs after carrageenan injection metered by plethysometer. The ratio of b/a equals or lower than 1/5 considered as the inhibition is effective *** P<0.001

### Table 1: Anti-inflammatory activity of Erynagium Caucasicum Trautv extract on foot edema (volume estimated by Plethysmometer) before and after Carrageenan injection

![Figure 1: Comparison of the percent of inflammation reduction in different doses of Erynagium Caucasicum Trautv extract](image1.png)

![Figure 2: Comparison of the percent of inflammation reduction in different doses of Erynagium Caucasicum Trautv extract with normal saline](image2.png)
the differences between groups of extract with control was significant and also was comparable with celecoxib (p<0.001).

As it has been shown in Figure 3, the ratios of inflammation (foot volume, after and before carrageenan) in groups of celecoxib, extract 200,400 and 800mg/kg compared with normal saline were significant (P<0.001).

It should be noted that intraperitoneal injection of the extract has not shown any toxicity. As waited, anti-inflammatory effect of Erynagium Caucasicum Trautv extract till dose of 400 mg/kg was dose-dependent and at higher dose, the reducing current of inflammation has not been observed.

Discussion

Researches has shown that phenols and poly-phenols components are in fruits and vegetables in large quantities and have anti-oxidant properties [22,23]. Erynagium species, especially Erynagium Caucasicum contains poly-phenol components as Gallic acid, quercetin and saponin [23].

Anti-inflammatory effect of Gallic acid and quercetin has been reported in previous studies and it was known that anti-inflammatory effect of quercetin is due to inhibition of enzymes as lipoxygenase and inflammatory mediators [23,24].

Also quercetin can inhibit histamine release from neutrophil and mast-cells and then inhibit inflammation. In a study at Niger Date university on inhibitory effect of quercetin and its’ metabolite 3-O methyl quercetin, all levels of inflammatory markers have been diminished [24].

Carrageenan method is a very sensitive approach for evaluating of anti-inflammatory effects of new drugs [25].

For anti-inflammatory studies, the response has been assayed three hours after carrageenan injection.

After three hours, prostaglandins have been released and the ratio of volume feet after carrageenan to before be considered as an index of anti-inflammatory effect which can be used for comparing treatment groups with controls [25].

According to some studies, Eryngium Caucasicum contains a lot of phenol and flavonoids constituents as Gallic acid and quercetin [26,27] which can reduce releasing of delayed proinflmation mediators: (High mobility group B) (HMGB) in animals [24].

In a study by Morikawa, the effect of quercetin on inflammation in rat by Carrageenan has been assayed, in which quercetin could have decreased inflammatory mediators and edema and decreased liquid axillary fluids of rat’s dorsum field after carrageenan injection [28].

A result of recent research has been shown that Eryngium Caucasicum has anti-inflammatory effect at 200 and 400 mg/kg but in higher dose, this effect has been diminished. So it seems with increasing the dose more than 400mg/kg, the neurotoxicity effect might be increased and the anti-inflammatory effect of the herb would be decreased.

Also it can be predicted that anti-inflammatory effect of Eryngium Caucasicum might be due to high concentration of Phenol and flavonoids as quercetin.

Conclusion

According to the results of this research, Eryngium Caucasicum has anti-inflammatory effect which is comparable with celecoxib as COX2 inhibitor but with lower adverse effect than chemical drugs, so it can be suggested for some inflammatory diseases as rheumatoid arthritis.

Acknowledgment

This article is as result as a project by pharmacy student, Dr. Azami, candidate for Pharm D which appreciated all efforts of deputy of research, Mazandaran University of Medical Sciences, for all financial and other executives supports.

References


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