ANTIHYPERTENSIVE AND ANTIHYPERLIPIDEMIC EFFECTS OF ACHILLEA WILHELMSII

ASGARY S., NADERI G.H., SARRAFZADEGAN N., MOHAMMADIFARD N., MOSTAFAVII S., VAKILI R.

Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

Summary: Achillea wilhelmsii C. Koch (Asteraceae) is widely found in different parts of Iran. This plant is full of flavonoids and sesquiterpene lactones, which have been shown to be effective in lowering blood lipids and hypertension. We conducted a double-blind placebo controlled clinical trial to study the antihyperlipidemic and antihypertensive effects of Achillea drops. We randomly selected 120 men and women, aged 40-60 years, and divided them in two distinct groups of moderate hyperlipidemic and primary hypertensive subjects. They were treated either with hydroalcoholic extract or with placebo in the form of 15-20 drops twice daily for more than 6 months. Blood pressure and serum lipids (total cholesterol, triglyceride, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol) were measured in the groups for 3 periods of 2 months each. The mean and standard deviation of alternations in these variables between the group taking placebo and that taking drugs was calculated by Student’s t-test. The results showed a significant decrease in triglycerides after of 2 months while decreases in triglycerides, total cholesterol and LDL-cholesterol were significant after 4 months. Levels of HDL-cholesterol were significantly increased after 6 months’ treatment. A significant decrease was observed in diastolic and systolic blood pressure after 2 and 6 months, respectively (p <0.05).

Introduction

Achillea wilhelmsii C. Koch (Asteraceae) is a wild growing herb widely distributed in different parts of Iran, especially in the central and western areas (1-3). It has long been used in traditional Persian medicine as a tonic and carminative substance in the treatment of pulmonary conditions (4). The aerial parts of the plant, such as the leaves, flowers, twigs and fruit are used for therapeutic applications (5-7). Phytochemical studies reveal that this species is a rich source of flavonoids and sesquiterpene lactones, which have a remarkable effect on blood lipids (5-10). Some highly diverse substances were isolated from this plant including alkaloids, volatile oils, saponin, tannins, resin, sterols, alkanoids, and carbohydrates (8).

Flavonoids have proved to be strong, free radical scavengers that affect cellular phosphorylation and inhibit lipid peroxidation, both enzymatically and nonenzymatically (11-14). The antioxidant com-
pounds of flavonoids and sesquiterpene provoke changes in fats and proteins through their own different mechanisms (15-16). Sesquiterpene lactone compounds have been shown to have numerous biological activities due to their strong electrophilic system, such as analgesic, antiinflammatory and antihyperlipidemic properties (3, 5, 6). Also, plant alkaloids decrease arterial blood pressure and have antispasmodic, enteric and uterine contraction inhibitory and antifebrile properties (17-19). Regarding the mechanism of the above mentioned active factors, this genus may reduce cardiovascular disease and its associated risk factors such as hypertension, hyperlipidemia and atherosclerosis. In the present study we report the antihypertensive and antihyperlipidemic effects of A. wilhelmsii.

Materials and methods

Plant gathering. Plant material was supplied from a wild species growing in Chatrood village in the province of Kerman in southeast Iran, at an altitude of 1,840 m in June 1995. The plant was identified in the Botany Garden of Philipps Marburg University in Germany and in the Karaj Forestry and Pasturage Research Center in Iran.

Preparation of herbal drops. Air-dried powder from aerial parts of flowering A. wilhelmsii were extracted with the 48 h percolation method using 70% ethanol at a ratio of 1:8, respectively (1 g of dried herb to 8 ml of 70% ethanol) (20).

Preparation of placebo drops. Alcoholic placebo, free from the plant material, was used to support the biological activity of the herb species through a placebo controlled, double-blind clinical trial.

Physicochemical controls. Physicochemical control tests were performed on the extract indicating the percentage of flavonoids, pH, density, alcoholic degree, dry left-over, color, smell and taste, as shown in Table I (20-21). The flavonoid extracts were determined by absorbance at 425 nm as follows:

\[
\frac{625 \times \text{extract absorbance}}{A_{1}^{\%} \times 1 \text{ cm} \times \text{powder weight}}
\]

where \(A_{1}^{\%}\) = hyperoside absorbance at 500.

<table>
<thead>
<tr>
<th>Table I</th>
<th>Results of the chemical and physical specifications of the herbal drops</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of test</td>
<td>Results</td>
</tr>
<tr>
<td>The dry leftover</td>
<td>3.4 g/100 ml</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>100-110 mg/100 ml</td>
</tr>
<tr>
<td>Percentage of alcohol</td>
<td>52</td>
</tr>
<tr>
<td>pH</td>
<td>5.47</td>
</tr>
<tr>
<td>Density</td>
<td>0.8961</td>
</tr>
<tr>
<td>Color</td>
<td>Light green</td>
</tr>
<tr>
<td>Smell</td>
<td>Almost bright</td>
</tr>
<tr>
<td>Taste</td>
<td>Bitter</td>
</tr>
</tbody>
</table>

Selection of patients. This study was a double-blind placebo controlled clinical trial. Subjects were selected randomly, based on the record numbers of patients referred to the regional Isfahan Cardiovascular Research Center in Isfahan, Iran. The patients were 120 equally randomized men and women, aged 40-60 years. They were divided into two distinct groups, one group of 60 patients with mild hypertension (systolic blood pressure: 140-160 mmHg; diastolic blood pressure: 90-95 mmHg) and another group of 60 patients with moderate hyperlipidemia (total cholesterol: 200-300 mg/dl; triglyceride: 200-400 mg/dl). Those who were undergoing medical treatment or dietary therapy were excluded. Exclusion criteria included uncontrolled hypertension and uncontrolled, hereditary or secondary hyperlipidemia. Patients who had both risk factors (hypertension and hyperlipidemia), coronary artery disease or any other disorders were also excluded. Blood pressure was
Concerning the limitations of this study, it would have been better to investigate the effect of *Achillea* extract on patients with severe hypertension and hyperlipidemia. In addition, the time taken to lower blood pressure is fairly long. An effect could be achieved earlier by different extract processing, increasing the recommended dosage or by preparing other phytopharmaceutical forms of this plant extract. Also, there are several reasons for the above mentioned differences not being significant: the validity of our data is based on the belief that our patients used the herbal drop according to the instruction (self-reporting). A biomarker is needed to verify the results in our subjects. Choosing an appropriate sample size, adjusted to the different clinical characteristics of the patients, is another important consideration in achieving reliable results on *Achillea* medicine.

**References**

Antihypertensive and antihyperlipidemic effects of Achillea wilhelmsii

measured by the World Health Organization's standardized method using a random zero sphygmomanometer to determine mildly hypertensive subjects (22). For the hyperlipidemic group total cholesterol, triglycerides, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol were initially measured when patients were in a 14 h fasting state with enzymatic standardized method by an ELAN 2000 autoanalyzer. Blood lipids and blood pressure measurements were repeated for each patient after 2, 4 and 6 months of medication.

All patients were adjusted for age, body mass index and occupation and were divided into the drug or placebo groups in two separate antihyperlipidemic and antihypertensive studies. They were treated orally twice daily in a volume of 15-20 drops of the placebo or the plant extract for up to 6 months. Fifteen to twenty drops of the plant extract equal 1-1.1 mg flavonoids on the basis of hyperoside.

Statistical analysis. Data was entered by EPI6 software and statistically analyzed in SPSS/WIN. Student's t-test was used to compare alterations in lipid profiles and systolic blood pressure between the drug and placebo groups. To compare diastolic blood pressure, due to lack of normal distribution in the diastolic blood pressure data, the nonparametric test (Wilcoxon's) was used in the hypertensive groups. These comparisons were done after 2, 4 and 6 months of treatment.

Results

In the present study, some interesting results were obtained through a 6-month treatment with the Iranian species of *A. wilhelmsii*. Comparison of results indicates that in hypertensive patients, diastolic blood pressure showed a statistically significant decrease after 2 months' treatment and that this decrease continued until the end of the 6-month treatment period ($p = 0.003$). However, systolic blood pressure showed no significant alteration after 2, 4 or 6 months' treatment ($p = 0.005$).

In the hyperlipidemic group, a significant decrease in triglyceride levels was observed after 2 months' treatment in the group taking drugs ($p < 0.05$). When levels of LDL- and total cholesterol were assessed, the plant extract showed its possible effects through a significant drop in these levels after 4 months (Table II). However, HDL-cholesterol levels increased significantly only after 6 months' treatment ($p < 0.05$). These findings could be explained by the therapeutic improvements in lipid profiles after at least 2 months of drug administration. Moreover, an antihypertensive trend for the plant extract might be expected after 6 months of oral administration.

Except for the bitter taste of the extract, no adverse effects, such as constipation, hiccups, headaches, vomiting or nausea, were seen in the patients. In addition, the plant extract produced beneficial effects on alimentary discomforts.

Discussion

Several phytochemical studies have been performed on the therapeutic effects of the *Achillea* species, mainly for the major components of flavonoids and the sesquiterpene lactone (5-10). Al-Hindawi et al. (17) found that the plant has antihypertensive and antiinflammatory effects on rats, probably due to its alkaloids.

Antihypertensive and antihyperlipidemic medication are essential to diminish the high morbidity and mortality due to cardiovascular disease. Because of the body's adaptation to the chemical composition of plants and the low incidence of adverse effects associated with plant extract administration compared with the adverse effects and high expense of synthetic chemical medicine, the use of phytotherapy will probably increase.