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# Hypotensive effect of *Achillea wilhelmsii* aqueous-ethanolic extract in rabbit

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## Abstract

**Objective:** For many years in herbal medicine the antihypertensive and lowering blood lipid properties of *Achillea wilhelmsii (A. wilhelmsii)* have been suggested. In the present study the impacts of the plant extract on rabbit's blood pressure and heart rate have been investigated.
**Materials and Methods:** Twelve NWZ rabbits weighed 2-3 kg were randomly divided into two groups of 6 rabbits. The test group received *A. wilhelmsii* extract (20, 40 and 80 mg/kg) and the control group received normal saline by jugular vein cannula. Blood pressure and heart rate were measured via carotid cannula using pressure transducer connected to a power lab system.
**Results:** The blood pressure was significantly decreased (16.7± 1.4 mmHg) in 80 mg/kg dose of the extract ($p<0.05$). However, there were not any significant effects on heart rate in the other doses of the extract or normal saline.
**Conclusion:** the aqueous-ethanolic extract has blood pressure lowering property which may due to cardiac depressant and/or vasorelaxant effects.

**Keywords**: *Achillea wilhelmsii*, Heart rate, Blood pressure, Rabbit

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## Introduction

The prevalence of cardiovascular diseases is very high and increases dramatically worldwide. Hypertension is a very important risk factor for development of other cardiovascular diseases such as myocardial infarction and heart failure (Androulakis et al., 2009). These conditions are the most important causes of hospital admissions which are responsible for high mortality rates, disabilities and costs. Therefore, heart failure treatment particularly lowering blood pressure by pharmacological treatment is an essential step for preventing cardiovascular diseases. In the recent years, herbal medicine applications for the prophylaxis and treatment of cardiovascular diseases has been increased and scientists have been paying more attention to the cardiovascular effects of herbs (Ho and Jie, 2007).

*Achillea*, is one of the most important genera of the *compositae* family and comprises more than 120 species. Several pharmacological effects of *Achillea* such as anti-inflammatory (Benedek et al., 2007), antibacterial (Candan et al., 2003; Stojanovic et al., 2005), antitumor (Tozyo et al., 1994; Csupor-Löffler et al., 2009). Antispasmotic (Lemmens-Gruber et al., 2006; Yaeesh et al., 2006), choleretic (Benedek et al., 2006), antiulcer (Cavalcanti et al., 2006), antibacterial (Helicobacter pylori)( Mahady et al., 2005) and hepatoprotective ( Yaeesh et al., 2006) have been reported. Moreover, there are some reports on cardiovascular effects of *Achillea* such as changing of electrocardiogram and cardiac enzymes (Rahchamani et al., 2008) and negative inotropic and chronotropic effects on isolated heart (Niazmand and Saberi, 2010). *A. wilhelmsii* is the major species which grows in Iran (it is called "Boomadaran" in Iran) and widely used in Iranian traditional medicine. It has chemical components including alkaloids (achilleine), cineol, borneol, α and β pinen, luteolin, apigenin, lignans, camphor, caryophllene, thujene, rutin and carvacrol (Dokhani et al., 2005; Afsharypuor et al., 1996; Gherase et al., 2003; Javidian et al., 2004). Recently the antihypertensive and antihyperlipidemia effects of *A. wilhelmsii* were demonstrated in a clinical trial (Asgary et al., 2000). However, there is no comprehensive study to specify the pharmacological activities of *A. wilhelmsii* extract on cardiovascular system. Therefore, the present study was conducted to investigate the effects of aqueous-ethanol extract of *A. wilhelmsii* on heart rate and blood pressure in anesthetized rabbits.

## Materials and Methods

### Plant and extract

The aerial part of *A. wilhelmsii* was collected from Nishabour city (Khorasan Province, Iran) and was dried at room temperature. The plant was identified by the Ferdowsi University Herbarium (voucher No. 164-2218-2). Three hundred grams of aerial part of *A. wilhelmsii* were macerated with ethanol (50%) at 30°C for 24 hours and shaken intermittently. The solution was then filtered and dried in oven at 40°C. The average w/w yield was 13%. The dried extract was dissolved in the distilled water to make 20, 40 and 80 mg/kg concentrations.

### Animals and procedures

Twelve NWZ rabbits weighed (2-3 kg) were used. The animals were kept in standard conditions at 20 ± 2°C and fed with standard diet. The rabbits were randomly divided into two groups (n=6 in each group) as follows:

1- Control group which received normal saline with the same volume of the extract

2- Test group which received *A. wilhelmsii* extract (20, 40 and 80 mg/kg).

In control group, normal saline (37°C) with similar volumes of the extracts used to rule out the effects of blood volume changes on measured parameters. Animals were anaesthetised using

sodium thiopental (50 mg/kg, i.p) and then jugular vein and carotid artery were cannulated. The carotid cannula was filled with heparinized saline (50 IU/ml). *A. wilhelmsii* extracts were introduced through the jugular vein. Blood pressure and heart rate were measured by a pressure transducer (UFI 1050.1) which was connected to a power lab (ADInstruments, Australia) and the data were recorded by computer.

### Statistical analysis

The changes in blood pressure and heart rate before and after injections were analyzed by paired t-test. The results were represented as mean±SEM and the differences were considered significant if $p<0.05$.

## Results

In control group there was no significant difference in the normal saline injection for mean arterial blood pressure (MAP) and heart rate(HR); so injection of normal saline with the same volume of *A. wilhelmsii* extract did not affect measured parameters (Table 1).

Table 1. Effect of normal saline injection by the same volume of *Achillea wilhelmsii* extract on mean arterial pressure and heart rate. (n=6)

| Parameters | BINS | AINS | P-value |
|---|---|---|---|
| **MAP (mmHg)** | 77.75±5.9 | 78±6.1 | 0.79 |
| **HR (beat/min)** | 217±24.9 | 219±22.1 | 0.51 |

Before injection of normal saline (BINS).
After injection of normal saline (AINS).
MAP (mean arterial pressure), H.R (heart rate).

Treatment with *A. wilhelmsii* extract at 80 mg/kg significantly reduced MAP (96.9±4.6 *vs* 80.2±3.9 mmHg) (Figure.1). Moreover, in doses of 20 and 40 mg/kg of *A. wilhelmsii* extract, the MAP was decreased, but the changes didn't reach statistically significant level (Figure 1). The extract at 80 mg/kg significantly reduced systolic blood pressure (SBP) and diastolic blood pressure (DBP) compared to the control group (Figure 2). The *A. wilhelmsii* extract did not affect HR.

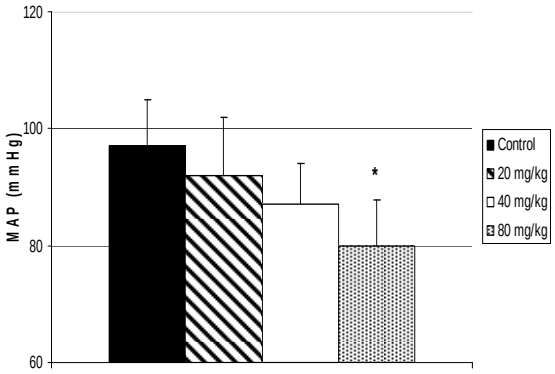


Figure 1. Effect of aqueous-ethanolic extract of *A. wilhelmsii* on mean arterial pressure (MAP) in rabbits. Only dose of 80mg/kg of extract significantly decreased MAP compared to the control group. (n =6, * $p<0.05$)

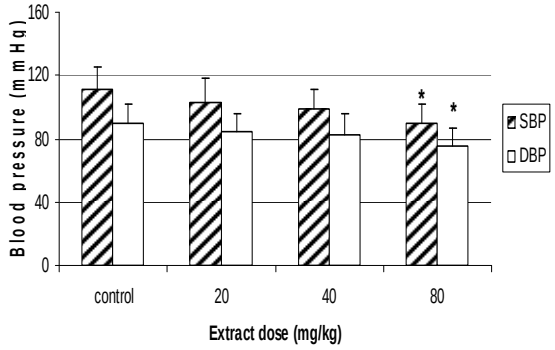


Figure 2. Effect of aqueous-ethanolic extract of *A. wilhelmsii* on Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP). The extract reduced SBP and DBP by 80 mg/kg dose significantly. (n=6, * $p<0.05$)

## Discussion

In the present study the impacts of *A. wilhelmsii* extracts on MAP and HR were investigated. In control group, injection of normal saline with the same volume of *A. wilhelmsii* extract did not affect the measured parameters, thus the results of

test groups could be attributed to *A. wilhelmsii* extract. This study demonstrated that *A. wilhelmsii* extract in 80 mg/kg was able to reduce MAP (17.5%) in normotensive conditions which may indicate a relaxation effect of the extract on vascular smooth muscles. The effect of *A. wilhelmsii* extract on SBP and DBP showed that 40% reduction in pulse pressure at 80 mg/kg dose which indicates reduction of arterial compliance due to arterial relaxation. Previous studies have demonstrated that *A. wilhelmsii* extract had antihypertensive effects (Asgary et al., 2000). Some other studies showed antispasmodic effects of other species of *Achillea* on ileum and duodenum smooth muscles (Lemmens-Gruber et al., 2006; Yaeesh et al., 2006; Babaei et al., 2007; Karamenderes and Apaydin, 2003). Moreover, *A. wilhelmsii* contains important ingredients such as carvacrol, luteolin, apigenin and 1,8-cineole which can influence vascular smooth muscle tone. In many studies the antispasmodic and vasorelaxant effects of carvacrol (Boskabady and Jandaghi, 2003; Baser, 2008; Peixoto-Neves et al., 2010), luteolin (Jiang et al., 2005; Qian et al., 2010), apigenin (Jin et al., 2009) and 1, 8-cineole (Lahlou et al., 2002; Nascimento et al., 2009) have been demonstrated. Luteolin has vasorelexant effect by inhibiting of sarcolemmal $Ca^{2+}$ channels, release from intracellular $Ca^{2+}$ stores and activation of $K^{+}$ channels (Peixoto-Neves et al., 2010).

Taken together, it seems that the *A. wilhelmsii* ingredients can induce hypotensive effects in rabbits. Blood pressure is not determined by vascular factors alone and cardiac interaction is also important for determining the final arterial blood pressure value. Previous studies on *Achillea* showed a negative cardiac inotropic and chronotropic effects (Niazmand and Saberi, 2010) and it is reasonable to suppose that reduction of MAP may partly due to this negative inotropic effect. However, to more clarify the exat mechanism of *A. wilhelmsii* extract effect on blood pressure further studies are needed. HR was not affected by the extract; however the pervious study on isolated heart showed negative chronotropic effect (Niazmand and Saberi, 2010). It may be due to difference of experiment protocols. Our study was performed in *in vivo* condition and the heart rate controlled by many factors which they are not present in *in vitro* condition.

## Conclusion

The results of the present study show that *A. wilhelmsii* extract has hypotensive effect in rabbit. It may be due to the vasorelaxant and/or cardiac depressant effect of the extract. These positive pharmacological properties should be investigated more to find the responsible ingredients and more reliable function of the herb on lowering blood pressure.

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