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HYPOTENSIVE AND CARDIOINHIBOTORY EFFECTS OF THE AQUEOUS AND ETHANOL EXTRACTS OF CELERY (APIUM GRAVEOLENS, APIACEAE)

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In this study, we present the effects of aqueous and ethanol extracts of celery (Apium graveolens, Apiaceae) investigated on the mean blood pressure of anaesthetized rabbits and contractility of isolated atria of the rats. In our experiments, the rabbits and Wistar albino rats were used. The effects of extracts (0.5-15 mg/kg) on blood pressure were recorded directly from the carotid artery. Isolated rat atria were mounted in 10 ml tissue bath. An equilibrium period of 30 min was given before the application of the extracts (0.02-0.75mg/ml). In anesthetized rabbit, intravenous administration of aqueous extracts induced least hypotensive effects (14.35±2.94%), while the ethanol extract caused the greatest fall in the blood pressure (45.79±10.86%). Hypotensive effects of the extracts were partially blocked by atropine (0.3 mg/kg), an unselective muscarinic receptor antagonist. In isolated rat atria, both aqueous and ethanol extracts of celery exhibit a negative chronotropic and inotropic actions. Aqueous extract decreased the rate of contractions by 12.88±2.74% and amplitude by 8.73±0.89%. Ethanol extract inhibited the rate of atria contractions by 34.26±5.69% and amplitude by 25.40±3.61%. Pretreatment rat atria with atropine (1 μM) partially blocked inhibitory response of aqueous and ethanol extracts. Ethanol extract of celery significantly exhibited greater hypotensive and cardio-depressant activities compared to aqueous extract ($p<0.05$). These data suggest that both aqueous and ethanol extracts of celery caused the hypotensive, negative inotropic and chronotropic effects, which could partially be mediated via stimulation of muscarinic receptors. Inhibitory effect of ethanol extract was significant compared to aqueous extract of celery. *Acta Medica Medianae 2010;49(1):13-16.*

***Key words**: celery, extract, blood pressure, isolated atria*

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Introduction

Celery, Apium graveolens L. is a plant from the family of Apiaceae that has been used as food and as medicine. A review of the literature indicates that celery has been cultivated for the last 3.000 years (1). Apium graveolens has been used in traditional medicine primarily as a diuretic, and to treat bronchitis, asthma, liver and spleen diseases (2). Extracts of the celery seed have been shown to inhibit arthritic pain (3). Also, it is known that celery in combination with other plants can help lower blood pressure (4).

A. graveolens has been extensively studied for its biological activities. Aqueous extract of celery caused significant reduction in serum total cholesterol level in hypercholesterolemic rats (5). Nitrogenous compounds from essential oil of celery seed have been reported to have effect on the central nervous system (6). A. graveolens posses antiinflamatory effect (7), and celery juice showed protective effect when applied with doxorubicine (8).

Aims

So far, no study related to the influence of celery on the cardiovascular system has been reported. In this study, we present the effects of aqueous and ethanol extracts of celery investigated on the mean blood pressure of anaesthetized rabbits and contractility of isolated atria of the rats.

Material and methods

Dried and pulverized aerial parts of the celery were extracted in ultrasonic bath with distilled water and 96% ethanol (10 minutes). After the separation of solvents, the extracts were concentrated in a rotary evaporator at reduced pressure (40°C) till a constant weight was achieved. The obtained dry residue was dissolved in the distilled water and ethanol solution.

In this study, rabbits (around 1 kg) and Wistar albino rats (200-250 g) bred in the Animal Research Center of Medical Faculty, University of Niš, Serbia were used. The animals were housed

in stainless steel cages under standard laboratory conditions. These animals were maintained at 20-24°C with a 12 h light-dark cycle at least 1 week before the experiment. All animals had free access to food and water. All experimental procedures with animals were in compliance with the European Council Directive from November 24, 1986 (86/609/EEC).

The rabbits were anesthetized intravenously with urethane (750 mg/kg). The animals were implanted with carotid arterial catheter for blood pressure recording. The arterial catheter was connected to the blood pressure transducer (P-1000-A) coupled with a Narcophysiograph (NARCO Bio system, Houston, USA) for measurement arterial pressure. The recording speed was set at 10 mm/s. The parameters of blood pressure were recorded in mmHg as systolic pressure (SP) and diastolic pressure (DP), and were expressed as mean arterial pressure (MBP).

After a period of equilibrium (30 min), animals were injected with 0.2 ml saline intravenously or with the same volume of plant extracts. The extracts were administrated in a rising concentrations (0.5-15 mg/kg) at intervals of 15-20 min. Arterial pressure was allowed to return to the resting level between injections. The blood pressure was recorded before and after the administration of plant extracts.

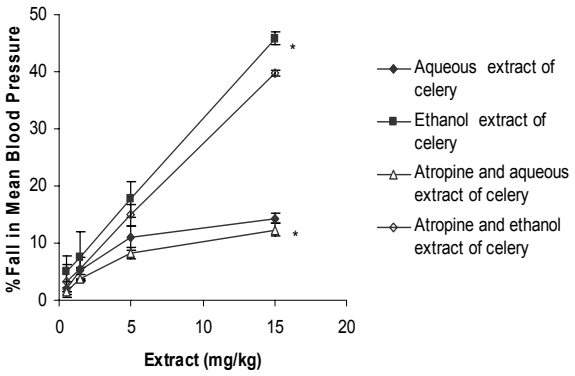
Rat atria were dissected, and cleaned off the fatty tissue. The spontaneously beating atria were suspended in 10 ml tissue baths, containing Tyrode solution for isolated atria, maintained at 32oC and continuously aerated with carbogen gas. After equilibrium period of 30 min, the extract of celery (0.02-0.75mg/ml) was added cumulatively. The changes in tension were recorded using system TSZ-04-E; Spell Iso (Experimetria Ltd).

Statistical analysis

Data were analyzed statistically. The results were expressed as mean ± standard deviation of six determinations. Statistical evaluation was performed using the Student`s t-test. The probability value of $p<0.05$ was considered significant.

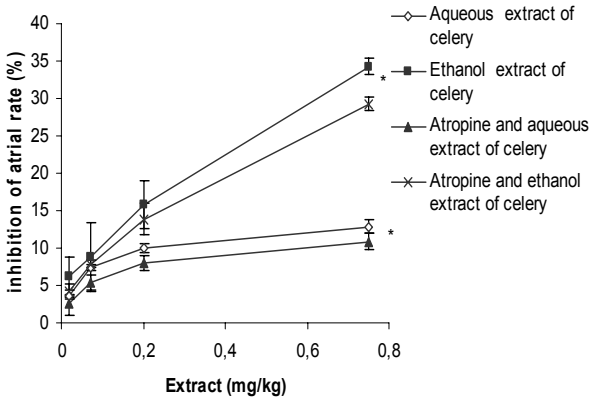
Results

Intravenous administration of the aqueous and ethanol extracts of A. graveolens (0.5-15 mg/kg) immediately caused a fall in systolic, diastolic and mean arterial blood pressure in anaesthetized rabbits. The aqueous extracts of A. graveolens at doses of 15 mg/kg induced a dose-dependent hypotensive effect hypotensive effects (14.35±2.94%) (Graph 1). The ethanol extract of celery at doses of 15 mg/kg caused the greatest fall in the blood pressure (45.79±10.86%). After the hypotensive peak, blood pressure increased progressively and reached the basal value in about 3-4 min. Hypotensive effects of the extracts were significantly blocked by atropine (0.3 mg/kg), an unselective muscarinic receptor antagonist ($p<0.05$).



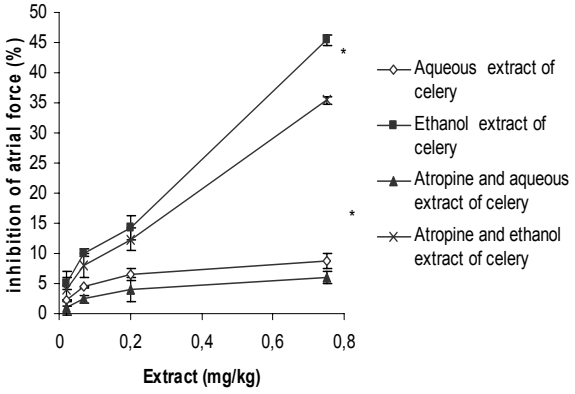
p<0.05 (vs control)

Graph 1. Hypotensive effect of the aqueous and ethanol extract of celery (Apium graveolens) without or with atropine in anaesthetized rabbits



p<0.05 (vs control)

Graph 2. Effect of the aqueous and ethanol extracts of celery (Apium graveolens) without or with atropine on the rate of rat atrial contraction



p<0.05 (vs control)

Graph 3. Effect of the aqueous and ethanol extract of celery (Apium graveolens) without or with atropine on the force of rat atrial contraction

The administration of the aqueous and ethanol extracts of A. graveolens (0.02-0.75mg/ml) to the spontaneously beating atria, caused negative inotropic and chronotropic effects (Graph 2 and Graph 3). Aqueous extract at the concentration of

0.75mg/ml decreased the rate of isolated rat atria contractions by 12.88±2.74% and amplitude by 8.73±0.89%. Ethanolic plant extract at the concentration of 0.75mg/ml inhibited the rate of atria contractions by 34.26±5.69% and amplitude by 25.40±3.61%. Pretreatment atria rat with atropine (1μM) significantly blocked inhibitory response of aqueous and ethanol extracts. Ethanol extract of A. graveolens significantly exhibited greater hypotensive and cardio-depressant activities compared to aqueous extract. ($p<0.05$).

Discussion

In this paper, we studied the hypotensive and cardioinhibitory effects of the aqueous and ethanol extract of A. graveolens. The study has shown that the intravenous injection of the aqueous or ethanol extract of A. Graveolens causes a dose-dependent decrease of the mean blood pressure of anaesthetized rabbits. The hypotensive effect was short-term and the blood pressure reached the basal value in about 3-4 min. At higher doses, the duration of hypotensive responses to A. graveolens extracts was long-lasting. The results are in line with our previous studies showing that the extract of Mistletoe induced hypotension in rats (9).

Blood pressure is a product of cardiac output and vascular resistance (10). Hence, we evaluated the effect of the A. graveolens extract in isolated rat atria. The results demonstrated that the plant extract induced a negative inotropic and chronotropic effect on the spontaneously contracting cardiac tissues of atria. Hypotensive effect of the extract was due to inhibitory effect on the rate and force of atrial contractions. Similar results were also obtained for the aqueous and ethanol extracts of Peroselinum crispum (11).

In order to evaluate the mechanism of hypotensive effect of A. graveolens extracts, we performed experiments in the presence of atropine, non-selective muscarinic antagonists. In these conditions, both hypotensive and bradycardic responses were partially inhibited. A partial blockade with atropine indicated the presence of cholinergic components in hypotensive and cardio-inhibitory activity of A. graveolens.

Phytochemical analysis of the A. graveolens demonstrated the presence of flavonoids apigenin, luteolin and quercentin (12-15). The compound of celery apigenin have been studied for their effect on blood vessels, where were found to produce vasodilatatory effect (16-18). Flavonoids from other plants may exhibit hypotensive, cariodepressant and vasodilatatory activities. In an experiment in isolated rat vascular smooth muscle, Duarte et al. (19) found that the contractile responses induced by high KCl and Ca2+ were inhibited by quercetin in a concentration-dependent manner. The presence of such compounds in A. graveolens might possibly contribute to hypotensive, negative inotropic and chronotropic effects of the celery extracts.

Conclusion

These data suggest that the aqueous and ethanol extracts of celery, Apium graveolens L., caused the hypotensive, negative inotropic and chronotropic effects, which could partially be mediated possibly via stimulation of muscarinic receptors. Inhibitory effect of ethanol extract was significant compared to aqueous extract of A. graveolens.

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HIPOTENZIVNI I KARDIOINHIBITORNI EFEKTI VODENOG I ETANOLNOG EKSTRAKTA CELERA (APIUM GRAVEOLENS)

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Ispitivani su efekti vodenog i etanolnog ekstrakta celera (Apium graveolens L., Apiaceae) na srednjem arterijskom krvnom pritisku anesteziranih kunića i kontraktilnosti izolovanih pretkomora pacova.

U studiji su korišćeni kunići i Wistar pacovi. Efekti ekstrakata A. graveolens (0.5-15 mg/kg) na arterijskom krvnom pritisku registrovani su direktnom metodom u karotidnoj arteriji. Izolovane pretkomore pacova postavljane su u kupatilo za izolovane organe. Adaptacija preparata je iznosila 30 min, nakon čega su primenjivani ekstrakti A. graveolens (0.02-0.75 mg/ml).

Kod anesteziranih kunića, intravenozna primena vodenog ekstrakta A. graveolens u dozi 15 mg/kg uzrokovala je manje hipotenzivne efekte (14.35±2.94%), dok je etanolni ekstrakt iste koncentracije izazvao veće snižavanje arterijskog krvnog pritiska (45.79±10.86%). Hipotenzivni efekti A. graveolens su delimično blokirani atropinom (0.3 mg/kg), neselektivnim antagonistom muskarinskih receptora. Kod izolovanih pretkomora pacova vodeni i etanolni ekstrakti ove biljne vrste su izazvali negativne hronotropne i inotropne efekte. Vodeni ekstrakt celera (koncentracije 0.75mg/ml) je umanjio frekvenciju kontrakcija pretkomora za 12.88±2.74%, a amplitudu kontrakcija za 8.73±0.89%. Etanolni ekstrakt A. graveolens (koncentracije 0.75mg/ml) je inhibisao frekvenciju kontrakcija pretkomora za 34.26±5.69%, a amplitudu kontrakcija za 25.40±3.61%. Primenom atropina (1μM), efekti ekstrakata celera su delimično umanjeni. Etanolni ekstrakt celera, u odnosu na vodeni ekstrakt, izazivao je statistički značajno veće hipotenzivne i kardio-depresivne efekte ($p<0.05$).

Dobijeni rezultati su pokazali da su vodeni i etanolni ekstrakti A. graveolens izazvali hipotenzivne, negativne inotropne i hronotropne efekte, koji su se verovatno delimično ostvarili posredstvom muskarinskih receptora. U odnosu na vodeni ekstrakt, etanolni ekstrakt A. graveolens je uzrokovao statistički značajno veće hipotenzivne i kardio-inhibitorne efekte. *Acta Medica Medianae 2010;49(1):13-16.*

***Ključne reči**: celer, ekstrakt, krvni pritisak, izolovane pretkomore*