Original article

UDC: 612.334.08:582.794.1
doi:10.5633/amm.2015.0201

SPASMOLYTIC EFFECT OF ANETHUM GRAVEOLENS L. METHANOL EXTRACT ON ISOLATED RAT ILEUM

Marija Gočmanac Ignjatović[1], Dušanka Kitić[2], Milica Kostić[2], Bojana Miladinović[2], Milica Milutinović[2], Milica Veljković[1], Suzana Branković[1]

Anethum graveolens L. is a member of the *Apiaceae* family and more commonly known as dill. Dill has been used for gastrointestinal ailments such as flatulence, indigestion, stomach ache and colic. It has therapeutic effects such as mucosal protective, antisecretory, antimicrobial, antispasmodic, antihypercholesterolaemic and antihyperlipidaemic. The aim of our study was to examine the effects of the dill methanol extract on spontaneous and acetylcholine-induced contractions on isolated rat ileum. Segments of the rat ileum were suspended in an organ bath. The isolated ileum had been treated with the methanol extract of dill in cumulative concentrations (0.003-1mg/mL). In the second series of experiments, acetylcholine (5-1500nM) was cumulatively added to the bath in the absence and presence of methanol extract of dill (0.3-1mg/mL). Cumulative concentrations of methanol extract of dill significantly reduced the spontaneous rat ileum contractions ($p<0.01$) with EC_{50} value of 6.45 ±0.87mg/mL. The methanol dill extract concentration-dependently inhibited the contraction induced with acetylcholine ($p<0.01$), with an EC50 value of 0.41±0.057nM and 1.10±0.29nM (the EC_{50} value of acetylcholine was 0.06±0.0097nM). Our results showed the relaxant effect of the methanol dill extract on the isolated rat intestine. Extract of dill inhibited the spontaneous ileum contractions and contractions induced by acetylcholine. *Acta Medica Medianae 2015;54(2):5-10.*

Key words: *dill, Anethum graveolens L., methanol extract, acetylcholine, rat, ileum*

University of Niš, Faculty of Medicine, Niš, Serbia[1]
University of Niš, Faculty of Medicine, Department of Pharmacy, Serbia[2]

Contact: Marija Gočmanac-Ignjatović
University of Niš, Faculty of Medicine
Bul. dr Zorana Đinđića 81, 18000 Niš, Serbia
E-mail: marija_gocmanac@yahoo.com

Introduction

Study of contractility of the small intestine is very important for investigating the mechanisms involved in intestinal physiological and patho-physiological processes. Intestinal spasms are uncontrolled contractions in the muscles of the small and large intestines. The spasm of intestinal smooth muscle may produce symptoms such as abdominal pain, colic, flatulence, constipation and diarrhea. It is very important to find plants or plant products that relax the intestinal muscle and that may be used for treatment of intestinal cramps. Dill (Anethum graveolens L.) is an important member of the Apiceae family. This plant originates from the southwest Asia and is cultivated in many areas worldwide (1,2). It is well-known as aromatic herb in cooking and as a medicinal herb (3). Dill has been used in traditional phyto-theraphy for centuries to treat digestive disorders, convulsion, vomiting and menstrual problems (4,5). It is known that dill fruits have been given to increase milk secretion in nursing mothers (6). Treatment with seeds of dill may be effective in improving the symptoms of halitosis (7). Also, dill has therapeutic properties such as mucosal protective, antidiabetic, anti-cancer, antioxidant, antimicrobial, anti-inflammatory diuretic, antipyretic, antihypercholesterolaemic and antihyperlipidaemic (8-23).

In experimental study, dill induces a stimulatory effect on the female reproductive system. Hekmatzade et al. and Mirmolaee et al. reported that boiled dill seeds reduced pain intensity and duration of labor stages (24,25). Dill reduces pain severity in primary dysmenorrhea in female students who received powder of dill seed (26). On isolated rat uterus, dill extract induced the spasmolytic effect (27).

Intravenous application of dill oil to cats increased respiratory volume and depressed arterial blood pressure (28). Aqueous extract of

Anethum graveolens seeds decreased food intake, body weight and increased the level of serotonin in brain and plasma of experimental animals (29). Dill extracts possess anticonvulsant activity (30, 31).

It is reported that dill has been used as a household remedy for gastrointestinal ailments such as flatulence, indigestion and stomachache. Dill is given for treating baby colics (32). Extract of dill fruit has antisecretory effect on mice gastric mucosa.

Aims

Although some studies have found that dill is an effective treatment for gastrointestinal diseases, yet more research is needed to clarify the underlying mechanism that mediates its action. The present study was aimed to evaluate the possible spasmolytic activity of methanol extract of dill on isolated rat ileum.

Materials and methods

Drugs

The drugs used in biological tests were: acetylcholine chloride (Sigma, USA), atropine sulphate (Sigma, USA) and papaverine hydrochloride (Merck, Germany). All drugs were dissolved in distilled water for each experimental protocol. The composition of Tyrode solution (in mM) was: NaCl (136), KCl (2.7), $CaCl_2$ (1.8), $NaHCO_3$ (12), NaH_2PO_4 (0.3) $MgCl_2$ (1.8) and glucose (5.6).

Plant material

The dill was purchased from a local grocery. Aerial parts of the dill were open-air dried in the shadow. Dried and pulverized aerial parts of the dill were extracted 10 minutes in ultrasonic bath with methanol. After the filtration, the extracts were concentrated in a rotary evaporator at reduced pressure till a constant weight was achieved. The obtained dry residue was dissolved in distilled water in order to get 10% solution used in the experiment. For experimental purposes, the plant extracts were dissolved in the Tyrode solution in the appropriate concentration. The volume of dill extracts added to the organ bath never exceeded 5% of its total volume.

Animals

In this study, Wistar albino rats aged 3-4 months, with body weight 200–300g, were obtained from the Animal Research Center of the Faculty of Medicine, University of Niš, Serbia. The rats were housed in stainless steel cages under standard laboratory conditions. These animals were maintained at 20–24°C with a 12h light-dark cycle at least 1 week before the experiment. They had free access to food and water. All experimental procedures with animals were in compliance with the European Council Directive of September 22th, Directive 2010/63/EU and were also approved by the Local Ethics Committee (number 01-206-7).

Experimental protocol

The ileum portions were isolated out and cleaned off mesenteries. Preparations of 2cm long parts of the ileum were mounted in 10ml tissue baths containing the Tyrode`s solution maintained at 37°C and aerated with a mixture of 5% carbon dioxide in oxygen. The fragments were stretched to a sufficient tension and equilibrated for at least 30min before starting experiments. The change of intestinal contractility was recorded using system TSZ-04-E; Spell Iso (Experimetria Ltd). After each assay, tissues were washed with fresh Tyrode and equilibrated for around 10min.

Rat ileum exhibits spontaneous rhythmic contractions. The isolated ileum had been treated with the methanol extract of dill in cumulative concentrations (0.003-1mg/mL). Papaverine (0.01–3μg/mL) was used as a control. Relaxant effect of the methanol extract of dill was expressed as a percentage of regular spontaneous ileum contractions.

In the second series of experiments, isolated intestinal segments were contracted by the agonists of muscarinic receptors acetylcholine (5-1500nM). Acetylcholine was cumulatively added to the bath in the absence and presence of methanol extract of dill (0.3-1mg/mL). Atropine (140nM) was used as a control. The contraction caused by maximal concentration of acetylcholine in the absence of the dill extract or atropine was considered as the 100% contraction.

Statistical analysis

Mean and standard error values were calculated for each group of results (n=6 for each set of experiments) and significance of differences between the means were determined by the Student`s t-test. A probability value of $p<0.05$ or less was taken as statistically significant. An EC_{50} value (concentration of drugs causing half-maximal responses) was established by regression analysis.

Results

The experimental data indicated that methanol dill extract (0.003-1mg/mL), concentration-dependently decreased the amplitude and tension of ileal muscle contractions. Cumulative concentrations of methanol extract of dill significantly reduced the spontaneous rat ileum contractions ($p<0.01$) with EC_{50} value of 6.45± 0.87mg/mL (Figure 1.). Papaverine (0.015–5lμg / mL) also relaxed the rat ileum in a concen-tration-dependent manner.

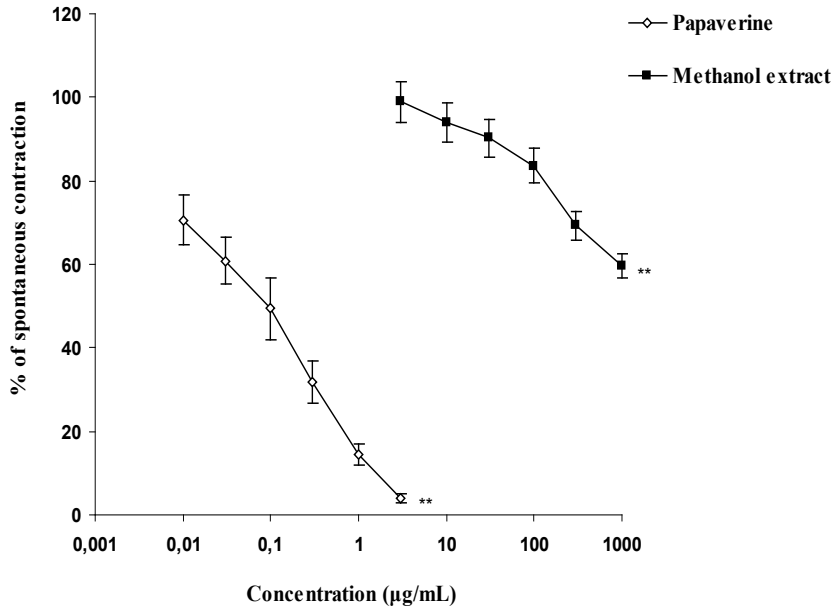

Figure 1. Inhibitory effect of the methanol extract of dill and papaverine on spontaneous contractions of isolated rat ileum

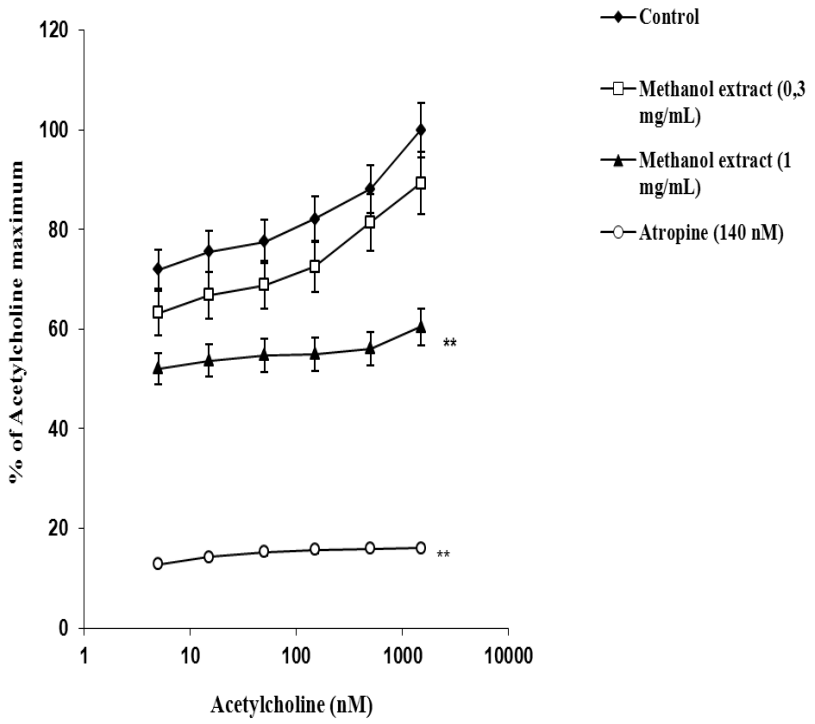

Figure 2. Inhibitory effect of the methanol extract of dill and atropine on acetylcholine-induced contraction of isolated rat ileum

The methanol dill extract (0.3-1mg/mL) concentration-dependently inhibited the contraction induced with acetylcholine ($p<0.01$), with an EC_{50} value of 0.41±0.057nM and 1.10±0.29nM (the EC_{50} value of acetylcholine was 0.06±0.0097nM) (Figure 2.). Atropine (140nM) exerted inhibitory effect on the contractile response of acetylcholine in isolated rat ileum.

Discussion

In this paper, we studied the possible spasmolytic effect of the methanol extract of dill in the isolated rat ileum. The present results showed that methanol extract of dill is a potent relaxant of spontaneous rat ileum contractions. The spasmolytic effect was reversible after washing the

ileum with the fresh Tyrode solution, suggesting that the inhibition was not due to the damage of the intestine by the dill extract. Our findings are in agreement with Naseri et al. (27) study, in which they found that dill fruit hydro-alcoholic extract produced the spasmolytic effect on the isolated rat ileum.

We also wanted to investigate the mechanism underlying the action of methanol dill extract on muscle contractions of isolated rat ileum. In order to explain the possible mode of spasmolytic activity, we examined the influence of the dill extract on acetylcholine-induced intestinal smooth muscle contraction. In our study, we also found that methanol extract of dill reduced acetylcholine-induced contractions of the isolated rat ileum. Treatment of tissues with atropine, nonselective blocker of muscarinic receptors inhibited intestinal muscle contractions induced by acetylcholine. These findings suggest that the action of methanol dill extract on rat ileum motility is mediated by the influence on muscarinic receptors. The enteric nervous system regulated motor and secretory functions of the gastrointestinal system. Acetylcholine is a very widely distributed neurotransmitter that is released from excitatory cholinergic neurons and plays an important role in the stimulation of intestinal smooth muscle contractions. Activation of muscarinic receptor in the rat ileum by acetyl-choline induces an increase in intracellular calcium concentration through the second messenger inositol triphosphate and by facilitating the influx of extracellular calcium (32-34).

Phytochemical analysis of the dill demonstrated the presence of flavonoids quercetin, rutin, isorhamnetin and their derivatives (35,36). Flavonoids as an important class of natural compounds exert physiological properties (37). Quercetin and rutin produced relaxation in the isolated ileum contraction (38,39). Also, isohamnetin produced the spasmolytic effect on the isolated intestine of mice. Vizcaino et al. found that quercetin and isorhamnetin induced endothelium-independent vasodilator effects in rat conductance and resistance arteries (40,41). Quercetin and isorhamnetin prevent angiotensin II-induced endothelial dysfunction in rat aorta (42).

According to the literary sources, monoterpenes have been isolated from dill (43). The monoterpene carvone and limonene produced ileum relaxation (44) and have a protective effect against induced convulsion in experimental animals (45,46).

Spasmolytic effects of dill methanol extract in isolated rat ileum may be due to the presence of these physiologically active components. Our results may explain the traditional use of dill in traditional medicine to treat gastrointestinal diseases.

Conclusion

In the present study, we investigated the effects of methanol dill extract on spontaneous smooth muscle contractions and those induced by acetylcholine in isolated rat ileum. The results suggest that methanol dill extract exerted a spasmolytic activity. Our findings are in agreement with the use of dill in traditional medicine for the treatment of gastrointestinal disorders.

Acknowledgment

The authors are grateful for the financial support of the Ministry of Education and Science of the Republic of Serbia, Grants Nr.III 46013 and III 41018, and in part to U.S. Natl. Inst. of Health, Fogarty International Center (2 D43 TW00-641), to the Institute of International Health at Michigan State Univ. for the Training and Research in Environmental Health in the Balkans program. The authors are also thankful to the assistant professor Bojan Zlatkovic from the Department of Biology and Ecology, Faculty of Sciences and Mathematics, University of Niš, Serbia for the taxonomical identification of the plant material.

References

1. Shyu YS, Lin JT, Chang YT, Chiang CJ, Yang DJ. Evaluation of antioxidant ability of ethanolic extract from dill (*Anethum graveolens* L.) flower. Food Chem 2009;115:515-21. [CrossRef]
2. Kaur GJ, Arora DS. In vitro antibacterial activity of three plants belonging to the family Umbelliferae. Int J Antimicrob Ag 2008;31(4):393-5. [CrossRef] [PubMed]
3. Callan NW, Johnson DL, Westcott MP, Welty LE. Herb and oil composition of dill *(Anethum graveolens* L.): Effects of crop maturity and plant density. Ind Crop Prod 2007;25:282-7. [CrossRef]
4. Yazdanparast R, Bahramikia S. Evaluation of the effect of *Anethum graveolens* L. crude extracts on serum lipids and lipoproteins profiles in hypercholesterolaemic rats. DARU 2008;16:88-94.
5. Monsefi M, Ghasemi M, Bahaoddini A. The effects of *Anethum graveolens* L. on female reproductive system. Phytother Res 2006;20:865-8[CrossRef] [PubMed]
6. Ishikawa T, Kudo M, Kitajima J. Water-soluble constituents of dill. Chem Pharm Bull 2002;50:501-7. [CrossRef][PubMed]

7. Saini N, Singh GK, Nagori BP. Spasmolytic potential of some medicinal plants beloging to family Umbelliferae: a review. IJRAP 2014;5: 74-83.
8. Kazemi M. Phenolic profile, antioxidant capacity and anti-inflammatory activity of *Anethum graveolens* L. essential oil. Nat Prod Res 2014;26:1-3. [PubMed]
9. Jirovetz L, Buchbauer G, Stoyanova AS, Georgiev EV, Damianova ST. Composition, quality control, and anti-microbial activity of the essential oil of long-time stored dill (*Anethum graveolens* L.) seeds from Bulgaria. J Agr Food Chem 2003;51:3854-7. [CrossRef][PubMed]
10. Chen Y, Zeng H, Tian J, Ban X, Ma B, Wang Y. Dill *(Anethum graveolens* L.*)* seed essential oil induces Candida albicans apoptosis in a metacaspase-dependent manner. Fungal Biol 2014;118:394-01. [CrossRef][PubMed]
11. Maheran MM. Investigation of diuretic drug plants. Phytochemical investigation and pharmacological evaluation of *Anethum graveolens* L., *Apium graveolens* L., *Daucus carota* L. and *Eruca sativa* Mill. Phytother Res 1992;5:169-72. [CrossRef]
12. Rezaee-Asl M, Bakhtiarian A, Nikoui V, Sabour M, Ostadhadi S, Maryam-Sadat Yadavar-Nikravesh MS et al. Antinociceptive properties of hydro alcoholic extracts of *Anethum graveolens* L. (dill) seed and aerial parts in mice. Clin Exp Pharmacol 2013;3 (2):122.
13. Kaur GJ, Arora DS. Bioactive potential of *Anethum graveolens*, *Foeniculum vulgare* and *Trachyspermum ammi* belonging to the family Umbelliferae-Current status. J Med Plants Res 2010;4(2):87-94.
14. Singh G, Maurya S, Lampasona MO, de Catalan C. Chemical constituents, antimicrobial investigations and antioxidative potentials of *Anethum graveolens* L. essential oil and acetone extract. J Food Sci 2005;70:208-15. [CrossRef]
15. Rabeh NM, Aboraya AO, Raheem ZH, Jebor AA, Mohammed SK, Saulawa LA, et al. Hepatoprotective Effect of dill (*Anethum graveolens* L.) and fennel (*Foeniculum vulgare*) oil on hepatotoxic rats. PJN 2014;13(6):303-9. [CrossRef]
16. Shewale RS, Doijad RC, Sankpal PS, Pisal SR, Patil YA. Investigation of In-vitro anthelmintic activity of *Anethum graveolens* against *Pheretima posthuma*. WJPPS 2014;3(8):1281-7.
17. Stavri M, Gibbons S. The antimicobacterial constituents of dill *(Anethum graveolens)* Phytother Res 2005;19:938-41. [CrossRef][PubMed]
18. Hosseinzadeh H, Karimi GR, Ameri M. Effects of *Anethum graveolens* L. seed extracts on experimen tal gastric irritation models in mice. BMC Pharmacol 2002;2:21. [CrossRef][PubMed]
19. Lopez P, Sanchez C, Battle R, Nerin C. Solid and vapour phase antimicrobial activities of six essential oils: susceptibility of selected food-borne bacterial and fungal strains. J Agr Food Chem 2005;53:6939-46. [CrossRef][PubMed]
20. Panda S. The effect of *Anethum graveolens* L (dill) on corticosteroid induced diabetes mellitus: involvement of thyroid hormones. Phytother Res 2008;22:1695-7. [CrossRef][PubMed]
21. Yang Y, Huang CY, Peng SS, Li J. Carotenoid analysis of several dark-green leafy vegetables associated with a lower risk of cancers. Biomed Environ Sci 1996;9:386-92. [PubMed]
22. Lanky PS, Schilcher H, Phillipson JD, Loew D. Plants that lower cholesterol. Acta Hortic 1993;332:131-6.
23. Chaurasia SC, Jain PC. Anribacterial avtivity of essential oils of four medicinal plants. Ind J Hosp Pharm 1978;15:166-8.
24. Hekmatzadeh SF, Bazarganipourb F, Malekzadehc J, Goodarzid F, Aramesh S. A randomized clinical trial of the efficacy ofapplying a simple protocol of boiled *Anethum graveolens* seeds on pain intensity and duration of labor stages. Complement Ther Med 2014;22:970—6. [CrossRef][PubMed]
25. Mirmolaee ST, Hekmatzadeh SF, Kazemnazhad A, Aidenlou F, Shamsi M. Evaluating the effects of dill *(Anethum graveolens)* seed on the duration of active phase and intensity of labor pain. J Herb Med. In press 2014.
26. Heidarifar R, Mehran N, Heidari A, Tehran HA, Koohbor M, Mansourabad MK. Effect of dill (*Anethum graveolens*) on the severity of primary dysmenorrhea in compared with mefenamic acid: A randomized, double-blind trial. J Res Med Sci 2014;19(4):326–30. [PubMed]
27. Naseri MKG, Heidari A. Antispasmodic effect of *Anethum graveolens* fruit extract on rat ileum. Int J Pharmacol 2007;3:260-4. [CrossRef]
28. Shipochliev T. Pharmacological study of a group of essential oils. Vet Med Nauki 1968;5:87-92.
29. Bano F, Ahmed A, Ahmed M, Parveen T. *Anethum graveolens* seeds aqueous extract stimulates whole brain 5-hydroxytryptamine metabolism and reduces feeding behavior and body weight in obese rats. Pak J Pharm Sci 2015;28(1):221-5. [PubMed]
30. Arash A, Mohammad MZ, Jamal MS, Mohammad TA, Azam A. Effects of the Aqueous Extract of *Anethum graveolens* Leaves on Seizure Induced by Pentylen etetrazole in Mice. Malays J Med Sci 2013;20(5):23-30. [PubMed]
31. Rostampour M, Ghaffari A, Salehi P, Saadat F. Effects of Hydro-alcoholic Extract of *Anethum graveolens* Seed on Pentylenetetrazol-induced Seizure in Adult Male Mice. BCN 2014;5(3):199-204. [PubMed]
32. Elorriaga M, Anselmi E, Hernandez JM, Docon P, Ivorra D. The source of Ca^{2+} for muscarinic receptor-induced contraction in rat ileum. J. Pharm Pharmacol 1996;48:817-9. [CrossRef][PubMed]
33. Eglen RM, Hedge SS, Watson N. Muscarinic receptor subtypes and smooth muscle function. Pharmacol Rev 1996;48:531-65. [PubMed]
34. Zhang WW, Li Y, Wang XQ, Tian F, Cao H, Wang MW, et al. Effects of magnolol and honokiol derived from traditional Chinese herbal remedies on gastrointestinal movement. World J Gastroentero 2005;11:4414-8. [PubMed]
35. Gebhardt Y, Witte S, Forkmann G, Lukacin R, Matern U, Martens S. Molecular evolution of flavonoid dioxygenases in the family Apiceae. Phytochemistry 2005;66:1273-84. [CrossRef][PubMed]
36. Moehle B, Heller W, Wellmann E. UV-induced biosynthesis of quercetin 3-O-beta-D-glucuronide in dill *Anethum graveolens* cell cultures. Phytochemistry 1985;24:465-8. [CrossRef]
37. Dirscherl K, Karlsteller M, Ebert S, Kraus D, Hlawatsh J, Walezak Y, et al. Luteolin triggers global changes in the microglial transcriptome leading to a unique anti-inflammatory and neuroprotective phenotype. J Neuroinflamm 2010;7:3. [CrossRef][PubMed]
38. Lozoya X, Meckes M, Abou-Zaid M, Tortoriello J, Nozzollilo C, Amason J. Quercetin glycosides in *Psidum guojava* L. leaves and determination of a spasmolytic principle. Arch Med Res 1994;25:11-55. [PubMed]
39. Cimanga RK, Mukenyi PN, Kambu OK, Tona GL, Apers S, Totté J, et al. The spasmolytic activity of extracts and some isolated compounds from the leaves of *Morinda morindoides* (Baker) *Milne-Redh.* (Rubiaceae). J Etnopharmacol 2010;127(2):215-20. [CrossRef][PubMed]

40. Perez-Vizcaino F, Ibarra M, Cogolludo AL, Duarte J, Zaragoza-Arnaez F, Moreno L, et al. Endothelium-independent vasodilator effects of the flavonoid quercetin and its methylated metabolites in rat conductance and resistance arteries. J Pharmacol Exp Ther 2002;302(1):66-72. [CrossRef][PubMed]
41. Perez-Vizcaino F, Duarte J. Flavonols and cardio vascular disease. Mol Aspects Med 2010; 31(6):478-94. [CrossRef][PubMed]
42. Sanchez M, Lodi F, Vera R, Villar IC, Cogolludo A, Jimenez R, et al. Quercetin and isorhamnetin prevent endothelial dysfunction, superoxide production, and overexpression of p47phox induced by angiotensin II in rat aorta. J Nutr 2007;137(4):910-5. [PubMed]
43. Taher M, Ghannadi A, Karimiyan R. Effects of volatile oil extracts of *Anethum graveolens* L. and *Apium graveolens* L. seeds on activity of liver enzymes in rat. J Qazvin Uni Med Sci 2007;11:8–12.
44. De Sousa DP, Junior GA, Andrade LN, Calasans FR, Nunes XP, Barbosa-Filho JM, et al. Structure and spasmolytic activity relationships of monoterpene analogues found in many aromatic plants. Z Naturoforsch C 2008;63(11-12):808-12. [CrossRef] [PubMed]
45. Sayyah M, Moaied S, Kamalinejad M. Anticonvulsant activity of Heracleum persicum seed. J Etnopharmacol 2005;98(1-2):209-11. [CrossRef] [PubMed]
46. De Sousa DP, De Farias Nobrega FF, De Almeida RN. Influence of the chirality of (R)-(-)- and (S)-(+)-carvone in the central nervous system: a comparative study. Chirality. 2007;19(4):264-8. [CrossRef] [PubMed]

SPAZMOLITIČKI EFEKAT METANOLNOG EKSTRAKTA MIROĐIJE (*ANETHUM GRAVEOLENS L.*) NA IZOLOVANI ILEUM PACOVA

Marija Gočmanac-Ignjatović[1], Dušanka Kitić[2], Milica Kostić[2], Bojana Miladinović[2], Milica Milutinović[2], Milica Veljković[1], Suzana Branković[1]

Univerzitet u Nišu, Medicinski fakultet Niš, Srbija[1]
Univerzitet u Nišu, Medicinski fakultet Niš, Odsek za farmaciju, Niš, Srbija[2]

Kontakt: Marija Gočmanac-Ignjatović
Univerzitet u Nišu, Medicinski fakultet, Niš, Srbija
Bul. dr Zorana Đinđića 81, 18000 Niš, Srbija
E-mail: marija_gocmanac@yahoo.com

Anethum graveolens L, mnogo poznatija kao mirođija, pripada porodici Apicacea. Koristi se kod gastrointestinalnih poremećaja kao što su nadimanje, loše varenje, bol u stomaku i grčevi. Mirođija ima terapeutske efekte, poput antisekretornih, antimikrobnih, mukozoprotektivnih, spazmolitičkih, antihiperholesterolemijskih i antihiperlipidemijskih.

Cilj našeg ispitivanja bio je da istraži efekte metanolnog ekstrakta mirođije na spontane i acetilholinom indukovane kontrakcije izolovanog ileuma pacova.

Delovi ileuma pacova su postavljani u kupatila za izolovane organe. U prvom delu eksperimenta je u kupatila sa izolovanim delovima ileuma aplikovan metanolni ekstrakt mirođije u rastućim koncentreacijama (0,003-1mg/ml). U drugom delu eksperimenta je davan acetilholin u rastućim koncentracijama (5-1500nM) do dobijanja maksimalnog kontrakcijskog odgovora ileuma. Zatim je acetilholin (5-1500nM) aplikovan nakon davanja metanolnog ekstrakta mirođije (0,1-1mg/mL).

Metanolni ekstrakt mirođije u rastućim koncentracijama značajno redukuje spontane kontrakcije ileuma pacova ($p<0,01$), sa vrednošću EC_{50} od 6,45±0,87mg/mL.

Metanolni ekstrakt mirođije u dozno-zavisnom odnosu inhibiše kontrakcije indukovane acetilholinom ($p<0.01$) sa vrednostima EC_{50} od 0,41±0,057nM i 1,10±0.29nM (EC_{50} vrednost za acetilholin je bila 0,06±0,0097nM).

Naši rezultati su pokazali spazmolitički efekat metanolnog ekstrakta mirođije na izolovano tanko crevo pacova. Ekstrakt inhibira kako spontane kontrakcije tako i kontrakcije creva indukovane acetilholinom. *Acta Medica Medianae 2015;54(2):5-10.*

Ključne reči: *mirođija, Anethum graveolens L., metanolni ekstrakt, acetilholin, ileum pacova*