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Original Research

Mutagenic, antimutagenic, antioxidant, anti-lipoxygenase and antimicrobial activities of *Scandix pecten-veneris* L.

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Abstract: *Scandix pecten-veneris* L. or Shepherd's-needle is a weed species used in some countries for medicinal purposes. In this study *S. pecten-veneris* leaves were shade dried, powdered and extracted with methanol. The purpose of this study was to assay the *in vitro* mutagenic, antimutagenic, antioxidant, antilipoxygenase and antimicrobial activities of *S. pecten-veneris* leaf extract. The methanolic extract indicated no mutagenicity when tested with *Salmonella typhimurium* strains TA98 and TA100. Antimutagenic activity was reported with inhibition of mutagenicity in a concentration dependent fashion. The methanolic extract demonstrated antioxidant activity in the DPPH radical-scavenging test (IC_{50} = 4.57 mg/mL), comparable to ascorbic acid and BHT. Moreover, the extract presented a remarkable and potent inhibition against soybean lipoxygenase (IC_{50} = 641.57 µg/mL). The methanolic extract was examined for its antimicrobial powers against four different bacteria with MIC values >100. Our results introduced this plant as a useful factor for the treatment of cancer, inflammatory and infectious diseases.

Key words: *Scandix pecten-veneris*, Shepherd's-needle, mutagenic activity, anti-mutagenic activity, antimicrobial activity, antioxidant activity, anti-lipoxygenase activity.

Introduction

The excessive and repeated use of the same drugs used in modern medicine has led to the evolution of antibiotic-resistant microbes (1). Many medicinal plants are considered as important natural remedies for the treatment of various diseases. Recently, natural products have played an important role in drug discovery and development especially for agents against infectious diseases (2-5). Plants are very important natural sources due to production of complex molecular substances (6). The plants produce structures such as secondary metabolites (phenolic compounds, alkaloids, flavonoids, tannins, coumarins, glycosides, terpenes and isoflavonoids) and their derivatives have antimicrobial and antifungal properties (7-14). Although plants have been extremely exploited in traditional healing systems, only in some cases have their curative potential in humans been substantiated (15). The need of herb-based medicines, cosmetics, health products, food supplements, and pharmaceuticals is successively expanding all over the world, since in some cases, natural products *i*) are non or low toxic, *ii*) have low side effects and *iii*) are available at affordable costs (16).

Mutagenesis is a complex action and many mutagens and carcinogens may serve through the generation of reactive oxygen species (ROS). The worry about the role of diet in human cancer has caused the search of compounds in ordinary foods as well as routinely used medicinal plants that may serve as antimutagens. Several reports have shown that the plant secondary metabolites can serve as antimutagenic compounds (17, 18). Antimutagens have also been touted as cancer chemopreventive factors. Then, the routine consumption of antimutagens can lower genotoxic effects of mutagenic and carcinogenic agents (19, 20).

Antioxidants have been consumed as food additives to prevent degradation. Also, it has been broadly documented that they have a valuable function in the avoidance of aging and diseases such as cancer, atherosclerosis, and Alzheimer's, which are closely linked to the production of reactive oxygen and nitrogen species (21). There is much attention in natural antioxidants to replace synthetic ones such as butylated hydroxyl anisole (BHA) and butylated hydroxytoluene (BHT), because of their likely activity as promoters of carcinogenesis (22). Therefore, in recent years, there has been considerable interest in the antioxidant activity of natural subs-

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tances (23, 24). Examination of plant antioxidants such as flavonoids, phenolic acids and diterpenes (25, 26) and contrasting their antioxidant potential with those of commercial antioxidants and synthetic products, will help discover new sources of natural antioxidants (27).

Lipoxygenases are members of a class of iron-containing dioxygenases that catalyze the attachment of molecular oxygen to fatty acids including a *cis*,*cis*-1,4-pentadiene system to yield unsaturated fatty acid hydroperoxides. It has been discovered that these lipoxygenase products play an important role in a variety of diseases such as bronchial asthma, inflammation (28), tumor angiogenesis (29), chronic obstructive pulmonary disease, cancer, osteoporosis and atherosclerosis (30, 31). There has been increasing interest in the development of lipoxygenase inhibitors for therapeutic symptoms (32, 33). Though anti-inflammatory drugs are consumed widely, prolonged using of these medications is usually associated with many side effects (34, 35). Consequently, there is a need to investigate other procedures to reduce the formation of inflammatory mediators with the use of natural dietary products.

The therapeutic influences of many plant spices and herbs suggest the presence of antioxidative and antimicrobial constituents in their tissues (25). The necessity of new antimicrobial agents and procedures for use in the treatment of problematic Gram-negative and Gram-positive infections is clear and is greater than ever because of the appearance of multidrug-resistance in typical pathogens, the rapid appearance of new infections, and the possibility for use of multidrug–resistant factors in bioweapons (26, 36).

The genus *Scandix*, in the Apiaceae, includes 20 species with 15 of them found mainly in the Mediterranean region (37-39) and only *Scandix pecten-veneris* L. broadly distributed (40). *S. pecten-veneris* (Umbelliferae or Apiaceae; Common name: Shepherd's-needle, Venus's comb, Venus's needle) is a species of arable land and waste places, associated with arable cultivation and is very abundant in grain fields. The plant is annual, and when found in arable crops, it is able to grow and set seed in the time between the sowing of the crop and post-harvest cultivation (41). The aim of this study was to evaluate the *in vitro* mutagenic, antimutagenic, antioxidant, anti-lipoxygenase and antimicrobial activities of *S. pecten-veneris*.

Materials and Methods

Collection and preparation of extracts

The *S. pecten-veneris* L. leaves (Figure 1) were collected in May 2014 from Zabol region, in Sistan and Baluchestan Provinces of Iran. The plant was taxonomically recognized by a botanist at the Herbarium of Pharmacognosy, Department of the Faculty of Pharmacy affiliated to Shahid Beheshti University of Medical Sciences of Iran. The leaves were air-dried in the shade at ambient temperature (18-25 °C) for 5 days. The plant leaf was powdered in a knife mill. Ground sample (100 g) was mixed with 300 mL of 85% methanol using a shaking water bath for 24 h at room temperature (25±3 °C). The extract was separated from the solid concentrate by filtering through Whatman No. 1 filter paper. The remaining residue was re-extracted twice and the extract was pooled. The solvent was removed under vacuum at 30 °C using a rotary vacuum evaporator (Laborota 4000, Heidolph, Germany). The final yield of the extract was 9 g, which was stored for future assays.

Figure 1. *Scandix pecten-veneris* plant used for biological activity assays in this study.

Mutagenic and antimutagenic activity

Bacterial strains

In this study, *Salmonella typhimurium* TA100 and TA98 were used for the mutagenity and antimutagenity assays. The strains were examined for their biotin requirement, histidine requirement, rfa mutation, the combination of both, excision repair capability, the presence of the plasmid pKM101, and spontaneous mutation rate according to Mortelmans and Zeiger (42). Working cultures were prepared by inoculating nutrient broth with the frozen cultures, followed by an overnight incubation at 37 °C with gentle agitation (43).

Viability assays and determination of test concentrations

A cytotoxic dose of the *S. pecten-veneris* methanolic extract was determined by the method of Mortelmans and Zeiger (42). The toxicity of methanolic extract toward *S. typhimurium* TA100 and TA98 was determined as described in previous studies (44, 45). These tests confirmed that there was normal growth of the background lawn, spontaneous colony numbers within the regular range, and no significant reduction in cell survival. Therefore, for the concentrations and conditions reported here, no toxicity or other adverse effects were observed.

Mutagenicity and antimutagenicity tests

The plate incorporation method was used for mutagenicity and antimutagenicity assays (46). The mutagens sodium azide (NaN_3) (8 μg/plate) for *S. typhimurium*TA100 and 4-nitro-*o*-phenylenediamine (4-NPD) (3 μg/plate) *S. typhimurium* TA98 were used as positive controls and methanol/water (1:1, v/v) was used as negative control in mutagenicity and antimutagenicity tests. For mutagenicity assay carried out with TA100 and TA98 strains of *S. typhimurium*, 100 μL of the overnight bacterial culture, 100 μL of test compounds at different concentrations (2.5, 0.25, and 0.025 mg/plate), and 400 μL of phosphate buffer were added to 2 mL

of the top agar containing 0.5 mM histidine/biotin. The mixture was poured onto minimal glucose plates. Histidine-independent revertant colonies (HIRCs) and viable cells were scored on plates after incubation at 37°C for 72 h.

For antimutagenicity assay performed with the same strains, 100 µL of the overnight bacterial culture, 100 µL of mutagen, 100 µL of test compounds at different concentrations (2.5, 0.25, and 0.025 mg/plate), and 400 µL of phosphate buffer were added to 2 mL of the top agar containing 0.5 mM histidine/biotin. The mixture was poured onto minimal glucose plates. HIRCs and viable cells were scored on plates after incubation at 37 °C for 72 h. The plate incorporation method was used to assess the results of mutagenicity and antimutagenicity tests (47).

For the mutagenicity assays, the mutagenic index was calculated for each concentration, which is the average number of revertants per plate divided by the average number of revertants per plate with the negative control. For the antimutagenicity tests, the % inhibition was calculated according the formula: % Inhibition = (1-T/M) ×100

Where T is the number of revertants per plate in the presence of mutagen, and the test sample, and M is the number of revertants per plate in the positive control.

The antimutagenic effect (%inhibition) between 25-40% was defined as moderate antimutagenicity, 40% or more as strong antimutagenicity and 25% or less inhibition as no antimutagenicity (48). The possible antimutagenic potential of the extract was examined against 4-nitro-*o*-phenylenediamine (4-NPD) and NaN_3 in *S. typhimurium* TA98 and TA100, respectively.

Antioxidant activity

Determination of 2, 2-diphenyl-1-picrylhydrazyl radical scavenging activity

Antioxidant activity of the extract was determined based on its ability to react with the stable 2,2-diphenyl-1-picryl hydrazyl (DPPH) free radical (16). Aliquots (50 µL) of the extract [1.25, 2.5, 5, and 10 mg/mL in methanol/water (1:1, v/v)] was added to 4 mL DPPH solution (0.004%) in ethanol. After incubation at room temperature for 45 min, the absorbance of each solution was determined at 517 nm. The % inhibition and the concentration of sample required for 50% scavenging of the DPPH free radical (IC_{50}) were determined. Butylated hydroxytoluene (BHT) and ascorbic acid were used as controls.

Total antioxidant activity

Total antioxidant activity of *S. pecten-veneris* extract was determined by the *β*-carotene-linoleic acid method (49). About 0.5 mg of the *β*-carotene in 1 mL of chloroform, 25 µL of linoleic acid, and 200 mg of Tween-40 (polyoxyethylene sorbitan monopalmitate) were mixed. The chloroform was completely evaporated using a vacuum evaporator and the resulting solution was diluted with 100 mL of oxygenated water. A volume of 2.5-mL aliquots of this mixture were transferred into different tubes containing 0.5 mL of samples at 1, 5, 10, 20, and 30 mg/mL concentrations in methanol/water (1:1, v/v). The same process was repeated with butylated hydroxytoluene (BHT), ascorbic acid as positive control and blank. The emulsion system was incubated for up to 2 h at 45°C. The measurement of absorbance was continued until the color of *β*-carotene disappeared in the control. After this incubation, the absorbance of the mixtures was measured at 490 nm.

The bleaching rate (R) of *β*-carotene was calculated using the following formula: R = ln (a/b)/t where, ln = natural log, a = absorbance at time 0, b = absorbance at time t (120 min). The total antioxidant was calculated in terms of % inhibition relative to the control using the formula

Total antioxidant = $[(R_{Control} - R_{Sample})/R_{Control}] \times 100$.

Antioxidative activities of the extracts were compared with those of BHT and ascorbic acid at 0.5 mg/mL.

Total Phenolic compounds determination

The phenolic constituent of *S. pecten-veneris* extract was determined by the Folin-Ciocalteu reagent method or gallic acid equivalence (GAE) method (50). The extract solution (200 µL) containing 0.1 mg extract was added to a test tube. Afterwards, 100 µL of Folin-Ciocalteu reagent was added, and the tube was shaken vigorously. After 5 min, 2 mL solution of Na_2CO_3 (0.5%) was added, and the mixture was shaken intermittently for 2 h. Then, absorbance was measured at 760 nm. The total phenolic content was determined as mg gallic acid equivalents per gram of extract (mg/g GAE extract) using the following linear equation based on the calibration curve: A = 0.0265C, R^2 = 0.993 where A is the absorbance and C gallic acid equivalents.

Anti-lipoxygenase activity

Anti-lipoxygenase activity was assayed using linoleic acid as substrate and lipoxidase as enzyme (Sigma, USA) (51). The plant extract sample (100, 200, 300, 600, and 900 µg/mL) was dissolved in 0.25 mL of 2 M borate buffer pH 9.0 and added 0.25 mL of soybean lipoxidase enzyme solution (final concentration of 20,000 U/mL). This mixture was incubated for 10 min at 25 °C. After which, 1.0 mL of linoleic acid solution (0.6 mM) was added, mixed well, and absorbance was measured at 234 nm by a Shimadzu UV 1601 spectrophotometer (Kyoto, Japan). The % inhibition was calculated from the following equation:

% inhibition = ([Absorbance of control - Absorbance of test sample]/Absorbance of control) × 100

A dose-response curve was plotted to determine the IC values. IC_{50} is defined as the concentration sufficient to obtain 50% of a maximum scavenging capacity. Indomethacin was used as reference standard.

Antimicrobial activities

Microorganisms strains

The leaf plant extracts were assayed against two fungi (*A. niger* and *C. albicans*) and two Gram-positive bacteria (*B. subtilis* and *S. aureus*) and two gram-negative bacteria (*P. aeruginosa* and *K. pneumoniae*). All microorganisms were obtained from the Persian Type Culture Collection, Tehran, Iran.

Antimicrobial assays

The fungi and bacteria were cultured for 14-24 h at 37 °C and the densities were adjusted to 0.5 McFarland standards at 530 nm. The antibacterial tests were carried

out by the disc diffusion method (52). Of the 100 µL microbial suspensions was spread on nutrient agar (Merck, Germany) plates (100 mm × 15 mm). Discs (6 mm diameter) were impregnated with 100 µL of different concentrations of extract (50,100, 150, 200, 250, 300, 400, and 500 µg/mL) and placed on the inoculated agar. All the inoculated plates were incubated for 24 h at 37 °C. We used positive control discs included ketoconazole, gentamicin and ampicillin (10 mg/disc) for fungi, gram-negative and Gram-positive bacteria, respectively. Also, we used 5% dimethyl sulfoxide (DMSO) as the negative control. Antimicrobial activity was appraised by measuring the zone of inhibition. Minimum inhibitory concentration (MIC) was determined using serial dilutions of the extracts (0-500 µg/mL) using microdilution assay approved by Clinical and Laboratory Standards Institute (53). The bacteria and fungi were suspended in Luria-Bertani media and the densities were regulated to 0.5 McFarland standards at A_{530} nm (10^8 CFU/mL). The extract (100 µL) and the bacteria and fungi suspensions (100 µL) were added to microtiter plates and incubated at 37 °C for 24 h. In this study, medium without bacteria and fungi was as sterility control and medium with bacteria and fungi but without extract was as growth control. Growth in each well with that of the growth in the control well was compared. The MICs were visually detected in comparison with the growth in the control well and delineated as the lowest concentration of the components with >95% growth inhibition.

Statistical analysis

The all experiments were carried out in triplicate at each experimental time. Data were subjected to one-way analysis of variance (ANOVA) followed by Tukey's HSD (honestly significant difference) *post-hoc* test at $P < 0.05$ using SPSS v. 11.5. Data are expressed as mean ± standard deviation.

Results and Discussion

S. pecten-veneris is a weed species used in some countries such as Iran and Turkey for medicinal purposes. The *S. pecten-veneris* extract, which was tested at three different concentrations, did not exhibit any mutagenic effect in the mutagenicity tests carried out with *S. typhimurium* TA100 and TA98 (data not shown). The lack of mutagenicity reveals that DNA does not appear to be a target for this methanolic extract (54).

The antimutagenic potential of the extract is shown in Table 1. In the antimutagenicity tests performed with TA98 and TA100 strains, the extract showed antimutagenic effects at 2.5, 0.25, and 0.025 mg/plate concentrations. The strongest antimutagenic activity was observed at 2.5 mg/plate concentration against *S. typhimurium* TA98 strain. The results showed that only one concentration (0.025 mg/plate) of the extract did not have any antimutagenic effect against *S. typhimurium* TA98. The antimutagenic activity of the extract was determined as being dose dependent. Anticarcinogenic and antimutagenic activity of medicinal and food plants may be due to a diversity of mechanisms such as inhibition of genotoxic influences, inhibition of cell proliferation, signal transduction modulation, scavenging of free radicals, induction of detoxification enzymes, induction of cell-cycle stop and apoptosis, modulation of cytoskeletal proteins that represent an important function in mitosis, and the inhibition of topoisomerase I or II activity (55). Additionally, the mechanism of the antimutagenic activity may be due to its antioxidant activity, as proposed for other extracts from plant sources by several other researches (56-62). Zahin *et al*. (63) have shown that *Carum copticum* (L.) fruit extract, a plant of Apiaceae, is a hopeful source of antimutagenic compounds. In another study, *Pituranthos chloranthus* (Coss. et Dur.) (Apiaceae) essential oils indicated promising antimutagenic influence (64).

The free radical-scavenging capacity of the corresponding extract measured by DPPH test, and the IC_{50} values of the extract, BHT, and ascorbic acid are shown in Table 2. Total antioxidant activities of the methanolic extract of *S. pecten-veneris* are shown in Table 3. When screened for its radical scavenging and total antioxidant

Table 1. The antimutagenicity assay results of *Scandix pecten-veneris* extract for *Salmonella typhimurium* TA98 and TA100 bacterial strains.

Test items	Concentration (mg/plate)	*S. typhimurium* TA100		*S. typhimurium* TA98	
		Number of revertants	% inhibition	Number of revertants	% inhibition
Extract	2.5	427.87 ± 3.29[§]	56.41	567.54 ± 3.49	77.78
	0.25	397.45 ± 4.36	46.22	436.83 ± 6.37	49.34
	0.025	456.99 ± 3.22	32.43	677.74 ± 4.22	18.25
Negative control	-	7.45 ± 1.12	-	184.82 ± 2.11	-
4-NDP	3	-	-	284.9 ± 1.5	-
NaN_3	8	305.8 ± 3.43	-	-	-

[§]Data are expressed as means ± SD. 4-NDP and NaN_3 were use as positive controls for *S. typhimurium* TA98 and AT100 strains, respectively. 4-NDP: 4-nitro-o-phenylenediamine.

Table 2. Free radical scavenging capacities of *Scandix pecten-veneris* extract and standards measured in the DPPH radical-scavenging assay.

Sample	IC_{50} (mg/mL)
Extract	4.57 ± 0.32[§] a
BHT	0.54 ± 0.00 b
Ascorbic acid	0.35 ± 0.00 c

[§]Data are expressed as means ± SD. The values with different letters within a column are significantly different ($P < 0.05$; LSD). BHT: Butylated hydroxytoluene.

Table 3. Antioxidant activity (%) of *Scandix pecten-veneris* extract in the *β*-carotene-linoleic acid test system.

Sample	Concentration (mg/mL)					
	0.5	1	5	10	20	30
Extract	-	32.59 ± 1.45	44.82 ± 2.36	56.97 ± 3.76	81.44 ± 2.22	85.99 ± 2.69
BHT	99.45 ± 1.4	-	-	-	-	-
Ascorbic acid	87.79 ± 2.3	-	-	-	-	-

[§]Data are expressed as means ± SD. BHT: Butylated hydroxytoluene.

properties, the methanolic extract of *S. pecten-veneris* provided dose-dependent results in the different assays. The results showed that the radical-scavenging activity of BHT and ascorbic acid were higher than that of the extract. In this study, the phenolic content of the methanolic extract of *S. pecten-veneris* was found to be 377.94 ± 3.41 mg GAE/g extract. The data obtained from this part show a correlation with those obtained from the *β*-carotene-linoleic acid test system. The total antioxidant feature of a plant extract is usually examined as the result of the mixed activity of a large area of compounds, containing phenolics, peptides, organic acids and other components (65). The identified compounds from *Foeniculum vulgare* Mill. (Apiaceae) show the connection between its radical-scavenging activity and chemical composition (66). This study contrasted 11 commercially available organic spices of the Apiaceae for their antioxidant capacity, and these workers found that phytochemicals in aqueous extracts are stronger antioxidants than in nonaqueous extracts (67). Meot-Duros and Magne (68) expressed that *Crithmum maritimum* L. (Apiaceae) can be counted as a useful source of antioxidant products. Antioxidant activity was also indicated in the extracts of coriander and parsley, also from the Apiaceae (69, 70).

The *S. pecten-veneris* methanolic extract was assessed in vitro for its capability to inhibit soybean lipoxygenase, as a measure of its possible anti-inflammatory activity, by the UV absorbance based enzyme test. *S. pecten-veneris* leaf extract indicated a considerable and marked inhibitory activity against lipoxygenase (IC_{50} = 641.57 µg/mL, $P < 0.05$) compared with the reference standard, that is Indomethacin (IC_{50} < 100 µg/mL). The % inhibitions of the plant extract were 3.5, 16.42, 34.62, 44.56, and 77.49 for concentrations of 100, 200, 300, 600, and 900 µg/mL, respectively. The reference standard indomethacin showed a % inhibition higher than 50% at all concentrations (Figure 2). Lipoxygenase-mediated products obtain different biological activities which are needed for neoplastic cell growth, influencing growth factor and transcription factor activation, oncogene induction, stimulation of tumor cell adhesion, and regulation of apoptotic cell death. Lipoxygenase inhibitors are promising therapeutics in many inflammatory diseases, asthma, increase immune response to viral and bacterial infections, leukemia, lymphoma and autoimmune disorders, cancer (71, 72). Umbelliprenin, the natural prenylated coumarin found in members of the Apiaceae, demonstrated a powerful inhibition against soybean lipoxygenase (73). Ali Shah *et al*. (74) indicated the anti-lipoxygenase activity of methanolic extracts of medicinal plants such as *Cuminum cyminum* (Apiaceae). Kim *et al*. (75) has shown that the MeOH root extract of *Dystaenia takeshimana* (Nakai) Kitagawa (Apiaceae) exhibited 5-lipoxygenase inhibitory activity.

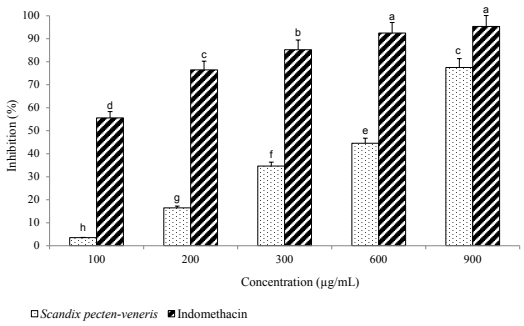

Figure 2. . Lipoxygenase inhibitory activities of leaf extracts of *Scandix pecten-veneris*. Different letters indicate significant differences at $P < 0.05$; all results are expressed as mean ± SD (n = 3).

The results of antifungal tests are shown in Table 4. The leaf extracts significantly inhibited the growth of *C. albicans* and *A. niger* in all assayed concentrations ($P < 0.05$). The maximum inhibition zone observed in concentration 500 µg/mL of extract for the fungi, but the MICs both of the fungal were >100 µg/mL. The methanolic extract showed strong activity against *C. albicans* fungus with inhibition zone of 25.2 ± 0.1 mm at 500 µg/mL concentration.

The Antibacterial screening results are summarized in Table 5. The plant extract showed the maximum inhibition zones at concentration of 500 µg/mL of the leaf extract on the growth of all bacteria. Inhibition zones at concentration of 500 µg/mL of the leaf extract were 34.9±0.3, 30.5±0.2, 47.5±0.1, and 10.5±0.3 mm for *S. aureus*, *B. subtilis, K. pneumoniae, P. aeruginosa*, respectively (Table 5). Among several bacteria, *K. pneumoniae* (MIC >100 µg/ml) disclosed a high sensitivity to methanolic extracts of *S. pecten-veneris*. The screening results show that the methanol leaf extract exhibited a dose-dependent antibacterial effect on the growth of all

Table 4. Antifungal activity of *Scandix pecten-veneris* leaf.

Extract concentrations (µg/mL)	*C. albicans*	*A. niger*
50	8.5± 0.1 g [§]	7.5±0.1 h
100	8.5± 0.3 g	8.8± 0.2 g
150	11.3± 0.1 f	8.3± 0.1 g
200	14.2±0.1 e	9.5± 0.2 f
250	15.8± 0.2 d	12.3± 0.1 e
300	18.9± 0.7 c	14.5± 0.4 d
400	19.6± 0.3 b	16.9± 0.5 c
500	25.2± 0.1 a	19.9±0.4 b
DMSO[a]	0.0±0.0 h	0.0± 0.0 i
Ketoconazole (µg/mL)	24.8±0.2 a	22.5±0.2 a
MIC[b]	>100	>100

[§]Data are expressed as means ± SD of inhibition zone diameter (mm); [a]DMSO: Dimethyl sulfoxide (Negative control); [b]MIC: Minimum inhibitory concentration (µg/mL); The values with different letters within a column are significantly different ($P < 0.05$; LSD).

Table 5. Antibacterial activity of *Scandix pecten-veneris* leaf extracts against Gram-positive and Gram-negative bacteria.

Extract concentrations (µg/mL)	*S. aureus*	*B. subtilis*	*K. pneumoniae*	*P. aeruginosa*
50	4.5±0.2 i§	7.5± 0.4 i	15.5±0.1 f	0.0±0.0 g
100	6.8± 0.4 h	8.3± 0.1 h	18.3±0.2 e	0.0±0.0 g
150	8.5±0.2 g	9.5± 0.3 g	18.5±0.2 e	0.0±0.0 g
200	12.3±0.1 f	10.9±0.2 f	19.2±0.2 d	3.5±0.1 f
250	15.5±0.1 e	15.9± 0.5 e	19.5±0.1 d	4.5±0.3 e
300	24.8±0.3 d	22.9± 0.3 d	33.5±0.2 c	7.7±0.3 d
400	29.7±0.3 c	25.8± 0.1 c	35.8±0.2 b	8.9±0.5 c
500	34.9±0.3 b	30.5± 0.2 b	47.5±0.1 a	10.5±0.3 b
DMSO	0±0.0 j	0±0.0 j	0±0.0 g	0.0±0.0 g
Ampicillin	39.8±0.5 a	35.5±0.1 a	-	-
Gentamicin	-	-	35.5±0.1 b	19.9±0.31 a
MIC	>100	>100	>100	>100

§Data are expressed as means ± SD of inhibition zone diameter (mm) for different concentration of leaf extracts, controls and minimum inhibitory concentration (MIC) (µg/mL); DMSO: Dimethyl sulfoxide (Negative control). The values with different letters within a column are significantly different ($P < 0.05$; LSD).

bacteria tested, which differed only slightly for the different bacterial strains. This result might be due to the inherent characteristics of each bacterial cell wall. The interest in drugs from natural medicinal plants in preference to commercial antimicrobial drugs has increased in recent years (76). It is well understood that active phytochemicals were produced for protection of plants against microbial pathogens and those plants can be promising sources of new compounds with biological activities such as antioxidant and antimicrobial activities (77, 78). Sonboli *et al*. (79) have shown that the essential oil of *Tetrataenium lasiopetalum* (Apiaceae) demonstrates moderate to high antimicrobial activity. The review of Christensen (80) has indicated that aliphatic C_{17}-polyacetylenes of the falcarinol type, which appear in typical food plants of the Apiaceae such as carrot, celery, parsnip and parsley, can be utilized in the treatment or avoidance of a long list of diseases including inflammatory diseases, antimicrobial effects, cancer, etc. In studies of Brković *et al*. (81), the aqueous, ethyl acetate and ethanol extracts of 12 plants from the Apiaceae were evaluated for antibacterial activities against chosen phytopathogenic bacteria; all the plants investigated demonstrated antimicrobial activities against the bacteria tested. Christova-Bagdassarian *et al*. (82) examined antibacterial activity of methanolic extracts of dry seeds from members of the Apiaceae, and they found that the methanol seed extracts did not show antimicrobial activity against *Escherichia coli* strains but did have activity against *P. aeruginosa*. Also they documented that phenolic and flavonoid content correlated with antibacterial activities of the extracts. Radulović *et al*. (83) have shown that all chosen microorganisms, except for the bacterium *E. coli*, were susceptible to the essential oil of *S. pecten-veneris* aerial parts and the novel esters of long-chain alcohols. Ebrahimabadi *et al*. (84) reported that the methanol extracts of the leaves and flowers of *Chaerophyllum macropodum* Boiss. (Apiaceae) exhibited antioxidant and antibacterial activities. The study of Oroojalian *et al*. (85) found the essential oils of three Apiaceae species, *Bunium persicum*, *Cuminum cyminum* and *C. copticum*, to have significant antibacterial activity with promising application in the food industry. The essential oils and various extracts from coriander (*Coriandrum sativum* L.), a hardy annual member of the Apiaceae, have been illustrated to have antibacterial (86-89), antidiabetic (90), anticancerous and antimutagenic (91), activities. Flavonoids and phenolic combinations, which are present in medicinal and dietary plants, have been stated to exert multiple biological effects, including free radical scavenging capabilities, anti-carcinogenic, antimutagenic, inhibition of hydrolytic and oxidative enzymes, anti-inflammatory activity etc. (92-101). In our study, also the antibacterial activity can be related to these compounds in the plant extract. The mechanisms concept to be responsible for the activity of these phytochemicals against bacteria may include enzyme inhibition by the oxidized compounds which act as an origin of stable free radical and often lead to deactivation of the protein and loss of function.

Conclusions

Due to the emergence of unpleasant side effects from the use of synthetic chemical combinations, the extracts from different plant species, especially edible and medicinal plants, have attained substantial importance among the research community. The history of useful essential oils, extracts and constituents of members of the Apiaceae and important antimutagenic, antioxidant, anti-lipoxygenase and antimicrobial capabilities for this family in conjunction with this current report suggest *S. pecten-veneris* to be a suitable candidate for treatment of some types of diseases. In addition, it can be used as food supplement and material for food in food industries. Furthermore, isolation of bioactive phytochemicals from *S. pecten-veneris* leaf extract should be done in search of new chemotherapeutic agents.

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