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Investigation of Angiotensin-Convertings Enzyme Inhibitory Effects of Medicinal Plants Used in Traditional Persian Medicine for Treatment of Hypertension: Screening Study

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ARTICLE INFO	A B S T R A C T
<i>Article type:</i> Original Article	Background: Angiotensin converting enzyme (ACE) inhibitors are used widely in the treatment of hypertension and heart failure. These inhibitors such as captopril and enal-april are derived from natural products.
Article history:	Materials and Methods: In the present study 135 plants used in Traditional Persian Medi-
Received: 17 Sep 2011	cine have been investigated for their angiotensin converting enzyme (ACE) inhibitory
Revised: 20 Oct 2011	activity. They were selected on the basis of their usage as antihypertensive, cardiotonics
Accepted: 5 Dec 2011	& diuretics. Dried powdered plant material was extracted with mix solution of water and ethanol in ultrasonic bath. The extracts were filtered and concentrated in vacuum except
Keywords:	for the water extracts, which were freeze-dried. Test solutions were made by dissolving
Medicine, Traditional	extract in assay buffer, corresponding to a final concentration of 0.33 mg of crude plant
Hypertension	extract in 1 ml test volume. Enzyme assay was performed by HPLC method. Plants exhibit-
Angiotensin-Converting Enzyme Inhibitors Tannins	ing inhibition levels with more than 50% were further tested for the presence of tannins in order to eliminate possible false positives.
Plants, Medicinal	Results: In total, 52 Species out of the 135 (39%) screened, gave more than 50% ACE inhibition. Forty Species were found to possess a high ACE inhibiting ability and were low in their tannin content.
	<i>Conclusions:</i> Traditional medicine based on certain plants could be of beneficial effects in hypertension treatment.

▶ Implication for health policy/practice/research/medical education: Introducig of new antihypertensive medications.

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1. Background

Angiotensin I-converting enzyme activity (ACE, peptidyldipeptide hydrolase, kininaseII, EC 3.4.15.1) plays an important role in regulation of blood pressure (1). ACE is an important blood pressure regulator that catalyzes the release of His-Leu from the carboxyl terminal of angiotensin I, which, in turn, generates a potent vasopressor octapeptide, angiotensin II. ACE is also involved in the degradation of vasodilator bradikinin (2). Most if not all commercialized ACE inhibitors have utilized peptides from the venom of the Brazilian viper Bothrops Jararaca as model substances(3). Besides this animal source, microorganisms and plants deliver compounds with ACE inhibitory activity which could serve as model substances in the development of new ACE inhibitors. ACE inhibitors prevent the formation of angiotensin II by ACE and thereby reduce peripheral vascular resistance and blood pressure. However, these synthetic drugs are believed to have certain side effects such as cough, taste disturbances and skin rashes (4). Therefore, for safe and economical use, interest in identifying food sources as ACE inhibitor has increased. More potent ACE inhibitors have also been designed and synthesized to treat hypertension effectively. Oral administration of these drugs frequently results in unwanted side effects; a nutritional approach might be a better medium by which blood pressure in controlled.

Screening for antihypertensive effects in traditional medicines has been performed over many years and certain animal models have been utilized (5). In western medicine, drug development has become increasingly more mechanistic in the focus of excluding unwanted side-effects (5). The rationale behind this approach is to identify a molecular target (receptor or enzyme) which has an essential role both in the regulation of the disease and the search for ligands, substrates or inhibitors of the target. In the treatment of hypertension, inhibition of the ACE is established as one the current therapeutic principles.(6)

In Persian the different traditional medicine systems make use of a number of plants for treating of the hypertension. In order to evaluate the biological activity of Persian medicinal plants, this study was conducted to evaluate the antihypertensive activity of some of these plants based on an in vitro bioassay for ACE inhibition. A number of screening studies have been made on the ACE inhibitory activities of higher plants and different screening methods have been used. To researchers, a variety of methods (e.g. spectrophotometry and fluorometry) are available by which ACE activity can be detected and analyzed (7, 8). High performance liquid chromatography (HPLC) is widely used because of its effective separation of the substrate and product from the ACE reaction mixture in order to ensure accurate measurements. More recently, Braga et al. (2000) investigated 20 species used to treat hypertension in Brazilian flora (9); Somanadhan et al. (1999) investigated 73 plant species used in Indian folk medicine to treat hypertension (10); Duncan et al. (1999) reported the result of screening 20 species from Zulu (11); Nyman et al. (1998) screened 75 species belonging to 42 plants family from Indian traditional medicine (12); 54 plants from Reunion Island with alleged antihypertensive & diuretic effects have been investigated by Anderson et al. (1997) (13), and Hansen et al. (1995) reported the result of screening of 31 species from India, China & Chile in which all of them used HPLC assay method for these screening. Arisawa et al. (1985) investigated some 38 samples of crude drugs by means of spectrophotometric & fluorimetric assay (14); Yun et al. (1981) investigated 27 plant species used to treat hypertension in Korean folk medicine (15).

Furthermore, some studies have been made on single plant species where several classes of ACE inhibitory compounds have been identified, for example proanthocyanidins (16-18), flavonoids (18, 19), xanthones (20), peptides (17), and secoiridoids (21) for a comprehensive review of these compounds (22).

To authors' knowledge and research in relevant literature, no documents have been reported in Traditional Persian Medicine regarding the systematically screening for this target. Thus, the present study may represent an opportunity to find new non-chemical agents to develop new antihypertensive drugs.

2. Materials and Methods

2.1. Plants Material

In this study 135 plants used in Traditional Persian Medicine have been investigated for their ACE inhibitory activity. They were selected on the basis of their usage as antihypertensive, cardio-tonics, and diuretics.

Plants material was collected throughout the years 2004 – 2005 from different zones of Persia. They were identified according to Herbarium of Tehran University and a voucher specimen of the plants was deposited in the Herbarium of the Faculty of Pharmacy of Tehran University.

2.2. Preparation of Crude Extracts

All plant materials were air dried in the shade before extraction. After grinding, a 1g weight of the dried plant material was extracted with 10 ml water or ethanol (96%) respectively for 2 hours in an ultrasonic bath. The extract were filtered and concentrated in vacuum except for the water extracts, which were freeze-dried. Then the extracts were kept at 2-6°C (refrigerator).

2.3. Chemicals and Buffers

Hippuryl-L-Histidyl-L-Leucine (HHL) and hipuric acid (HA), were purchased from Sigma; all other reagents were analytical grade.

1) Assay buffer: HEPES-NaOH, 50mM, and pH 8.0 contain 300mM NaCL (11.92g of HEPES and 17.52g of NaCL are dissolved in 900 ml bidistilled water, adjusted to pH 8.0 with NaOH and diluted to liter). Before use, buffer is filtered using a filter with a pore diameter of 0.45μ m.

2) Substrate (3.5 mM): 5.2 mg of HHL (Hippuryl-L-Histidyl-L-Leucine) are solved in 1ml assay buffer. This solution should be prepared freshly before each assay.

3) Stop solution (0.1N): 11.92g of HPES are dissolved in 800 ml bidistilled water, adjusted to pH 9.0 with NaOH 1 M and diluted to liter). Before use, solution is filtered us-

ing a filter with a pore diameter of 0.45µm.

2.4. Enzyme

For these studies, a commercially available angiotensin-converting-enzyme preparation from rabbit lung (EC 3.4.15.1-purchased from sigma) has been used.1 unit angiotensin-converting enzyme with the specific activity of 3 units/mg protein is dissolved in 2500 μ L assay buffer. The enzyme solution is highly active and stable for at least 3 months at 2-6°C (refrigerator).

2.5. Preparation of Crude Extracts

Solutions of inhibitors are made by dissolving 1mg of test compound in 1mL of buffer which may contain up to 10% of an organic solvent such as ethanol. This corresponds to a final concentration of 0.33 mg test compound in 1mL assay volume.

2.6. ACE-assay

ACE activity was assayed according to the method described by Horiuchi et al. (1982) and modified by Schnaith et al. (1994) (23, 24) with some modifications for micro assay. This method is based on the ACE-catalyzed cleavage of the HHL (Hippuryl-L-Histidyl-L-Leucine), into Hippuric acid, which is quantitatively measured by High Performance Liquid Chromatography (HPLC). The reaction can be represented as shown in Figure 1. 25 µL of inhibitor solution or assay buffer (for control incubation) are placed into a micro tube and mixed with 25 µL enzyme solution. The micro-tube is placed for 5 min in a thermo-mixer at 37° C and the reaction is started by the addition of $25 \,\mu$ L substrate solution (3.5Mm). After incubation at 37°C, the enzyme reaction is stopped by the addition of 50 µL 0.1N Na2EDTA. The incubation time depends on the activation of the applied enzyme batch. No internal standard was used in this procedure. The incubation mixtures are transferred to HPLC tubes. Assays were performed in duplicate. A blank assay was performed for each extracts tested. (Figure 2)

2.7. High Performance Liquid Chromatography (HPLC)

The product (HA) and unreacted substrate (HHL) are separated and quantified by reversed phase HPLC with UV detection at 228nm. (1) Instrumentation: Pump: Knauer, K-1001; Injector: Autosampler, Maraton, 20μ L loop; Detector: UV-Visible, K-2501, oprated at 228nm; Integrator: Chromogate. (2) Solvent System: Column: Perfectsill target (125×4 mm) and ODS-35 Mobile phase: 10 mM Phosphate buffer (pH = 3) - Methanol HPLC grade (60:40), gradient, Flow rate: 1mL/min, Detection wavelength: 228nm. Using this gradient elution system, the total separation is achieved within 5 min.

2.8. Quantitative Analysis

It was established that the percentage conversion of the substrate by the enzyme was an accurate method to determine the percentage inhibition of the samples. The following formula was used to calculate the percentage of enzyme activity. This method assumed that the control (without the presence of any inhibitors) would have the highest percentage of the ACE activity. A sample exhibiting high inhibition levels would have low percentage of the ACE activity.Using the following equation, the percentage inhibition of the sample could be calculated: Inhibition (%) = 100-Activity (%)

2.9. Tannins Tes

The tannins test was performed by extracting 5g of dry plant material with 50 mL of water or ethanol (96%). After evaporation of the solvents, the extracts were re-dissolved in 13 mL hot water (90-100°C) and allowed to cool to the room temperature. Two drops of 10% NaCL were added to 'salt' out any non-tannin compounds which could cause a false positive reaction. After vacuum filtration, 3 mL of the filtrate was added to each of four test tubes. The following solutions were added to the test tubes:

1. 4-5 drops of 1% gelatin solution,

2. 4-5 drops of 1% gelatin + 10% NaCL solution,

$$Activity(\%) = \left[\frac{Peak \ area(Hippuric \ acid \ Sample) - Peark \ area(Hippuric \ acid \ Blank)}{Peak \ area(Hippuric \ acid \ Control^+)}\right] \times 100$$

Figure 1. HHL (Hippuryl-L-Histidyl-L-Leucine), is cleaved by ACE into Hippuric acid, which can be quantified (HPLC).

Sample: $25\mu l Enzyme + 25\mu l$ Inhibitor $\xrightarrow{37^{\circ}C, 5'} 25\mu l$ Substrate $\xrightarrow{37^{\circ}C, 35'} 50\mu l EDTA$ Blank: $25\mu l Enzyme + 50\mu l EDTA + 25\mu l$ Inhibitor $\xrightarrow{37^{\circ}C, 5'} 25\mu l$ Substrate $\xrightarrow{37^{\circ}C, 35'}$ Control: $25\mu l Enzyme + 25\mu l$ Buffer $\xrightarrow{37^{\circ}C, 5'} 25\mu l$ Substrate $\xrightarrow{37^{\circ}C, 35'} 50\mu l EDTA$

Figure 2. The incubation methods.

3. 3-4 drops of 10% ferric chloride,

4. Control (no solution added).

The first and second tubes were observed for the formation of precipitate and the third tube was observed for color produced.

The test would be considered negative if test tubes 1 and 2 showed no precipitation or if 3 showed no color formation, and positive if test tubes 1 and 2 showed precipitation and 3 shows color formation (either blue-black for hydrolysable or brownish-green for condensed tannins) (12).

2.10. Statistical Analysis

For statistical analysis ANOVA (Analysis of variance) and t-test in SPSS ver.11 software were used to determine significant differences between groups and P < 0.05 were considered significant.

3. Results

3.1. Hippuric acid Standard Curve (Figure 3) 3.2. Linearity of Enzyme Reaction

The time course action of the enzyme was determined by reacting HHL at a concentration of 3.5mM with 1 units of ACE enzyme at varying incubation times. By plotting the percentage of product (HA) against time, it was possible to determine over what time period the enzymatic activity was constant. *Figure 4* shows that the enzymatic rate was constant over a period of 35 min which it would indicate the optimum incubation time from the bioassay.

3.3. Establishing the Sensitivity of the ASssay System

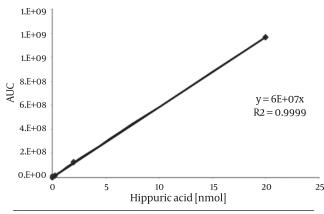
The sensitivity of the assay was tested by determination of the IC50 value of the competitive inhibitor captopril and comparing the value cited in the literature (*Figure* 5).The values in the literature were similar to the one determined in this study. From the data, the IC50 value of 20 nM was established. The reference value in the literature for captopril is 23 nM (25).

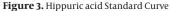
3.4. ACE Inhibitory Activity of Medicinal Plants

The results of the screening are presented in Table 1. In total, 52 Species out of 135 (39%) are screened, have resulted in an ACE inhibition around or above 50%, redering them suitable for closer investigation and isolation of active constituents. these species are further screened for their content of tannins and results are summarized in Table 1. In total, 40 species (29% of total investigated) have been found to possess a high ACE inhibiting ability, not depending on the presence of tannins.

4. Discussion

To obtain the active substances for ACE inhibition the





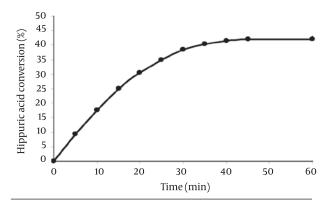


Figure 4. The Time Course of the ACE Reaction

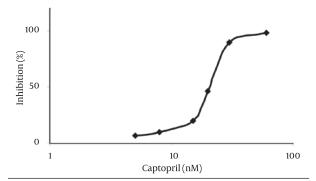


Figure 5.Inhibition of ACE by Captopril at varying concentrations. The IC50 value was determined to be 20 nM

screening was performed on 135 species which were selected on the basis of their usage as antihypertensive, cardio-tonics & diuretics, using water and ethanol (96%) extraction.

As far as possible, the traditionally used part of the plant was employed for the screening. However, in certain cases other parts were also tested. A literature survey on pharmacological activity of all the plants screened for ACE inhibitory activity was carried out and summarized in *Table 1*.

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Allum sativum LIliacaeBulb $14-67$ $14-67$ $13-7$ 76 Ale vera LLuliacaeResin 6.8 5.8 5.8 7.9 76 Ale vera LLuliacaeLaff & 6.8 6.8 7.9 7.9 70 Ale vera LLuliacaeLaff & 6.8 6.8 7.9 7.9 7.9 Ale vera LUnbelliferaeSeed 6.8 6.8 $7.23-6.8$ 7.9 Aretium lapa LCompositaeRotRot $1.3-4.6$ 7.7 7.9 Artemisa dracunculus LRomostaeRotRot $1.3-4.6$ 7.7 $7.9-6.8$ Artemisa dracunculus LCompositaeRotRot 7.7 $1.9-6.6$ 7.7 7.7 Artemisa dracunculus LCompositaeRotRot $8.7-7$ $7.7-7$ $1.9-6.6$ $7.7-7$ Artemisa dracunculus LCompositaeRotRot $7.7-7-7$ $1.9-6.6$ $7.7-7-7$ $7.7-7-7-7$ $1.9-6.6-7$ Artemisa dracunculus LCompositaeRotRot $8.7-7-7-7-7-7-7-7-7-7-7-7-7-7-7-7-7-7-7-$	10	Allium porrum L.	Liliaceae	Leaf	6-8	6-8	1-3-6-8	52	62	ı
Aloeveral.ItiliacaeResin 63 68 10 Aloeveral.ItiliacaeLeaf & Gel 6 6 3 3 Aloeveral.UmbelliferaeSeed 5 6 3 3 Arethum graveolensl.UmbelliferaeSeed 5 5 12346 5 Armin lapal.CompositaeRoot 1 13446 5 1 Armeniaca vulgaris LCompositaeRoot 1 1 1 2 Armeniaca vulgaris LCompositaeRoot 1 1 1 2 Armeniaca vulgaris LRosaceaeLeaf 1 1 1 1 2 Armeniaca vulgaris LCompositaeRoot 1 1 1 2 2 Armeniaca vulgaris LGramineaeRoot 2 2 2 2 2 Armeniaca vulgaris LGramineaeRoot 2 2 2 2 2 Armeniaca vulgaris LBerberia deceeFruit 2 2 2 2 Breberis vulgaris LBerberia deceeFruit 3 3 4 5 5 Brassica olarea LCurciferaeSeed 2 3 3 4 5 <td>11</td> <td>Allium sativum L.</td> <td>Liliaceae</td> <td>Bulb</td> <td>1-4-6-7</td> <td>1-4-6-7</td> <td>1-3-7</td> <td>76</td> <td>68</td> <td>,</td>	11	Allium sativum L.	Liliaceae	Bulb	1-4-6-7	1-4-6-7	1-3-7	76	68	,
Aloe veral.LielacaeLeaf & Gel6.86.839Anethum graveolens L.UmbelliferaeSeed6.86.81.2.36.81Apium graveolens L.UmbelliferaeSeed6.81.2.36.811Artetum lappa L.UmbelliferaeSeed6.81.2.36.811Artetum lappa L.CompositaeRootLeaf1111Artemisia dracuculus LCompositaeRootArtenisia dracuculus L1111Asparagus officinalis L.AsparaginaceaeRootArteni at a trait1111Asparagus officinalis L.AsparaginaceaeRootArteni at a trait1111Asperugo procumbens LBorraginaceaeRoot22222Avena sativa L.GraminaeaMole plant4633346Berberis integerrima Bge.BerberidaceaeFruit3346333463Berberis integerrima Bge.BerberidaceaeFruit3346555 <td>12</td> <td>Aloe vera L.</td> <td>Liliaceae</td> <td>Resin</td> <td>6-8</td> <td>6-8</td> <td></td> <td>10</td> <td>3</td> <td></td>	12	Aloe vera L.	Liliaceae	Resin	6-8	6-8		10	3	
Anethum graveolens L.UmbelliferateSeed $:= 1:2:3:68$ $:= 1:2:3:68$ $:= 1:3:4:6$ $:= 1:3:4$	13	Aloe vera L.	Liliaceae	Leaf & Gel	6-8	6-8		39	32	
Apium graveolens L.UmbelliferaeSed6.81-23-6.8-Arctum lappa L.CompositaeRoot1-34-6Armeniaca vulgaris LRomositaeRoot1-34-6Armeniaca vulgaris LRosaceaeLeaf11-Armeniaca vulgaris LRosaceaeRoot-1-34-6Armeniaca vulgaris LRosaceaeRoot-1Armeniaca vulgaris LRosaceaeRoot-1-3Asperugo procumbens LBorraginaceaeRoot222-Arena sativa L.GramineaeArrial part2222Arena sativa L.GramineaeFruit33465Berberis integerrima Bge.BerberidaceaeFruit33465Berberis vulgaris L.BerberidaceaeFruit33465Brasica oleracea L.CruciferaeLeaf63-5855Bunium persicum (Boiss) B.UnbelliferaeSeed3-5855Bunium persicum (Boiss) B.UnbelliferaeSeed3-5855Bunium persicum (Boiss) B.UnbelliferaeSeed5-585Bunium persicum (Boiss) B.UnbelliferaeSeed5-585Bunium persicum (Boiss) B.Unbelliferae	14	Anethum graveolens L.	Umbelliferae	Seed			1-2-3-8	ı	ı	
Arctium lapa L.CompositaeRoot1-34-6-Armeniaca vugaris LRosaceaeLeaf11-Armeniaca vugaris LRosaceaeLeaf11-Artemisia dracunculus LCompositaeAerial part1Asparagus officinalis L.RoparaginaceaeRoot-1-631Asperugo procumbens LBorraginaceaeRoot-1-3-Avena sativa L.GramineaeAerial part222Avena sativa L.GramineaeFruit33465Berberis integerrima Bge.BerberidaceaeFruit33465Berberis ungaris L.BerberidaceaeFruit33465Brassica napus L.CruciferaeSeedBrassica oleracea L.CruciferaeLeaf63-58Bunum persicum (Boiss)B.UmbelliferaeSeedBunum persicum (Boiss)B.UmbelliferaeSeedBunum persicum (Boiss)B.MolelliferaeSeedFedschBunum persicum (Boiss)B.MolelliferaeSeedFedschFedsch <t< td=""><td>15</td><td>Apium graveolens L.</td><td>Umbelliferae</td><td>Seed</td><td>6-8</td><td>6-8</td><td>1-2-3-6-8</td><td>ı</td><td>ı</td><td></td></t<>	15	Apium graveolens L.	Umbelliferae	Seed	6-8	6-8	1-2-3-6-8	ı	ı	
Armeniaca vulgaris LRosaceaeLeaf1-Artemisia dracunculus LCompositaeAerial part1-631Asparagus officinalis LAsparaginaceaeRoot1-31-631Asperugo procumbens LBorraginaceaeRoot222Avena sativa L.GramineaeAerial part222Avena sativa L.GramineaeWhole plant41-32Avena sativa L.GramineaeFruit3345Berberis integerima Bge.BerberidaceaeFruit33465Berberis vulgaris L.BerberidaceaeFruit33465Brassica napus L.CruciferaeSeed53-5-855Bunium persicum (Boiss) B.UnbelliferaeSeed1-3-5-81-3-5-855Fedtsch.CruciferaeSeed1-3-5-81-3-5-855	16	Arctium lappa L.	Compositae	Root			1-3-4-6	ı	ı	
Artemisia dracunculus LCompositaeAerial part1-631Asparagus officinalis L.AsparaginaceaeRoot1-3-Asperugo procumbens LBorraginaceaeRoot222Asperugo procumbens LBorraginaceaeAerial part222Avena sativa L.GramineaeWhole plant441-32Berberis integerrima Bge.BerberidaceaeFruit33465Berberis uugaris L.BerberidaceaeFruit33465Brassica napus L.CruciferaeSeed53-5-855Bunium persicum (Boiss) BUmbelliferaeSeed63-5-855Bunium persicum (Boiss) BUmbelliferaeSeed71-3-5-855	17	Armeniaca vulgaris L	Rosaceae	Leaf			1	ı	ı	
Asparagus officinalis L.AsparaginaceaeRoot1-3-Asperugo procumbens L.BorraginaceaeAerial part222Avena sativa L.GramineaeWhole plant441-32Avena sativa L.GramineaeFruit334-Berberis integerrima Bge.BerberidaceaeFruit33465Brassica napus L.CruciferaeSeed.3-5-8Burium persicum (Boiss) B.UmbelliferaeSeed.1-3-5-8Burium persicum (Boiss) B.UmbelliferaeSeed.1-3-5-8	18	Artemisia dracunculus L.	Compositae	Aerial part			1-6	31	50	+
Asperugo procumbens LBorraginaceaeArrial part222-Avena sativa L.GramineaeWhole plant441:32Avena sativa L.GramineaeFruit334-Berberis integerrima Bge.BerberidaceaeFruit3346Berberis vulgaris L.BerberidaceaeFruit3346Brassica napus L.CruciferaeSeed335-8-Brassica oleracea L.CruciferaeLeaf635-8-Bunium persicum (Boiss) B.UmbelliferaeSeed1:3-5-8-Fedtsch.CruciferaeSeed1:3-5-8-	19	Asparagus officinalis L.	Asparaginaceae	Root			1-3	I	68	+
Avena sativa L.GramineaeWhole plant41-32Berberis integerrima Bge.BerberidaceaeFruit34-Berberis vulgaris L.BerberidaceaeFruit33465Brassica napus L.CruciferaeSeed3-5-8-Brassica oleracea L.CruciferaeLeaf63-5-8-Bunium persicum (Boiss) B.UmbelliferaeSeed1-3-5-8-Fedtsch.CruciferaeSeed-1-3-5-8-	20	Asperugo procumbens L.	Borraginaceae	Aerial part	2	2	2		52	+
Berberis integerrima Bge.BerberidaceaeFruit34-Berberis vulgaris L.BerberidaceaeFruit3465Brassica napus L.CruciferaeSeed3-5-8-Brassica oleracea L.CruciferaeLeaf63-5-8-Bunium persicum (Boiss) B.UmbelliferaeSeed1-3-5-8-Fedtsch.CruciferaeSeed-1-3-5-8-	21	Avena sativa L.	Gramineae	Whole plant	4	4	1-3	2	ı	
Berberis ulgaris L.BerberidaceaeFruit3465Brassica napus L.CruciferaeSeed3-5-8-Brassica oleracea L.CruciferaeLeaf63-5-8-Bunium persicum (Boiss) B.UmbelliferaeSeed1-3-5-8-Fedtsch.	22	Berberis integerrima Bge.	Berberidaceae	Fruit	3	3	4	ı	81	,
Brassica napus L.CruciferaeSeed3-5-8-Brassica oleracea L.CruciferaeLeaf63-5-8-Bunium persicum (Boiss.)B.UmbelliferaeSeed1-3-5-8-Fedtsch.	23	Berberis vulgaris L.	Berberidaceae	Fruit	3	3	4	65	23	,
Brassica oleracea L.CruciferaeLeaf63-5-8-Bunium persicum (Boiss.)B.UmbelliferaeSeed1-3-5-8-Fedtsch.	24	Brassica napus L.	Cruciferae	Seed			3-5-8	ı	ı	
Bunium persicum (Boiss.)B. Umbelliferae Seed I-3-5-8 - Fedtsch.	25	Brassica oleracea L.	Cruciferae	Leaf	6	9	3-5-8	ı	ı	
	26	Bunium persicum (Boiss.)B. Fedtsch.	Umbelliferae	Seed			1-3-5-8		51	

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						,				+			,		,				,			,			+			
tract Ethanol Extract	72		,	18	1	70	,	60	11	62	1	1	35	1	56	ı	11		57	ı	13	13	1	1	64	,	,	
Water Extract	33			3	,	77			7	51	19	19	67	2	60		ı	ı	64	ı	I	62	I	ı	42	,	16	
Cardiotonic	9	6	6			6	6	6	5	J.	J.		1-3-6	3-6	3-6	3-6	1-3-6	3	7				3	6	6	3	2	
pertensive Diuretic Cardio	6	1	1	3-5	1-3	1-2-3-4-6	2-3	1-3-8	1-2-3-4-6-8	1-2-3-4-6-8	1-2-3-4-6-8	3	1-6		2-3		1-6	1	3-7	1-3-5	1-3-5	1-3-5	1-3-4	5-8	5-8	2-3-4-5-7		
Antihypertensive	1					3-9	3-9	3-9	3-8	3-8	3-6-8	9	1-6	6		3		9	7	C.	6	6				1		
used	Whole plant	Leaf	Leaf	Seed	Fruit	Fruit tail	Fruit tail	Fruit	Leaf	Root	Seed	Seed	The peel	The peel	Fruit	The peel	Leaf	Seed	Flower	Seed	Fruit	Seed	Seed	Seed	Fruit	Seed	Leaf	
•	Compositae	Theaceae	Theaceae	Cannabaceae	Solanaceae	Rosaceae	Rosaceae	Rosaceae	Compositae	Compositae	Compositae	Cucurbitaceae	Rutaceae	Rutaceae	Rutaceae	Rutaceae	Rutaceae	Umbelliferae	Iridaceae	Cucurbitaceae	Cucurbitaceae	Cucurbitaceae	Cucurbitaceae	Rosaceae	Rosaceae	Umbelliferae	Labiatae	
	Calendula officinalis L.	Camellia thea Link.	Camellia thea Link.	Cannabis Sativa L.	Capsicum annuum L.	Cerasus avium (L.) Moench	Cerasus vulgaris Miller.	Cerasus vulgaris Miller	Cichorium intybus L.	Cichorium intybus L.	Cichorium intybus L.	Citrullus vulgaris Schard.	Citrus aurantifolia (Christm.) Swingle	Citrus aurantium L.	Citrus aurantium L.	Citrus Medica L.	Citrus sinensis(L.) Osbeck	Coriandrum sativum L.	Crocus sativus L.	Cucumis melo L.	Cucumis sativus L.	Cucumis sativus L.	Cucurbita pepo Dc.	Cydonia oblonga Mill.	Cydonia oblonga Mill.	Daucus carota L.	Dracocephalum moldavica L.	
	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	

AntihypertensiveDiurreticpart1797991:3:5:791:3:5:791:2:3:693:4:8111	No.	Scientific Name	Family Name	Plant part	Traditional use (literature Source)*	e (literature	Source)*	ACE Inh	ACE Inhibition (%)	Presentce of
Equisetum arvenset.EquisetaceeAerial part1Fab avulgaris Moench.PapilionaceaeSeed3Feus carical.MoraceaeFrut73Feus carical.UmbelliferaeSeed3Feus carical.UmbelliferaeRoot3-45Feuntum vulgare Miller.UmbelliferaeRoot3-46Feunaria parvifora Jam.HumariaceaeAerial part1Feunaria parvifora Jam.CompositaeRoot3-46Hellanthus amus LCompositaeRoot3-6Grycyrthizaglabrat.CompositaeBulb9Hellanthus amus LCompositaeFrut2-9Hibiscue gosspifolius MillMalvaceaeAerial part1Humukus lupulus LCompositaeFrut2-9Hypericam Perforatum LHypericaceaeAerial part1Jugans regal.JugandaceaeSeed5Jugans regal.JugandaceaeKerial part2Jugans regal.JugandaceaeAerial part1Jugans regal.JugandaceaeKerial part2Jugans regal.JugandaceaeAerial part				used	Antihypertensive	Diuretic	Cardiotonic	Water Extract	Ethanol Extract] tannins
Fab avugaris Moench,PaplitonaceaeSeed1Fuce carical.MoraceaeFruit73Four culum vugare Miller,UmbelliferaeSeed13357Foeniculum vugare Miller,UmbelliferaeRoot9Furmaria parvifora lam,EmartaceaeRoot9Furmaria parvifora lam,FurmariaceaeRoot9Gvyyrthiza glabal.PaplitonaceaeRoot9Helianthus unus.l.CompositaeRoot9Helianthus unus.l.CompositaeBulb9Helianthus unus.l.CompositaeFlutter29Humulus tuputus.l.CompositaeHutter19Hypericum Perforatum.l.Hypericum Perforatum19Hypericum Perforatum.l.HypericaeAerialpart19Hypericum Perforatum.l.HypericaeeAerialpart19Hypericum Perforatum.l.HypericaeeAerialpart19Hypericum Perforatum.l.HypericaeeAerialpart19Hypericum Perforatum.l.HypericaeeAerialpart19Hypericum Perforatum.l.HypericaeeAerialpart19Hypericum Perforatum.l.HypericaeeAerialpart19HypericaeeBulbSeed5193567HypericaeeBulbSeed52HypericaeeBulbSeed52HypericaeeBulbSeed52HypericaeeBulbSeed52HypericaeeBulbSe	56	Equisetum arvense L.	Equisetaceae	Aerial part		1				
Heure artical.MoraceaeFutir73Feeniculum vulgare Miller.UmbelliferaeSeed13457Feeniculum vulgare Miller.UmbelliferaeRoot9Fumaria parvifora lam.FumariaceaeRoot9Fumaria parvifora lam.FumariaceaeRoot9Gvyrthiza glabral.RopitonaceaeRoot9Helianthus amus l.CompositaeRoot9Helianthus unberosur.CompositaeBulb9Helianthus unberosur.CompositaeFlower14Hypericum Perforatum LAnvaceaeFrutt29Hypsopus officinalis l.LabhatcaeAerial part12Hypericum Perforatum LHypericaeRoot25Hypericum Perforatum LJugandaceaeFrutt29Hypericum Perforatum LLabhatcaeAerial part12Hypericum Perforatum LHypericaeAerial part13Hypericum Perforatum LBulbatcaeAerial part13Hypericum Perforatum LHypericaeAerial part13Hypericum Perforatum LBulbatcaeAerial part13Hypericum Perforatum LHypericaeAerial part13Hypericum Perforatum LBulbatcaeAerial part13Hypericum Perforatum LBulbatcaeAerial part13Hypericum Perforatum LBulbatcaeAerial part13Hypericum Perforatum LBulbatcaeAerial part2Hypericum Perforatum LAerial part <t< td=""><td>57</td><td>Faba vulgaris Moench.</td><td>Papilionaceae</td><td>Seed</td><td></td><td>6</td><td></td><td>50</td><td></td><td>+</td></t<>	57	Faba vulgaris Moench.	Papilionaceae	Seed		6		50		+
Feeniculum vulgare Miller.UmbelliferaeSeed3-3-5Feeniculum vulgare Miller.UmbelliferaeRoot2-3-6Fumaria parviflora Lam.HumariaceaeRoot3-4-8Gycyrthiza glabra L.PapilionaceaeRoot3-6-Gycyrthiza glabra L.CompositaeSeed3-6Helianthus amus LCompositaeBulb9Helianthus amus LCompositaeBulb9Helianthus tuberosus L.CompositaeBulb2-9Humulus lupulus LCompositaeEruit2-9Humulus lupulus LCompositaeAerial part1-1Humulus lupulus LLamabaceaeAerial part1-2-3-5Humulus lupulus LLamabaceaeAerial part1-2-3-5Humulus lupulus LLabitaeAerial part1-2-3-5Humulus lupulus LLabitaeSeed5Humulus lupulus LLabitaeSeed5Humulus lupulus LLabitaeSeed5Humulus lupulus LLabitaeSeed5Humulus lupulus LLabitaeSeed5Latuca sativa LLabitaeSeed5Latura sativa LLabitaeLeaf1-5Latura sativa LLabitaeSeed5Latura sativa LLabitaeSeed5Latura sativa LLabitaeSeed5Latura sativa LLabitaeSeed5Latura sativa LLabitaeSeed5Latura sativa LLabitaeAe	58	Ficus carica L.	Moraceae	Fruit	7	ŝ	3-6	53	7	,
Foenclum vulgare Miller, Fumaria parviffora Lam.Root2.3-6Fumaria parviffora Lam.Fumaria parviffora Lam.Aerial part3-48Gycyrthiza gabrat.PapilionaceaeRoot93-66Helianthus amust.CompositaeBulb93-66Helianthus unust.CompositaeBulb91Helianthus tuberosust.CompositaeBulb93-66Helianthus tuberosust.CompositaeBulb93-66Humulus tuputs.CompositaeFruit2-91Humulus tuputs.MalvaceaeFruit2-93-3567Humulus tuputs.LambaceaeAerial part11Uglans regat.Jugland ceaeFruit2-93-3567Uglans regat.Jugland ceaeSeed622Latruc satival.LabiateeSeed622Latruc satival.Jugland ceaeLaff111Latruc satival.LabiateeLaff122Latruc satival.LabiateeLaff112Latruc satival.LabiateeLaff122Latruc satival.LabiateeLaff122Latruc satival.LabiateeLaff122Latruc satival.LabiateeLaff122Latruc satival.LabiateeLaff122Latruc satival.LabiateeLaff12<	59	Foeniculum vulgare Miller.	Umbelliferae	Seed		1-3-5-7	9	56	7	,
Fumaria parviflora lam.Humaria createAerial part3-48Glycyrthiza glabra LPapilionaccaeRoot93-6Heliamthus amus LCompositaeSeed1Heliamthus amus LCompositaeBulb9Heliamthus tuberosus LCompositaeBulb9Heliamthus tuberosus LCompositaeBulb29Heliamthus tuberosus LCompositaeFruit29Humulus tupulus LCompositaeRent29Hypericum Perforatum LHypericaceaeAerial part1Hypericum Perforatum LJuglandaceaeFruit29Hypericum Perforatum LJuglandaceaeAerial part1Juglans rega LJuglandaceaeSeed5Juglans rega LJuglandaceaeSeed5Juglans rega LJuglandaceaeSeed6Juglans rega LJuglandaceaeSeed7Juglans rega LJuglandaceaeSeed6Juglans rega LJuglandaceaeSeed2Jugandu officinalis LJublaceaeLatrus nobilis L1Jurus nobilis LJublaceaeJublaceae1Jurus nobilis LJubaceaeLatrus nobilis L1Jubra citritofora H & et KJubra citritofora H & et K3Juppia citritofora H & et KJubra citritofora H & et K1Juppia citritofora H & et KJubra citritofora H & et K1Juppia citritofora H & et KJubra citritofora H & et K1Juppia citritofora	09	Foeniculum vulgare Miller.	Umbelliferae	Root		1-2-3-6	9	50	61	
Glycyrthizaglabra.L.PaplilonaceaeRoot936Helianthus amus.L.CompositaeSeed1Helianthus amus.L.CompositaeHower4Helianthus tuberosus.L.CompositaeBulb9Humulus tuperosus.L.CompositaeBulb29Humulus tuperosus.L.CompositaeEruit29Hypericum Perforatum.L.HypericaeeFruit29Hypericum Perforatum.L.HypericaeeAerial part1Hyseopus officinalis.L.LabiataeAerial part1Jugans regia.L.JugandaceaeKruit5Jugans regia.L.JugandaceaeSeed5Lactuca sativa.L.OunositaeSeed5Lactuca sativa.L.LadiataeSeed5Laurantia roykean (Wall.)RthLadiataeLadiata5Laurantia roykean (Wall.)RthLadiataeLadiata5Laurantia roykean (Wall.)RthLadiataeLadiata5Laurantia roykean (Wall.)RthLadiataeLadiata5Laurantia roykean (Wall.)RthLadiataeLadiatae1Laurantia roykean (Wall.)RthLadiataeSeed5Laurantia roykean (Wall.)RthLadiataeLadiatae1Laurantia roykean (Wall.)RthLadiataeLadiatae1Laurantia roykean (Walu.)LadiataeLadiatae1Laurantia roykean (Walu.)LadiataeLadiatae1Laurantia roykean (Walu.)LadiataeLadiatae1<	61	Fumaria parviflora Lam.	Fumariaceae	Aerial part		3-4-8		ı	ı	
HelianthusamustCompositaeSeed1Helianthusamust.CompositaeFlower4Helianthus tuberosust.CompositaeBulb94Humuls lupulust.CompositaeBulb94Humuls upulust.CompositaeFruit294Hyserus perforatumt.HypericaceaeFruit291Hyserus perforatumt.HypericaceaeAerial part11Uglans regiat.UglandeceaeFruit21Uglans regiat.UglandeceaeSeed63:567Jugans regiat.UglandeceaeSeed63:567Laturus ativat.CompositaeSeed63:567Laturus noblist.LabiataeSeed63:567Laurus noblist.LabiataeLeaf63:567Laurus noblist.LabiataeLeaf62Laurus noblist.LabiataeKerla part11Laurus	62	Glycyrrhiza glabra L.	Papilionaceae	Root	6	3-6		ı	53	,
Helianthus annus LCompositaeFlowerSlower4Helianthus tuberosus L.CompositaeBulb91Hibiscus gossypifolius Mill.MalvaceaeEruit2.91Humulus lupulus LCamabaceaeFruit2.91Humulus lupulus LCamabaceaeHower11Hysopus officinalis L.LabiateaAerial part11Uglans regia L.Juglans regia LJuglandeceaeSeed55Juglans regia L.JuglandeceaeSeed63-5675Juglans regia L.JuglandeceaeSeed63-5675Juglans regia L.JuglandeceaeSeed63-5672Juglans regia L.JuglandeceaeSeed63-5672Juglans regia L.JuglandeceaeSeed63-5672Juglans regia L.JuglandeceaeSeed63-5672Juglans regia L.JuglandeceaeSeed63-5672Jacutu as ativa L.CompositaeSeed711Laurus noblis L.Laurus noblis L.Laurus noblis LJuglandeceae3-673Laurus noblis L.Laurus noblis L.LauraceaeLeafAerial part1Laurus noblis L.Laurus noblis L.LauraceaeLeafAerial part1Laurus noblis L.Laurus noblis L.LauraceaeLeafAerial part1Laurus noblis L.LauraceaeLeafA	63	Helianthus annus L	Compositae	Seed		1	6	61	,	,
Helianthus tuberosusCompositaeBulb9Hibiscus gossypifolius Mill.MalvaceaeFruit29Humulus lupulus LCamabaceaeFlower14Hypericum Perforatum L.CamabaceaeAerial part12335Hysepus officinalis LLabiataeAerial part1Uglans rega L.Juglans regia LJugland ceae55Juglans rega L.Jugland ceaeSeed6Juglans rega L.Jugland ceaeSeed6Juglans rega L.Jugland ceaeSeed6Juglans rega L.Jugland ceaeSeed7Juglans rega L.Jugland ceaeSeed6Juglans rega L.Jugland ceaeSeed7Juguas rega L.Jugland ceaeSeed6Jaruus noblis L.LabiataeSeed7Laturus noblis L.LabiataeLaff1Lawandula officinalis L.LabiataeLeaf35-67Lawandula officinalis L.LabiataeSeed7Lawandula officinalis L.LabiataeLaff1-3-367Lawandula officinalis L.LabiataeAerial part6Lawandula officinalis L.LabiataeKerial part1-3-367Lawandula officinalis L.LabiataeAerial part2Lawandula officinalis L.LaffAerial part1-3-367Lawandula officinalis L.Malva sylvertris L.Malva sylvertris L.1-3-366Malva sylvertris L.Malva sylvertris L.Malva sylvertris L.1-3-3	64	Helianthus annus L	Compositae	Flower		4	6	,	,	
Hibiscue gossypfiolius MILMalvaceaeFruit29Humulus lupulus LCamabaceaeFlower1-4Hypericum Perforatum LHypericaceaeAerial part1-2-35Hysepus officinalis L.LabiataeAerial part1Juglans regia LJuglans regia LJuglans regia1Juglans regia LJuglans regia LJuglans regia2Juglans regia LJuglans regia LJuglans regia3Juglans regia LJuglans regia22Juglans regia LJuglans regia22Laurus nobilis LLauraceaeLeaf52Laurus nobilis LLauraceaeLeaf12Lavandula officinalis LLubraceaeKuholeplant52Lavandula officinalis LLubraceaeAerial part52Lavandula officinalis LLavaceaeKuholeplant62Lavandula officinalis LLavaceaeAerial part52Lavandula officinalis ULKuholeplant852LavacueaeLavaceaeAerial part72<	65	Helianthus tuberosus L.	Compositae	Bulb	6			71	,	,
Humulus lupulus LCamabaceaeHower 14 Hypericum Perforatum LHypericaceaeAerial part1Hyssopus officinalis LLabiataeAerial part1Hyssopus officinalis LJuglandsceaeKruit5Juglans regia LJuglandsceaeSeed5Juglans regia LJuglandsceaeSeed5Lactuca sativa LCompositaeSeed6Lactuca sativa LCompositaeSeed5Laurus nobilis LLaurus nobilis LLauraceaeLeaf1Laurus nobilis LLauraceaeLeaf562Laurus nobilis LLabiataeLeaf3-5-72Laurus nobilis LLabiataeLeaf3-5-72Laurus nobilis LLabiataeLeaf3-5-72Laurus nobilis LLabiataeLeaf3-5-72Lavonia inermis LLythraceaeAerial part2Lippia citriodora H.B. et KVerbenaceaeAerial part2Lippia citriodora H.B. et KVerbenaceaeAerial part2Malva sylvestris LMalva sylvestris LMalva sylvestris LMalva sylvestris L13-3-5-6Malva sylvestris LMalva sylvestris LMalva sylvestris LMalva sylvestris L13-3-5-6Malva sylvestris LMalva sylvestris LMalva sylvestris L13-3-5-6Malva sylvestris LMalva sylvestris LMalva sylvestris L13-3-5-6Malva sylvestris LMalva sylvestris LMalva sylvestris L13-3	99	Hibiscus gossypifolius Mill.	Malvaceae	Fruit	2-9			,	73	,
Hypericum Perforatum LHypericaceeAerial part112335Hyssopus officinalis LLabitaceeAerial part11Juglans regia LJuglandceaeFruit55Juglans regia LJuglandceaeSeed65Juglans regia LJuglandceaeSeed63Juglans regia LCompositaeSeed63Lactuca sativa LCompositaeSeed63Laurus noblifs LLancaceaeLancaceaeLeaf1Laurus noblifs LLauraceaeLeaf33Laurus noblifs LLabitaceaeLeaf33Laurus noblifs LLabitaceaeLeaf33Lavandula officinalis LLabitaceaeLeaf33Lavandula officinalis LLabitaceaeLeaf33Lavandula officinalis LLabitaceaeLeaf33Lavandula officinalis LLabitaceaeAerial part2Lavandula officinalis LLabitaceaeAerial part2Lavandula officinalis LNalva sylvestris LNalva sylvestris L3Malva sylvestris LMalva sylvestris LMalva sylvestris L1Matricaria chanonnilla LCompositaeHower1Matricaria chanonnilla LCompositaeHower1Matricaria chanonnilla LCompositaeHower1Matricaria chanonnilla LCompositaeHower1Matricaria chanonnilla LCompositae<	67	Humulus lupulus L	Cannabaceae	Flower		1-4		11	40	
Hyssopus officinalist.LabiataeAerial part11Juglans regia L.JuglandaceaeSeed5Juglans regia L.JuglandaceaeSeed5Juglans regia L.CompositaeSeed5Lactuca sativa LCompositaeSeed5Laurus nobilis L.LauraceaeLeaf1Laurus nobilis L.LauraceaeLeaf2Laurus nobilis L.LauraceaeLeaf5Laurus nobilis L.LabiataeVhole plant5Lawondula officinalis L.LabiataeLeaf7Lawondula officinalis L.LabiataeLeaf7Lawondula officinalis L.LabiataeKhole plant5Lawona inermis L.LythraceaeLeaf76Lawona inermis L.LabiataeAerial part2Lippia citriodora H.B.et KVerbenaceaeAerial part2Lippia citriodora H.B.et KVerbenaceaeAerial part2Lippia citriodora H.B.et KVerbenaceaeAerial part2Malus orientalis Ug.RosaceaeAerial part2Malva sylvestris L.Malva ceaeMole plant1-3-56Malva sylvestris L.Malva ceaeMole plant1-3-356Malva sylvestris L.Malva ceaeMole plant1-3-356Malva sylvestris L.Malva ceaeMole plant1-3-356Marcaria chamonilla L.Malva ceaeMole plant1-3-356Marcaria chamonilla L.Malva ceaeMole plant1-3-356 </td <td>68</td> <td>Hypericum Perforatum L.</td> <td>Hypericaceae</td> <td>Aerial part</td> <td></td> <td>1-2-3-5</td> <td></td> <td>,</td> <td>66</td> <td>,</td>	68	Hypericum Perforatum L.	Hypericaceae	Aerial part		1-2-3-5		,	66	,
Juglans regia L.Jugland ceaeFruit5Juglans regia L.Jugland ceaeSeed5Juglans regia L.Jugland ceaeSeed6Lactuca sativa L.CompositaeSeed6Lanus nobilis L.CompositaeSeed2Laurus nobilis L.LauraceaeLeef2Laurus nobilis L.LauraceaeLeef2Lavandula officinalis L.LauraceaeLeef3Lawondula officinalis L.LauraceaeLeef3Lawondula officinalis L.LabiataeWhole plant5Lawondula officinalis L.LabiataeWhole plant5Lawondula officinalis L.LabiataeLeef3Lawondula officinalis L.LabiataeWhole plant5Lawondula officinalis L.LabiataeLeef16Lawondula officinalis L.LabiataeNetrial part2Lippia citriodora H.B. et KVerbenaceaeAerial part2Lippia citriodora H.B. et KVerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeMarti arguit9133-56Malva sylvestris L.Malva sylvestris L.Malva sylvestris L.Malva sylvestris L.12-33-56Matricaria chamonilla L.CompositaeFruit12-33-56133-56Matricaria chamonilla L.Malva sylvestris L.Malva sylvestris L.13-35-67Matricaria chamonilla L.CompositaeFruit13-57-7Matricaria chamonilla L.CompositaeFlower	69	Hyssopus officinalis L.	Labiatae	Aerial part	1	1		,		
Juglams regialJuglandaceaeSeed5Lactuca satival.CompositaeSeed635-67Laltemantia royleana (Wall.)BthLabitateeSeed2Laurus nobilislLauraceaeLeaf2Lavandula officinalis L.LauraceaeLeaf3Lavandula officinalis L.LabitateeWholeplant5Lavandula officinalis L.LabitateeLeaf3Lavandula officinalis L.LabitateeLeaf3Lavandula officinalis L.LabitateeLeaf3Lavandula officinalis L.LabitateeLeaf3Lavandula officinalis L.LabitateeLeaf3Lavandula officinalis L.LabitateeLeaf3Lippia citriodora H.B. et K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ug.RosaceaeAerial part2Malva sylvestris L.Malva sylvestris L.Malvaceae1Matricaria chamonilla L.CompositaeHower1Matricaria chamonilla L.CompositaeHower <td>70</td> <td>Juglans regia L.</td> <td>Juglandaceae</td> <td>Fruit</td> <td></td> <td>5</td> <td></td> <td></td> <td>42</td> <td></td>	70	Juglans regia L.	Juglandaceae	Fruit		5			42	
Lactuca sativa LCompositaeSeed63-5-67Lallemantia royleana (Wall.)BthLabiataeSeed2Laurus nobilis L.Laurus eaeLeaf1Laurus nobilis L.LauraceaeLeaf5Lavandula officinalis L.LabiataeWholeplant5-6Lawsonia inermis L.LythraceaeLeaf3-6-7Lawsonia inermis L.LythraceaeLeaf1-6Lepidium sativum L.LythraceaeLeaf1-6Lippia citriodora H.B et K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeAerial part1-3-3-67Malva sylvestris L.Malva sylvestris L.Malva sylvestris L.Malva sylvestris L.Matricaria chanomilla L.CompositaeHower1-3-3-67Matricaria chanomilla L.CompositaeHower1-3-3-67Matricaria chanomilla L.Malva sylvestris L.Malva sylvestris L.1-3-3-67Matricaria chanomilla L.CompositaeHower1-3-3-67Matricaria chanomilla L.Compositae1-3-3-671-3-3-67Matricaria chanomilla L.Malva sylvestris L.1-3-3-67Matricaria chanomilla L.Compositae1-3-3-67Matricaria chanomilla L.Malva sylvestris L.1-3-3-67Matricaria chanomilla L.Compositae1-3-3-67Matricaria chanomilla L.Compositae </td <td>71</td> <td>Juglans regia L.</td> <td>Juglandaceae</td> <td>Seed</td> <td></td> <td>5</td> <td></td> <td></td> <td></td> <td></td>	71	Juglans regia L.	Juglandaceae	Seed		5				
Laltemantia royleana (Wall.)BthLabiataeSeed2Laurus nobilis L.LauraceaeLeaf1Laurus nobilis L.LauraceaeLeaf5.61Lavandula officinalis L.LabiataeWholeplant5.63Lawsonia internis L.LythraceaeLeaf3.6-73Lepidium sativum L.CurciferaeLeaf1.61.23.6-7Lippia citriodora H.B. et K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeThe peel91.3-6-6Malva sylvestris L.MalvaceaeFruit1.2-3-5-6Matricaria chamonilla L.CompositeHower1.3-6-7Matricaria chamonilla L.CompositeHower1.3-6-7 <trtr>Matricaria chamonilla L.</trtr>	72	Lactuca sativa L.	Compositae	Seed	6	3-5-6-7	3-6	28		
Laurus nobilis L.LauraceaeLeaf1Lavandula officinalis L.LabiataeWholeplant5-63Lawsonia inermis L.LubthraceaeLeaf3-6-73Lepidium sativum L.LurciferaeLeaf1-61-2-3-6-7Lippia citriodora H.Bet K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ug.RosaceaeThe peel91-3-6Malva sylvestris L.MalvaceaeFruit1-2-3-5-6Matricaria chamonilla L.CompositeHower1-2-3-5-6Matricaria chamonilla L.CompositeHower1-3-5-6	73	Lallemantia royleana (Wall.)Bth	Labiatae	Seed		2	9	,		
Lavandula officinalis.LabiataeWhole plant5-6Lawsonia inermis.L.LythraceaeLeaf3-6-73Lepidium sativum.L.LythraceaeLeaf1-61-2-3-6-7Lippia citriodora H.B et K.VerbenaceaeAerial part2Lippia citriodora H.B et K.VerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeAerial part2Malus sylvestris.L.MalvaceaeFruit1-3-5-6Matricaria chanomilla.CompositeHower3-6-7Matricaria chanomilla.CompositeHower3-6-7	74	Laurus nobilis L.	Lauraceae	Leaf		1		,	51	+
Lawsonia inermis L.LythraceaeLeaf36-73Lepidium sativum L.CurciferaeLeaf161-23-67Lippia citriodora H.B et K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeThe peel91-3-66Malva sylvestris L.MalvaceaeFruit1-3-56Matricaria chamonilla L.CompositaeHower3-671-3-56	75	Lavandula officinalis L.	Labiatae	Whole plant	5-6		3	,		
Lepidium sativum L.CurciferaeLeaf1-61-23-6-7Lippia citriodora H.B et K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeThe peel91-3-6Malva sylvestris L.MalvaceaeFruit1-2-3-5-6Malva sylvestris L.MalvaceaeWhole plant1-2-3-5-6Matricaria chamonilla L.CompositaeHower3-6-71-3-5-6	76	Lawsonia inermis L.	Lythraceae	Leaf	3-6-7	3		55	68	+
Lippia citriodora H.B et K.VerbenaceaeAerial part2Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeThe peel91:3-6Malva sylvestris L.MalvaceaeFruit1:2-3-5-6Malva sylvestris L.MalvaceaeWhole plant1:2-3-5-6Matricaria chamomilla L.CompositaeFlower3-6-7	7	Lepidium sativum L.	Curciferae	Leaf	1-6	1-2-3-6-7		21		
Lippia citriodora H.B. et K.VerbenaceaeAerial part2Malus orientalis Ugl.RosaceaeThe peel91-3-6Malva sylvestris L.MalvaceaeFruit1-2-3-5-6Malva sylvestris L.MalvaceaeWhole plant1-2-3-5-6Matricaria chamomilla L.CompositaeHower3-6-71-3-5-6-7	78	Lippia citriodora H.B et K.	Verbenaceae	Aerial part		2	1-6	,		
Malus orientalis Ugl.RosaceaeThe peel91-3-6Malva sylvestris L.MalvaceaeFruit1-2-3-5-6Malva sylvestris L.MalvaceaeWhole plant1-2-3-5-6Matricaria chamomilla L.CompositaeFlower3-6-7	79	Lippia citriodora H.B. et K.	Verbenaceae	Aerial part		2	1-6			
Malva sylvestris L. Malvaceae Fruit Malva sylvestris L. Malvaceae Whole plant Matricaria chamomilla L. Compositae Flower 3-6-7	80	Malus orientalis Ugl.	Rosaceae	The peel	6	1-3-6	3-5-6		63	+
Malva sylvestris L. Malvaceae Whole plant Matricaria chamomilla L. Compositae Flower 3-6-7	81	Malva sylvestris L.	Malvaceae	Fruit		1-2-3-5-6				
Matricaria chamomilla L. Compositae Flower 3-6-7	82	Malva sylvestris L.	Malvaceae	Whole plant		1-2-3-5-6			72	
	83	Matricaria chamomilla L.	Compositae	Flower	3-6-7	1-3-5-6-7		5	1	
84 Medicago sativa L. Papilionaceae Seed 9	84	Medicago sativa L.	Papilionaceae	Seed		6			69	r

 Mentha longifolia (L.) Hudsom Mentha piperita L. Morus alba L. Morus nigra L. Morus nigra L. Noigella sativa L. Ocimum Basillicum L. Ocimum Basillicum L. Origanum vulgare L. Papaver somniferum L. Peganum harmala L. Persica vulgaris Miller. Petroselinum hortense Hoffin. Petroselinum hortense Hoffin. Pininella anisum L. Pininella anisum L. Pistacia vera L. Pininella anisum L. Pininella anisum L. Pininella anisum L. Pininella anisum L. 	Labiatae	r		(an incommunity) and minor innit				
	Labiatae	used	Antihypertensive	Diuretic	Cardiotonic	Cardiotonic Water Extract	Ethanol Extract	tannins
		Aerial part		1-5	1	1	,	
	Labiatae	Leaf	6	3-6	1-3	,	,	
	Moraceae	Leaf	1	3-5-7		26	53	,
	Moraceae	Leaf	2	J.		67	50	
	Ranunculaceae	Seed		3-4-5		I	1	
	Labiatae	Seed	9	3-6-7	3-5-6	ı	,	
	Oleaceae	Leaf	1-2-6	6-7	1	ı	,	
	Labiatae	Aerial part		1-2-3	3-6	ı	,	
	Papaveraceae	Seed		6	6	28	7	
	Zygophyllaceae	Seed	3-9	3-5		72	84	
	Geraniaceae	Aerial part	1		1	ı	,	
	Rosaceae	Leaf		1		ı	,	
	Umbelliferae	Leaf	6	2-4-6		68	,	,
_	Umbelliferae	Seed	9	2-4-6		18	,	
_	Umbelliferae	Seed		1-2-5-7	1	ı	,	
	Anacardiaceae	The peel			3	ı	,	
	Papilionaceae	Seed		1-3-7		ı	,	
	Liliaceae	Root	1-3	1-2-7	3-6	ı	,	
	Portulacaceae	Seed	6-5	1-3-6-7		5	32	
	Punicaceae (Granata- ceae)	Flower	5	3-5-6-7	7	55		
105 Pyrus communis L	Rosaceae	Fruit	9	1-6	9	I	1	
106 Pyrus communis L	Rosaceae	Leaf	6	1-6	6		,	
107 Rheum ribes L.	Polygonaceae	Steam & Flower			9		40	
108 Rhus coriaria L	Anacardiaceae	Fruit	6	3		ı	1	
109 Rosa damascena Mill.	Rosaceae	Flower	5	6	3-5-6	ı	,	
110 Rosmarinus officinalis L.	Labiatae	Aerial part		1-3-4	6			
111 Rubia tinctorum L.	Rubiaceae	Root	6	4		32	69	,
112 Rubus hyrcanus Juz.	Rosaceae	Leaf		1-2-3-6-7			60	
113 Ruta graveolens L.	Rutaceae	Leaf	3-4	1-3-7	3-4			

No.	Scientific Name	Family Name	Plant part used	Traditional use (literature Source)*	e (literature	Source)*	ACEInh	ACE Inhibition (%)	Presentce of tannins
				Antihypertensive	Diuretic	Cardiotonic	Water Extract	Ethanol Extract	
114	Salix babylonica L.	Salicaceae	Leaf		3-6-7	3-6	1	1	
115	Solanum Melongena L	Solanaceae	Fruit		1-3-6	6		,	
116	Solanum nigrum L.	Solanaceae	Fruit		9		19	C.	
117	Solanum tuberosum L.	Solanaceae	Bulb		6	6	4		
118	Spinacia oleracea L	Chenopodiaceae	Leaf		2-36				
119	Spinacia oleracea L	Chenopodiaceae	Seed		2-3-6		50	64	
120	Taraxacum officinale Weber	Compositae	Whole plant		1-5-6	6		28	
121	Teucrium polium L.	Labiatae	Flower	6		6	1	52	
122	Tribulus terrestris L.	Zygophyllaceae	Fruit		1-3		56	37	
123	Trifolium pratense L	Papilionacea	Seed			3-6	1	1	
124	Trigonella Foenum-graecum L.	Papilionacea	Leaf	1-6	6		55	23	,
125	Trigonella Foenum-graecum L.	Papilionaceae	Seed	1-6	9		,	,	
126	Urtica pilulifera L.	Urticaceae	Seed	2-6			,	66	+
127	Vaccinium Arctostaphylos L.	Ericaceae	Seed	2-6			,	51	
128	Valeriana officinalis L	Valerianaceae	Root		6	4-6	,	55	+
129	Viola odorata L.	Violaceae	Flower	5	3-4		3	,	
130	Vitis vinifera L.	Vitaceae (Ampelidaceae)	Leaf	1-6	1-4-6	9	,	35	
131	Zataria multiflora Boiss.	Labiatae	Aerial part		1-3-5		,	,	,
132	Zea mays L.	Gramineae	Fruit	4	1-2-6	1-4	60	75	
133	Zingiber officinale Rocs.	Zingiberaceae	Root		6-7		31	10	
134	Ziziphus vulgaris L.	Rhamnaceae	Fruit	2-6	1-6	3	,	68	+
135	Ziziphus vulgaris L.	Rhamnaceae	Leaf	2-6		3	50	62	
Literati	Literature Source:	-							

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This study showed that the water extract didn't give the same result as ethanol extract in each spices and this two groups showed significant differences, like the study of Adseren et al. (1997) (13). On the other hand, this is of considerable magnitude, no less when it is taken into account that the alleged effects are not necessarily medicated by ACE inhibition.

We have found a rather high positive hit rate (29%) among this figure which is based on crude extracts and inhibits the enzyme by more than 50% when there is 0.33 mg test compound in 1 ml assay volume, as described by Elbi and Wagner (1991) (17). However, the limit of 50% is a hypothetical value which is difficult to justify since we do not know anything about the compounds present in the crude extracts.

Several crude extracts in the present investigation have given an inhibition in the interval from 35 to 50% and should thus be regarded as negative. Our suggestion is that sample with an inhibition in this interval could well be worth a reinvestigation but this should be based upon a new collection of the plant material.

In some cases, identical plant materials were collected in different localities which also resulted in differences in ACE inhibition (Hibiscus gossypifolius Mill.). Nyman et al. (1998) reached the same conclusion (12); these contradictory results probably arise from differences in the ages of the plants specimens assayed and/or from variations in environmental conditions.

The presence of a strong ACE inhibitory activity, however, does not necessarily imply that the species could provide powerful antihypertensive drugs. As discussed by Wagner et al. (1991) (17), some flavonoids may show an in vitro activity due to the generation of chelate complexes within the active center of ACE. It must be remembered that if the plant exhibits low levels of ACE inhibitory activity, it may act on a different mechanism causing hypertension; as a result, it could be used as an antihypertensive agent.

In conclusion, the screening report in this paper has led to the identification of two species from the Persian flora with high potential antihypertensive activity by inhibition more than that of 80% of ACE activity: Peganum harmala L. and Berberis integrrima Bge. Berberis integrrima Bge is used traditionally in Persian as antihypertensive and, then, our results corroborated its popular use.

Further studies on the pure compounds isolated from the active extracts are necessary, and work in this area is presently going on in our laboratory.

Due to the abundant of plants in Persian, there lies an untapped reservoir of potentially useful chemical compounds; unique templates that could serve as the starting points for analog preparation by chemist, as well as interesting tools that can be applied to achieve a better understanding of biological processes involved in hypertension.

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