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Pharmacological Actions and Potential Neuroprotective Effects of Rhus coriaria L. and Echium amoenum L.: A Brief Review

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Corresponding Author:
Ms. Saba Khalilpour,
Saba Khalilpour, Department of Pharmacology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden 11800, Pulau Penang - Malaysia

Submitting Author:
Mrs. Ghazaleh Behnammanesh,
Ghazaleh Behnammanesh , Department of Pharmacology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden 11800 - Malaysia

Other Authors:
Dr. Aman Shah Abdul Majid,
Abdul Majid, AS, Advanced Medical and Dental Institute, Universiti Sains Malaysia, 13200 Bertam, Kepala Batas, Penang - Malaysia

Dr. Amin Malik Shah Abdul Majid,
Abdul majid, AMS, Department of Pharmacology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden 11800, Pulau Penang - Malaysia

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Author(s): Behnammanesh G, Khalilpour S, Abdul Majid A, Abdul Majid A

Abstract

In the present paper two plants (*Rhus coriaria L*. and *Echium amoenum L*.) have been reviewed for their pharmacological aspects. *Rhus coriaria L*. is a traditional medicinal herb belonging to the family of Anacardiaceae and variously known as Sicilian Sumac, Elm-Leaved Sumach, Tanner's Sumach. Historically, *Rhus coriaria L.* has possessed remarkable medicinal value. The leaves and berries of this herb have been used extensively as remedies in folk medicine. *Echium amoenum L.* is an annual herb belonging to the family of Boraginaceae. Flowers, stems, roots and leaves from this plant are used for medicinal purposes. Since, they have long been used in traditional medicine; it represents an interesting source to search for various pharmacological activities. The significant antioxidant efficacy of these herbs has been reported in previous studies. Antioxidants may have neuroprotective and neuroregenerative functions, by reducing or reversing cellular damage and by slowing the progression of neuronal cell loss. In conclusion, the plants contain antioxidant principles that may explain their neuroprotective properties and can be considered as a topic for future research studies.

Background

Plant-derived antioxidants are regarded as effective in controlling the effects of oxidative damage, and hence have had an influence in what people eat and drink (Sun A. Y., 2002). As the focus of medicine shifts from treatment of manifest disease to prevention, herbal medicine (with its four pillars of phytochemistry, phytopharmacy, phytopharmacology and phytotherapy) has come into consideration, being a renaissance of age-old human tradition (Weiss and Fintelmann, 2000). The ‘Green’ movement in Western society has changed attitudes in the general population, many of whom now consider naturally derived substances and extracts to be inherently safer and more desirable than synthetic chemical products, with the net effect of an increase in sales of herbal preparations (Houghton P.J. , 1998, Capasso R., 2000). About 80% of people in the developing world rely on phytomedicine for primary healthcare for man and livestock (Mccorkle C. M., 1996). However, despite the growing demand for phytotherapeutic agents, most medical and veterinary professionals still distrust the use of herbal medicines, due to the lack of scientific evidence of efficacy and safety. Hence there is a need for scientific validation before plant-derived extracts gain wider acceptance and use. In this regard, many plants have nevertheless been scientifically proved to be effective in control of acute and chronic nervous disorders. As herbal extracts are a complex mixture of compounds, it is difficult to evaluate their active molecules, mode of action, bioavailability and pharmacokinetics, and toxicity issues (Thompson, 1997). There is ample scientific and empirical evidence supporting the use of plant-derived antioxidants for the control of neurodegenerative disorders.

Botanical Description of Rhus coriaria L. and Echium amoenum L.

Rhus coriaria L. is a traditional medicinal herb belonging to the family of Anacardiaceae and variously known as Sicilian Sumac, Elm-Leaved Sumach and Tanner's Sumach (Sumac, 2014, Beltsville, 2007). The term sumac is derived from the Syriac word “sumâqâ”, meaning red. It is a common name belonging to the Rhus genus with more than 250 species of Anacardiaceae family. The genus Rhus has been introduced in tropical and temperate non-agriculturally viable regions. Rhus has medicinal and other applications in different cultures and geographical locations (Jalal Pourahmad, 2010).

Tanner's Sumach is a wild herb native to the Mediterranean region and is widespread from the Canary Islands, southern Europe, Turkey and Middle Eastern countries to Afghanistan (Beretta, 2009, Jalal Pourahmad, 2010, Bozan B, 2003, Candan and Sokmen, 2004b). Rhus coriaria L. is an annual plant which can attain small tree or a shrub height from 1 to 3 meters. It can grow 1000 meters above sea level

and is usually found in stony places (Kirjassa and Gathered by John Gerarde of London Master in Chirvrgeria, 1597). It grows on dry rocky slopes in forests and in mountainous areas, with high tolerance of temperatures as low as -20 °C (Kirjassa and Gathered by John Gerarde of London Master in Chirvrgeria, 1597).

Sicilian Sumac has alternate and odd-pinnate leaves. The surface of the leaf is dark green above and gray below, with 4-8 pairs of opposite toothed leaflets (Mills, 2010). The leaf is 15-20 cm in length and 1.5-3 cm in width (Pharmacy, 2014). The flowers are small, inconspicuous greenish-white and unisexual. They are clustered in large male and female panicles. Male panicles are 25 cm long and female panicles are 15 cm long with conical, apical and axillary buds. The petals are white, ovate and oblong and sepals are green rounded-ovate (Pharmacy, 2014). The plant flowers in northern hemisphere months of June and July, and the fruits are ripe in September and October. Sometimes a secondary bloom occurs in the fall (Pharmacy, 2014). The fruit is small and brownish-purple or drupe, with red seeds that are kidney-shaped or spherical (Mills, 2010, Chittenden, 1951).

Echium amoenum L. or Boraginaceae is an annual herb which grows in most of Europe, Mediterranean region and also in the northern mountains of Iran at an altitude ranging from 60-2200m (Mehrabani et al., 2005, Abolhassani, 2004, Ranjbar et al., 2006, Abed et al., 2012, Mehrabani et al., 2010). Flowers, stems, roots and leaves from this plant are used for medicinal purposes (Heidari et al., 2006, Ranjbar et al., 2006). Echium genus has 4 species however, only Echium vulgare, Echium amoenum have been used in traditional medicine of Iran for a long time (Ghassemi et al., 2003, Mehrabani et al., 2005, Fisch and Mey, 2005, Uysal et al., 2012).

Chemical Constituents

Recent phytochemical studies of Rhus coriaria L. have proved its richness in strong antioxidants called tannins (Pourahmad et al., 2010). The leaves contain up to 25-33% tannins (Pharmacy, 2014). Hydrolysable tannins, condensed tannins and gallic acid derivatives have been found (Mavlyanov M, 1997, Mavlyanov M, 1995). The hydrolysable gallotannins have not been structurally characterized by Nuclear magnetic resonance or physicochemical mass spectrometry. They have been extensively used in tanning leather (Mestres, 2004, Tang et al., 2005). Gallic acid, protocatechuic acid, linolenic acid, p-OH-benzoic acid, and vanillic acid were the phenolic acids found in the leaves of this herb (Pharmacy, 2014). In vitro testing has indicated that gallic acid is the active principle of sumac (Franziska Ferk, 2007). Anthocyanins like cyanidin, peonidin, pelargonidin and petunidin have also been reported in the leaf of Rhus coriaria L. The flavonoids detected in this herb are quercetin and kaempferol glycosides (Panico et al., 2009b, Zalacain A, 2003).

Echium amoenum L. is considered as a promising source of bioactive compounds with various beneficial biological activities. It has been reported that the petals of Echium amoenum L. is rich in rosmarinic acid (RA), a potent antioxidant (Abolhassani, 2004), Cyaniding, delphinidin, anthocyanins, gamma-linolenic acid (GLA), alpha-linolenic acid (ALA), delta6-fatty acyl desaturase, delta8-sphingolipid desaturase and flavonoids (Ranjbar et al., 2006, Sperling et al., 2001, Mehrabani et al., 2005, Abolhassani, 2004, Ghassemi et al., 2003). The Cyaniding 3-glucoside, the most common anthocyanin, which is present in petals of Echium amoenum L. attenuates prostaglandin production and cyclooxygenase-2 expressions by inhibiting activation and translocation of c-Jun and NF-κB factors into nucleus (Petersen & Simmonds, 2003) and reducing intracellular reactive oxygen species (ROS) levels via activating the glutathione (GSH) antioxidant system (Min et al., 2011). Its neuroprotective effect was related to attenuation of brain superoxide levels resulted from blocking apoptosis-inducing factor release in mitochondria (Toth et al., 2003, Kelley et al., 1976).

Ethno-pharmacology

Historically, Rhus coriaria L. has possessed remarkable medicinal value (Mohammad Moazeni, 2012). The leaves and berries of this herb have been used extensively as remedies in folk medicine (Panico et al., 2009a). The red fruit of Rhus coriaria L. that contains one seed is commonly consumed in Middle Eastern countries, especially in Turkey, as spice (Jalal Pourahmad, 2010, Beretta, 2009, Kosar, 2007). The ground dried drupes of this herb with salt have a sour, lemony taste and are usually used in salad and as a condiment sprinkled over the traditional Turkish cuisine, kebab. The citric acid and malic acids in Rhus coriaria L. create the sour taste (PH=2.5) of the spice (Mohammad Moazeni, 2012).

The main focus of studies of Rhus coriaria L. has been on the fruit and the leaf parts of this herb. The leaves with their high content of tannins have been used as a tanning agent; the berries have a diuretic and antimicrobial effect and have been used for wound healing, fever reduction, and intestinal discomfort (S and G, 2007, Sezik, 1991). Reports from the traditional medicine of Iran have shown an athero-protective effect of this herb (Jalal Pourahmad, 2010).

Studies of the biological activity of Rhus coriaria L. leaves have demonstrated that they have significant antimicrobial, antifungal, and antiviral activities (Sierra Rayne 2007). Studies of the methanolic extract of the leaves and the ethanolic and water extract of the fruits of this plant have shown antibacterial effects against twelve different species of bacteria and nine tested fungal strains (Mccutcheon Ar, 1992, Mccutcheon Ar, 1994).

The antioxidant properties of Rhus coriaria L. have been investigated by different experiments. Food products such as stored sunflower and peanut oil were tested for stabilizing with methanolic extracts of the seeds of Rhus coriaria L. and the antioxidant properties were reported (Ozcan, 2003b, Ozcan, 2003a, Bozan B, 2003, Candan and Sokmen, 2004a). Ozcan et al. (2003) reported that the extract of Rhus coriaria L. fruits showed antioxidant activity (Ozcan, 2003a). The property of this extract has been shown in cell-free oxidative stress models. For instance, the xanthine oxidase system has exhibited an inhibitory effect on superoxide anion formation and lipid peroxidation (Candan and Sokmen, 2004b, Candan, 2003). The protective effect of this herb extract has also been studied, due to its antioxidant properties. The water extract of fruits of Rhus coriaria L. have demonstrated a hepatoprotective effect against oxidative stress in isolated hepatocytes from Sprague–Dawley rat (Perchellet, 1992).

Beretta et al. (2009) investigated the cardiovascular protective activity of hydro-alcoholic extract of Rhus coriaria L. leaf extract and the gallotannin fraction in isolated rabbit heart. Limited postischemic myocardial injury was demonstrated (Beretta, 2009). The vasorelaxant ability of the extract also showed in isolated thoracic aorta of rabbit (Beretta, 2009). The antioxidant potency of gallic acid as an active compound of the extract of Rhus coriaria L. fruit was compared with vitamins C and E and was found to be 50 times more protective (Franziska Ferk, 2007).

The anticarcinogenic and tumor formation and growth inhibitory effect of tannins the active compound of Rhus coriaria L. leaves has also been exhibited in animals (Perchellet, 1992). Studies of sumac extracts have also demonstrated other bioactivities for this herb, such as antifibrogenic (Lee, 2003), anti-inflammatory (Fourie, 1984), antimalarial (Ahmed et al., 2001), antithrombin (Kuo et al., 1991), antiatherosclerosis (Zargham, 2008) properties, and astringent potency (Pharmacy, 2014). This herb can be used externally for burns, weeping ulcers, wounds, eczema, and internally for bleeding of the gastrointestinal tract, diarrhea, enteritis, and colitis, because of its high tannins content. In homeopathy, the infusion and crushed fresh leaves can be used for the treatment of diarrhea, rheumatism, gout, paralysis, ulcers, eczema, exhaustion and biliary tract problems (Pharmacy, 2014).

The petals of Echium amoenum L. are traditionally either brewed or boiled in water before drinking. The benefits of this traditional medication have initially been discovered by the Romans, 300 B.C. (Grieve, 1970). The flowers and the leaves has been used as an anti-inflammatory, antioxidant, demulcent, antibacterial, analgesic, antiviral, anxiolytic, antidepressant and mood enhancer and recently possible protective factor against cancer (Sayyah et al., 2009, Ghassemi et al., 2003, Ranjbar et al., 2006, Rabbani et al., 2004, Taravati et al., 2014).

The antioxidant activity of Echium amoenum L. petals aqueous extract has been investigated in human (Ranjbar et al., 2006). The results showed a significant reduction in blood lipid peroxidation after 14 days of extract (7 mg/kg) intake. It is suggested that the flavonoids in this plant play an important role in its potential antioxidant activity (Sayyah et al., 2009, Ranjbar et al., 2006). Flavonoids with anti-inflammatory, antioxidant, and gastroprotective effects are widely distributed in the plant kingdom (Talhouk et al., 2007). The influence of usage of the Echium amoenum L. petal extract on the oxidative stress of healthy subjects has been studied. It has been indicated that the concentration of reactive oxygen species (ROS) markedly decreased after consumption of Echium amoenum L. (Ranjbar et al., 2006). Its antioxidant property acts as a free radical scavengers which protects cells from free radical exposure and cellular damage (Ranjbar et al., 2006).

Various substances have been suggested to act as antioxidant in this plant. Numerous phenolic antioxidants such as flavonoids, rosmarinic acid, tannins, coumarins, xanthenes, and procyanidins have

been shown to scavenge radicals in a dose-dependent manner (Yao et al., 2004, Mehrabani et al., 2005, Uysal et al., 2012).

Rosmarinic acid, an important constituent of Echium amoenum L., is an ester of caffeic acid and 3,4-dihydroxyphenylacetic acid. It is commonly found in species of the Boraginaceae and the subfamily Nepetoideae of the Lamiaceae (Mehrabani et al., 2005, Ranjbar et al., 2006, Taravati et al., 2014). There are number of reports on the antioxidant activities of rosmarinic acid which all confirm that rosmarinic acid has strong antioxidant activity even higher than vitamin E. (Sanbongi et al., 2003, Englberger et al., 1988, Ranjbar et al., 2006).

Antioxidants and Neuroprotection

Antioxidants may have neuroprotective and neuroregenerative functions, by reducing or reversing cellular damage and by slowing the progression of neuronal cell loss (Bizimenyera et al., 2007). The lack of effective and widely applicable pharmacological treatments in the modern therapy for neurodegenerative disorders may explain the growing interest in traditional medicines. The traditional crude form of remedy has emerged as standardized herbal extracts, their formulations and even composite preparations. Moreover, particular components responsible for activity have also been isolated, some of which have been synthesized (Wasik, 1999, Eisenberg et al., 1993). Some available scientific literature has revealed the neuroprotective action of plants such as Clitoria ternatea, Hemidesmus indicus (Ambikar et al., 2009), Bacopa monniera (Schmidt et al., 1995, Hou, 2004, Deshmukh, 2006), Withania somnifera (Dhuley, 2001, Trigunayat, 2007), Centella asiatica (Joshi, 2006), Ocimum sanctum (Shukla, 2000), Semecarpus anacardium, Nardostachys jatamansi (Kirtikar, 1993, Shukla et al., 2006), Acorus calamus (Kennedy and Scholey, 2003), Panax ginseng (Limpeanchob N, 2008), Ginkgo Biloba (Ahlemeyer B, 2003, Dongen et al., 2003). An ethnopharmacological approach has provided leads to identify the potential of new drugs, including some for neurodegenerative disorders, from plant sources. It is apparent from the above publications that varieties of plants show or have the potential to show activities relevant for use in neurodegenerative disorders. This brief review on Rhus coriaria L. and Echium amoenum L. pharmacological properties can lead to further neuroprotection studies of these herbs.

References

Abed, A., Minaiyan, M., Ghannadi, A., Mahzouni, P. & Babavalian, M.R. (2012). Effect of Echium amoenum Fisch. et Mey a traditional Iranian herbal remedy in an experimental model of acute pancreatitis. *ISRN gastroenterology*.

Abolhassani, M. (2004). Antibacterial effect of borage (Echium amoenum) on Staphylococcus aureus. *Brazilian Journal of Infectious Diseases,* **8,** 382-385.

Ahlemeyer B, K.J. (2003). Neuroprotective effects of Ginkgo biloba extract. *Cell Mol Life Sci. ,* **60,** 1779 -1792.

Ahmed, M.S., Galal, A.M., Ross, S.A., Ferreira, D., Elsohly, M.A.*, et al.* (2001). A weakly antimalarial biflavanone from Rhus retinorrhoea. *Phytochemistry* **58,** 599-602.

Ambikar, D.B., Harle, U.N., Khandare, R.A., Bore, V.V. & Vyawahare, N.S. (2009). Neuroprotective effect of hydroalcoholic extract of dried fruits of Trapa bispinosa Roxb on lipofuscinogenesis and fluorescence product in brain of D-galactose induced ageing accelerated mice. *Indian Journal of Experimental Biology* **48,** 378-382.

Beltsville, M. 2007. *Germplasm Resources Information Network*. United States Department of Agriculture, Agricultural Research Service,USA: United States Department of Agriculture (USDA). Available: http://www.ars-grin.gov/npgs/aboutgrin.html.

Beretta, G. (2009). Anti-Ischemic Activity and Endothelium-Dependent Vasorelaxant Effect of Hydrolysable Tannins from the Leaves of Rhus coriaria (Sumac) in Isolated Rabbit Heart and Thoracic Aorta. . *Planta Med,* **75,** 1482-1488.

Bizimenyera, E.S., Aderogba, M.A., A, J.N.E. & A, G.E.S. (2007). Potential of Neuroprotective Antioxidant-Based Therapeutics from Peltophorum Africanum Sond.(Fabaceae). *Afr. J. Traditional,Complementary andAlternative Medicines,* **4** 99 -106.

Bozan B, K., Tunalier Z, Ozturk N, Baser Khc. (2003). Antioxidant and free radical scavenging activities of Rhus coriaria and Cinnamomum cassia extracts. Acta Alimentaria **32,** 5-61.

Candan, F. (2003). Effect of Rhus coriaria L. (Anacardiaceae) on superoxide radical scavenging and xanthine oxidase activity. *J Enzyme Inhib Med Chem Biodivers,* **18,** 59-62.

Candan, F. & Sokmen, A. (2004a). Effects of Rhus

coriaria L (Anacardiaceae) on lipid peroxidation and free radical scavenging activity. *Phytother,* **18,** 84-86.

Candan, F. & Sokmen, A. (2004b). Effects of Rhus coriaria L. (Anacardiaceae) on lipid peroxidation and free radical scavenging activity. *Phytother Res* **18,** 84-86.

Capasso R., I.a.A., Pinto L., Bifulco T., Vitobello C. And Mascolo N (2000). Phytotherapy and quality of herbal medicines. *Fitoterapia,* **71,** S58-S65.

Chittenden, F.J. (1951). *The Royal Horticultural Society Dictionary of Gardening,* Oxford University Press. London.

Deshmukh, A.A., Gajare, K.A., Pullajwar,V.S.,Ruiker, A.A.,Bule, P.P. (2006). *J.Cell TissueRes.,* **6,** 757-761.

Dhuley, J.N. (2001). Nootropic-like effect of ashwagandha (Withania somnifera L.) in mice. *PhytotherapyRes,* **15,** 524-528.

Dongen, M.V., Rossum, E.V., Kessels, A., Sielhorst, H. & Knipschild, P. (2003). Ginkgo for elderly people with dementia and age-associated memory impairment: A randomized clinical trial. *J Clin Epidemiol,* **56,** 367-376.

Eisenberg, D., Kessler, R., Foster, C., Norlock, F., Calkins, D*., et al.* (1993). Unconventional medicine in the United States. Prevalence, costs, and patterns of use. *N Engl J Med,* **328,** 246-252.

Englberger, W., Hadding, U., Etschenberg, E., Graf, E., Leyck, S*., et al.* (1988). Rosmarinic acid: a new inhibitor of complement C3-convertase with anti-inflammatory activity. *International journal of immunopharmacology,* **10,** 729-737.

Fisch, A. & Mey, C. (2005). Main phenolic compound of petals of Echium amoenum Fisch. and CA Mey., a famous medicinal plant of Iran. *Daru,* **13,** 65.

Fourie, T.G., Snyckers, F.O (1984). A flavone with antiinflammatory activity from the roots of Rhus undulata. . *J. Nat. Prod,* **47,** 1057-1058.

Franziska Ferk, A.C., Tatjana Simic, Michael Kundi, Siegfried Knasmüller (2007). Antioxidant and free radical scavenging activities of sumac (Rhus coriaria) and identification of gallic acid as its active principle. *BMC Pharmacology,* **7(Suppl 2),** A71.

Ghassemi, N., Sajjadi, S.E., Ghannadi, A., Shams-Ardakani, M. & Mehrabani, M. (2003). Volatile constituents of a medicinal plant of Iran, Echium amoenum Fisch. and CA Mey. *Daru,* **11,** 32-33.

Grieve, M. (1970). Modern Herbal Vol-I.

Heidari, M.R., Azad, E.M. & Mehrabani, M. (2006). Evaluation of the analgesic effect of< i> Echium amoenum< /i> Fisch & CA Mey. extract in mice: Possible mechanism involved. *Journal of ethnopharmacology,* **103,** 345-349.

Hou, F.F., Hao, R., Chen, J.X., Li, J.F., Chem, P.Y.Schmidt,A.M. (2004). *J.Am. Soc.Nephrol.,,* **15,** 1889-1896.

Houghton P.J. , R.A. (1998). *Laboratory handbook for the fractionation of natural extracts,* London, Chapman & Hall.

Jalal Pourahmad, M.R.E., Rashin Shakibaei, Mohammad Kamalinejad (2010). A search for hepatoprotective activity of aqueous extract of Rhus coriaria L. against oxidative stress cytotoxicity. *Food and Chemical Toxicology,* **48,** 854–858.

Joshi, H., Parle,M. (2006). Cholinergic basis of memory improving effect of Ocimum tenuiflorum linn. *Ind J. Pharma Sci* **68,** 364-365.

Kelley, C.J., Harruff, R.C. & Carmack, M. (1976). Polyphenolic acids of Lithospermum ruderale. II. Carbon-13 nuclear magnetic resonance of lithospermic and rosmarinic acids. *The Journal of Organic Chemistry,* **41,** 449-455.

Kennedy, D.O. & Scholey, A.B. (2003). Ginseng: potential for the enhancement of cognitive performance and mood. *Pharmacol. Biochem. Behav,* **75,** 687-700.

Kirjassa, T.I. & Gathered by John Gerarde of London Master in Chirvrgeria 1597. The Herball or Generall Historie of Plantes. London: Iohn Norton.

Kirtikar, K.R., Basu, B.D. (1993). *Indian medicinal plants* International book distributors,Deharadun.

Kosar, M. (2007). Antioxidant Activity and Phenolic Composition of Sumac (Rhus coriaria L.) Extracts. *Food Chemistry,* **103,** 952-959.

Kuo, S., C.M Teng, L.G Lee, T.H Chiu, T.S Wu*, et al.* (1991). 6-Pentadecylsalicylic acid: an antithrombin component isolated from the stem of Rhus semialata var roxburghii. *Planta Med,* **57,** 247-249.

Lee, S.H. (2003). The Chalcone Butein from Rhus verniciflua Shows Antifibrogenic Activity. *Planta Medica,* **69,** 990-994.

Limpeanchob N, J.S., Rattanakaruna S, Phrompittayarat W, Ingkaninan K (2008). Neuroprotective effect of Bacopa monnieri on beta-amyloid-induced cell death in primary cortical culture *Ethnopharmacology* **120,** 112-117.

Mavlyanov M, I.S., Ismailov Ai, Kamaev Fg (1995). Chemistry of Natural Compounds **31,** 268.

Mavlyanov M, I.S., Ismailov Ai, Karimdzhanou Ak, Ismalov Ai (1997). Chemistry of Natural Compounds. **33,** 209.

Mccorkle C. M., M.-M.E., Schillhorn Van Veen T. W. (1996). *In: Ethnoveterinary Research and Development. ,* London.

Mccutcheon Ar, E.S., Hancock Re, Towers Gh (1992). Antibiotic screening of medicinal plants of the British Columbian native peoples. *J Ethnopharmacol* **37,** 213-223.

Mccutcheon Ar, E.S., Hancock Re, Towers Gh (1994). Antifungal screening of medicinal plants of British Columbia native peoples. . *J Ethnopharmacol* **44,** 157-169.

Mehrabani, M., Ghassemi, N., Ghannadi, E.S.A. & Shams-Ardakani, M. (2005). Main phenolic compound of petals of Echium amoenum Fisch. and CA Mey., a famous medicinal plant of Iran. *DARU Journal of Pharmaceutical Sciences,* **13,** 65-69.

Mehrabani, M., Shams-Ardakani, M., Ghannadi, A., Ghassemi-Dehkordi, N. & Sajjadi-Jazi, S. (2010). Production of rosmarinic acid in Echium amoenum fisch. and CA mey. cell cultures. *Iranian Journal of Pharmaceutical Research***,** 111-115.

Mestres, R. (2004). A brief structured view of green chemistry issues. *Green Chem,* **6,** G10-G12.

Mills, C. 2010. *Hortus camdenesis*. Available: http://hortuscamden.com/plants/view/rhus-coriaria-l.

Min, J., Yu, S.-W., Baek, S.-H., Nair, K.M., Bae, O.-N*., et al.* (2011). Neuroprotective effect of cyanidin-3-< i> O< /i>-glucoside anthocyanin in mice with focal cerebral ischemia. *Neuroscience letters,* **500,** 157-161.

Mohammad Moazeni, M.M. (2012). Sumac (Rhus coriaria L.): Scolicidal Activity on Hydatid Cysst Protoscolices. *Surgical Science,* **3,** 452-456.

Ozcan, M. (2003a). Antioxidant activities of rosemary, sage, and sumac extracts and their combinations on stability of natural peanut oil. *I. J. Med. Food* **6,** 267-270.

Ozcan, M. (2003b). Effect of sumach (Rhus coriaria L.) extracts on the oxidative stability of peanut oil. *J Med Food* **6,** 63-66.

Panico, A., Cardile, V., Santagati, N.A. & Messina, R. (2009a). Antioxidant and Protective Effects of Sumac Leaves on Chondrocytes. *Journal of Medicinal Plants Research,* **3,** 855-861.

Panico, A., Cardile, V., Santagati, N.A. & Messina, R. (2009b). Antioxidant and protective effects of Sumac Leaves on chondrocytes. *Journal of Medicinal Plants Research* **3,** 855-861.

Perchellet, J.P., Gali, H.U., Perchellet, E.M., Klish, D.S., Armbrust, A.D. (1992). Antitumor-promoting activities of tannic acid, ellagic acid, and several gallic acid derivatives in mouse skin. *Basic Life Sci,* **59,** 783-801.

Pharmacy, G. 2014. *??????? ??????*. Available: http://www.fito.nnov.ru/special/glycozides/dube/rhus_coriaria/

Pourahmad, J., Eskandari, M.R., Shakibaei, R. & Kamalinejad, M. (2010). A search for hepatoprotective activity of aqueous extract of Rhus coriaria L. against oxidative stress cytotoxicity. *Food and Chemical Toxicology,* **48,** 854-858.

Rabbani, M., Sajjadi, S., Vaseghi, G. & Jafarian, A. (2004). Anxiolytic effects of< i> Echium amoenum< /i> on the elevated plus-maze model of anxiety in mice. *Fitoterapia,* **75,** 457-464.

Ranjbar, A., Khorami, S., Safarabadi, M., Shahmoradi, A., Malekirad, A.A*., et al.* (2006). Antioxidant activity of Iranian Echium amoenum Fisch & CA Mey flower decoction in humans: a cross-sectional before/after clinical trial. *Evidence-based Complementary and Alternative Medicine,* **3,** 469-473.

S, R. & G, M. (2007). Biological activities of extracts from sumac (Rhus spp.): a review. *Plant Foods Hum. Nutr,* **62,** 165-75.

Sanbongi, C., Takano, H., Osakabe, N., Sasa, N., Natsume, M*., et al.* (2003). Rosmarinic acid inhibits lung injury induced by diesel exhaust particles. *Free Radical Biology and Medicine,* **34,** 1060-1069.

Sayyah, M., Boostani, H., Pakseresht, S. & Malaieri, A. (2009). Efficacy of aqueous extract of< i> Echium amoenum< /i> in treatment of obsessive–compulsive disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry,* **33,** 1513-1516.

Schmidt, A.M., Hori, O., Chen, J.X., Crandali, J., Brett, J*., et al.* (1995). Advanced glycation endproducts interacting with their endothelial receptor induce expression of vascular cell adhesion molecule-1 (VCAM-1) in cultured human endothelial cells and in mice. A potential mechanism for the accelerated vasculopathy of diabetes. *J.Clin.Invest,* **96** 1395-1403.

Sezik, E., Tabata, M., Yesilada, E (1991). Traditional medicine in Turkey. Folk medicine in northeast Anatolia. . *Ethnopharmacol.,* **35,** 191-196.

Shukla, P.K., Khanna, V.K., M.M, A., Maurya, R. & Khan, M.Y. (2006). Neuroprotective effect of Acorus calamus against middle cerebral artery occlusion-induced ischaemia in rat. *Human.Expt Toxicol,* **25,** 187-194.

Shukla, S.D., Jain, S., Sharma, K., Bhatnagar, M

(2000). *Ind J.Expt.Bio.,,* **38,** 1007-1013.

Sierra Rayne , G.M. (2007). Biological Activities of Extracts from Sumac (Rhus spp.): A Review. *Plant Foods Hum Nutr* **62,** 165-175.

Sperling, P., Libisch, B., Zähringer, U., Napier, J.A. & Heinz, E. (2001). Functional Identification of a Δ< sup> 8< /sup>-Sphingolipid Desaturase from< i> Borago officinalis< /i>. *Archives of biochemistry and biophysics,* **388,** 293-298.

Sumac, S. 2014. *Encyclopadia Britannica*. Available: http://global.britannica.com/EBchecked/topic/542782/Sicilian-sumac.

Sun A. Y., S.A., Sun G. Y. (2002). The "French Paradox" and beyond: neuroprotective effects of polyphenols. . *Free Radic. Biol. Med.,* **32,** 314-318.

Talhouk, R., Karam, C., Fostok, S., El-Jouni, W. & Barbour, E. (2007). Anti-inflammatory bioactivities in plant extracts. *Journal of medicinal food,* **10,** 1-10.

Tang, S., Smith, R. & Poliakoff, M. (2005). Principles of green chemistry. *Green Chem* **7,** 761-762.

Taravati, G., Masoudian, N. & Gholamian, A. (2014). Evaluation of Medical Metabolites in Boraginaceae Family. *Journal of Chemical Health Risks,* **4**.

Thompson, A. (1997). As patients embrace herbal remedies, dearth of scientific evidence frustrates clinicians. *Am. J. Health Syst. Pharm,* **54,** 2656-2664.

Toth, J., Mrlianova, M., Tekelova, D. & Korenova, M. (2003). Rosmarinic acid–an important phenolic active compound of lemon balm (Melissa officinalis L.). *Acta Facultatis Pharmaceuticae Universitatis Comenianae,* **50,** 139-45.

Trigunayat, A., Raghavendra, M., Singh, R.K., Bhattacharya,A.K.,Acharya, S.B (2007). *J. Nat. Rem,* **7,** 234-246

Uysal, H., Kizilet, H., Ayar, A. & Taheri, A. (2012). The use of endemic Iranian plant, Echium amoenum, against the ethyl methanesulfonate and the recovery of mutagenic effects. *Toxicology and industrial health***,** 0748233712468019.

Wasik, J. (1999). The truth about herbal supplements. *Consumer's digest,* **July/August,** 75-79.

Weiss, R.F. & Fintelmann, V. (2000). Herbal Medicine. 2nd edition. *Thieme Stuttgart* 3-20.

Yao, L.H., Jiang, Y., Shi, J., Tomas-Barberan, F., Datta, N.*, et al.* (2004). Flavonoids in food and their health benefits. *Plant Foods for Human Nutrition,* **59,** 113-122.

Zalacain A, P.M., Carmona M, Alonso Gl (2003). Screening method for the detection of artificial colours in saffron using derivative UV-Vis spectrometry after precipitation of crocetin; . *Biosystem Eng,* **84,** 211.

Zargham, R., Zargham, H (2008). Tannin extracted from Sumac inhibits vascular smooth muscle cell migration. *McGill J. Med,* **11,** 119-123.