Berberis vulgaris: specifications and traditional uses

Mohammad Rahimi-Madiseh 1, Zahra Lorigoini 1, Hajar Zamani-gharaghoshi 2, Mahmoud Rafieian-kopaei 1*

1 Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran
2 Department of Chemistry, Faculty of Sciences, Shahrekord University, Shahrekord, Iran

ARTICLE INFO

Article type: Review article

Article history:
Received: Jun 5, 2016
Accepted: Apr 14, 2017

Keywords: Berberis, Iran, Plants Medicinal, Secondary Metabolism, Traditional

ABSTRACT

The medicinal plants from genus Berberis are particularly important in traditional medicine and the food basket of Iranians. Given various plants from genus Berberis and their economic, nutritional, and medicinal status in Iran, this study seeks to investigate the findings of recent studies on the phytochemical characteristics, specifications, and uses of Berberis vulgaris. In this review article, 350 articles were initially retrieved from reliable scientific databases using relevant search terms. Then, 230 articles were selected and 120 were excluded after a primary analysis. Finally, 98 articles related to the subject under study were meticulously examined and the required data were extracted and classified according to the research purposes. The findings were divided into eight separate sections: Introducing Berberidaceae family, different species of Berberis, pharmaceutical organs, B. vulgaris nutrition facts and minerals, the antioxidants and alkaloids compounds in fruit and other organs, action mechanisms of preventing and treating diseases, traditional uses of B. vulgaris, and its properties reported by recent studies. The results briefly indicate that B. vulgaris contains a large number of phytochemical materials including ascorbic acid, vitamin K, several triterpenoids, more than 10 phenolic compounds and more than 30 alkaloids. Therefore B. vulgaris may have anti-cancer, anti-inflammatory, antioxidant, anti-diabetic, antibacterial, analgesic and anti-nociceptive and hepatoprotective effects. Regarding the use of different organs of B. vulgaris in traditional medicine and their confirmed effects in the recent studies, it is possible to use different organs of B. vulgaris, especially fruit, to develop new drugs.

Introduction

Medicinal plants have been known among different nations since thousands of years ago and have been used throughout many centuries according to the traditional medicine of most countries. In recent decades and despite the emergence of synthetic drugs, medicinal plants continue to be welcomed and are being used in many countries due to safe use, efficiency, cultural acceptance, and fewer side effects than synthetic drugs (1, 2). As with other countries, in Iran, different medicinal plants, including those from genus Berberis, are used to treat diseases according to traditional medicine (3, 4).

Genus Berberis is native to moderate and semitropical regions of Asia, Europe, Africa, North America, and South America. Different plants of genus Berberis can occur in many regions across the world including Iran (5). Iran is the biggest producer of B. vulgaris fruit in the world, with 11,000 hectares of land under cultivation. Over 10,000 tons of dried B. vulgaris fruit are produced in Iran per year. Among the provinces of Iran, Southern Khorasan is one of the biggest producers of B. vulgaris. Over 97% of all the lands under B. vulgaris cultivation are located in Ghaenat County, Southern Khorasan province, producing 95% of the whole B. vulgaris fruit in Iran (6, 7).

Various species of the genus Berberis which occur around the world are cultivated and grown up for specific purposes (8). B. vulgaris is the most widely known Berberis which is mainly used as a food is cooked with rice (seedless or red), B. integerrima, also referred to as black barberry and wild barberry, are used mainly for juice extraction in food industries and as medication (9, 10).

Medicinal uses of B. vulgaris in Chinese medicine date back to over 3000 years ago and in some other countries to over 2500 years ago (3, 5). In Iran, Rhazes was the first one to introduce the medicinal properties of B. vulgaris and considered its use to be helpful for human being (11). There are a variety

*Corresponding author: Mahmoud Rafieian-Kopaei. Medical Plants Research center, Shahrekord University of Medical Sciences, Shahrekord, Iran. Tel: +98-383346692; email: rafieian@yahoo.com
of alkaloids in the various organs of this plant, most important of which is berberine. This alkaloid can exert different effects, including antioxidant, anti-inflammatory, hypoglycemic, hypotensive, and hypolipidemic activities (12, 13).

Different organs of *B. vulgaris* are used in food and pharmaceutical industries and the decorative species are used to decorate different places. According to traditional medicine, *B. vulgaris* is used to treat fever, cough, liver disease, depression, hyperlipidemia, hyperglycemia and bleeding (14, 15).

Over 500 plants from genus *Berberis* are accessible to people across the world with four pharmaceutical organs being used to treat different diseases. *B. vulgaris*, *B. orthobotrys*, *B. khorasanica*, *B. integerrima*, *B. crataegina*, *B. lycium*, and *B. aristata* are used in traditional medicine more frequently in Iran and other parts of the world (16-18). Hence, this study was conducted to present the phytochemical characteristics, the findings of the experimental studies and the clinical trials conducted on the most frequently used species of the plants from this genus in traditional medicine, focusing on *B. vulgaris* which is the most frequently used plant of this genus.

Therefore, the present review is mainly focusing the research reports on the pharmacological effects in traditional and modern medicine and various chemical constituents in *B. vulgaris*.

**Materials and Methods**

In this review article, 350 articles were initially retrieved from reliable scientific databases using relevant search terms. Then, 230 articles were selected and 132 ones were excluded after a primary analysis. Finally, 98 articles that were related to the subject under study were meticulously examined and the required data were extracted according to the research purposes and classified. In summary our method is presented as flow chart in Figure 1.

**Results**

The findings were presented in eight separate sections: Introducing *Berberidaceae*, family different plants of genus *Berberis*, pharmaceutical organs, *B. vulgaris* nutrition facts, vitamins, and minerals, the antioxidants and alkaloids in fruit and other pharmaceutical organs, action mechanisms of preventing and treating diseases, uses of *B. vulgaris*, and its properties reported by recent studies. Besides that, the pharmaceutical and therapeutic properties of the pharmaceutical organs of some species from Berberidaceae family are shown in Table 1.

**Berberidaceae**

The plants from Berberidaceae family are often acanaceous shrubs with 1-5 m height and rarely small. The internal surface of the bark and wood of these plants are yellow, brown, or purple.
The branches of these plants are cylindrical, angular, or striate and sometimes covered by wax. The leaves of long branches are transformed to single, binary, or triple thistles, sometimes clawed or leaf-like and located in short branches or short small branches with batch oriented, lint-less, without petioles or with short petioles, the lower surface is sometimes covered with a waxed layer.

The flowers are yellow and sometimes with a differently colored strip, red-striped, and with senary sepals or petals. Petals are often smaller than sepals. The stamens are scenery and often smaller than petals. The fruits of the plants from Berberidaceae family are bright red or blackish red and taste sour (19, 20). After falling leaves in autumn and passing through winter, the shrubs of barberries begin to flourish in March and flower in June. The fruits are rape and can be harvested in October (21).

Genus Berberis

The genus Berberis (Berberidaceae) includes about 500 species worldwide (22). Berberidaceae family includes approximate 14 genera and 700 species (23). Berberis is a major genus in dicotyledonous woody plants of Berberidaceae family. Different taxonomists have reported disparate number of species and in the family likewise species in the genus. For many, the family comprises upon ca. 17 genera containing 650 species (24), while for several others there are 14 genera and ca. 715 species (25). Furthermore, Whetstone et al (1997) and Nickol (1995) are in favor of 15 and 13 genera with ca. 650 and 570 species respectively in the family (26). Similarly, according to Ahrendt (1961) and Adhikari (2010), Berberis includes ca. 450 (excluding Mahonia ca. 100) and more than 500 (inc. Mahonia) species correspondingly. Berberis is the largest woody plant genus of the basal eudicots (12, 27). The genus includes four species in Iran: B. integrerrima Bunge, B. crataegina DC, B. vulgaris L. and B. orthobotrys Bienert (28).

Two species, B. orthobotrys and B. khorasanica occur exclusively in Iran, and B. integrerrima, B. crataegina and black barberry, occur also in Eastern Anatolia, eastern Iraq, Afghanistan, Upper Caucasus, Turkmenistan, western Pakistan, Kashmir, and Central Asia. Some species of genus Berberis have recently been imported into Iran and cultivated and propagated in different regions for decorative uses (8).

Pharmaceutical organs of B. vulgaris

In traditional medicine, different organs of this plant are used to treat diseases. Fruit, bark, root, and stem are the pharmaceutical organs of B. vulgaris. Fruit is the most frequently used organ of this plant in traditional and modern medicine (21, 29).

Nutrition facts of B. vulgaris fruit

B. vulgaris fruit is sour and contains different nutrients including dextrose, fructose, malic acid, tartaric acid, citric acid, pectin, and resin. It is also rich in vitamins C and A, calcium, iron, and potassium (16, 30). In B. vulgaris fruit, the concentrations of iron, zinc, copper, and manganese are estimated 2650 mg/kg, 27.5 mg/kg, 33.7 mg/kg, and 58.6 mg/kg, respectively (10). Decomposition of B. vulgaris fruit shows that this fruit contains 79.6% humidity, 1.16% fat, 2% protein, 16.24% carbohydrate, and 0.99% ash. The amount of anthocyanin is estimated 281 mg/l (31).

In Iran, dried B. vulgaris fruit is used in many foods. As well, the fruit or its derivatives are used to produce certain products such as sauce, jelly, juice, jam, marmalade, and carbonated drinks. Besides that, B. vulgaris, considered of nature-based and useful substance, is used to season, flavor, and garnish foods to satisfy different sapers (32, 33). This fruit is also used in industries. For example, the anthocyanin found in B. vulgaris fruit is used as a nature-based color (6).

Secondary metabolites of B. vulgaris fruit and other medicinal organs

Many metabolites of various species of B. vulgaris have been reported. Phytochemical analysis revealed the presence of alkaloids, tannins, carotenoid, vitamin, protein, lipid, anthocyanin and phenolic compounds. Most compounds are summarized in Table1. The highest amounts of phenolic compounds and anthocyanins can be found in B. vulgaris juice and the highest amount of flavonoid compounds in B. vulgaris leaves. Regarding the importance of investigating B. vulgaris quality, the amount of anthocyanin in the fruit to be an important index of B. vulgaris quality (21). The concentrations of flavonol, flavonoid, and phenol of B. vulgaris fruit are 25.3 mg/g, 12.2 mg/g, and 0.54 mg/g, respectively (10).

Action mechanism of B. vulgaris in preventing and treating diseases

In all organs of B. vulgaris, certain alkaloids such as berberine, oxyacanthine, berbamine, brolcin, and columbamine are found. The amount of alkaloid is higher in the root bark than other organs of B. vulgaris. Berberine is one of the most important alkaloids of this plant that can be effective in preventing coronary artery disease and possibly reducing the levels of total cholesterol and triglyceride (36). The most important property of berbamine is to block calcium channels. This alkaloid was found to be active in the tests of lipids peroxidation in red blood cells and can exert anti-myocardial ischemia and antiarrhythmic effects. Besides that, oxyacanthine has a sympatholytic and vasodilatory agent (37).
| Secondary Metabolite | Structure | References |
|----------------------|-----------|------------|
| Jatrorrhizine Chloride | ![Structure](image1.png) | (13) |
| Aromoline | ![Structure](image2.png) | (12, 13) |
| Berberine | ![Structure](image3.png) | (12, 13) |
| Berbamine | ![Structure](image4.png) | (12, 13) |
| Palmatine Chloride | ![Structure](image5.png) | (12, 13) |
| Oxyberberine | ![Structure](image6.png) | (12) |
Columbamine

Isocorydine

Lambertine

Magnilflorine

Bisbenzisooquinolines

(+-)Oxycanthine

N-(P-Trans-Coumaroyl) Tyramine

References:
(12)
| Compound                          | Structure |
|----------------------------------|-----------|
| Cannabis G                       | ![Cannabis G](image)
| (+)-Lyoniresinol                 | ![(+)-Lyoniresinol](image) |
| (+)-Aromoline                    | ![(+)-Aromoline](image) |
| (+)-Obamegine                    | ![(+)-Obamegine](image) |
| Thalifoline                      | ![Thalifoline](image) |
| 8-Oxyberberine                   | ![8-Oxyberberine](image) |

(12) ±Lyoniresinol

(13) (+)Obamegine

(13) Thalifoline

(13) 8-Oxyberberine
| Compound                | Structure |
|-------------------------|-----------|
| Baluchistanamine        | ![Baluchistanamine](image1) |
| (-)-Tejedine            | ![(-)-Tejedine](image2) |
| (+)-Obaberine           | ![(+)-Obaberine](image3) |
| (+)-Isotetrandrine      | ![(+)-Isotetrandrine](image4) |
| Magnoflorine Chloride   | ![Magnoflorine Chloride](image5) |
(±)-Thaligrisine

Beriambine

Berberrubine

Bargustanine

Columbamine

Berlambine

Hydroxycanthine

\[ \text{(13)} \]

\[ \text{(34)} \]

\[ \text{(34)} \]

\[ \text{(34)} \]

\[ \text{(14)} \]

\[ \text{(34)} \]

\[ \text{(14)} \]
Berberis vulgaris: Specifications and traditional uses

Rahimi-Madiseh et al

Iran J Basic Med Sci, Vol. 20, No.5, May 2017

| Substance                  | Structure | Reference |
|----------------------------|-----------|-----------|
| Berlambine                 | ![Berlambine](image) | (14)      |
| Triterpenoids              |           |           |
| Lupeol                     | ![Lupeol](image) | (12)      |
| Oleanolic Acid             | ![Oleanolic Acid](image) | (12)      |
| Stigmasterol               | ![Stigmasterol](image) | (12)      |
| Urosolic Acid              | ![Urosolic Acid](image) | (34)      |
| Phenolic Compound          |           |           |
| Chrysanthemin              | ![Chrysanthemin](image) | (34)      |
| Quercetin                  | ![Quercetin](image) | (13, 35)  |
| Pelargonin                 | ![Pelargonin](image) | (34)      |
Berberis vulgaris: Specifications and traditional uses

Petunidin-3-O-Beta-D-Glucoside

Caffeic Acid

Kaempferol

Hyperoside

Chrysanthemmin

Chlorogenic Acid

Aesculetin

Carbohydrate

Polysaccharide

(34)
| Molecule          | Structure | Reference |
|-------------------|-----------|-----------|
| Sucrose           | ![Sucrose Structure](image1) | (34)      |
| Xylan, Beta       | ![Xylan Structure](image2)   | (34)      |
| Pectin            | ![Pectin Structure](image3)  | (34)      |
| Glucan, Alpha     | ![Glucan Structure](image4)  | (34)      |
| Vitamin Ascorbic  | ![Ascorbic Acid Structure](image5) | (34)      |
| Vitamin K         | ![Vitamin K Structure](image6) | (34)      |
Recently, berberine has been reported to decrease cholesterol through a mechanism different from that through which statins decrease cholesterol. If a statin and berberine are used simultaneously, they seem to control cholesterol more efficiently. In a controlled study, berberine was found to cause increase in a type of protein receptor in the liver, which could bond to cholesterol and facilitate its excretion (38). Despite extensive use and several properties of different organs of *B. vulgaris*, the action mechanisms of this plant remain to be clearly known. Some of these properties can be attributed to the antihistaminic and anticholinergic effects of this plant (39). There are large amounts of vitamin C in *B. vulgaris* fruit. Vitamin C is an antioxidant and water-soluble organic compound. This vitamin is essential to the production and maintenance of collagen tissue and the strength of other tissues, and can help to reinforce immunity system and to speed up wound healing (40, 41). As well, vitamin C prevents the formation of carcinogenic nitrosamines and nitrous urases, and is considered a strong antioxidant agent and an effective cause of restoring cell enzymatic activities and electron transfer processes (42). It is also involved in the metabolism of carbohydrates, the conversion of folic acid to folinic acid, the metabolism of phenylalanine and thryosine, the conversion of plasma transferin to liver ferritin, and the production of serotonin in the body (43, 44).

A study on aqueous *B. vulgaris* fruit extract on antihistaminic and anticholinergic activities in guinea pig ileum confirmed that this extract could exert these effects (5).

**Uses of *B. vulgaris* in traditional medicine**

The oldest findings on the use of barberry fruit to purify blood were inscribed on clay tablets in the library of Assyrian (present day Iraq) emperor Asurbanipal during 650 BC. The stem bark, stem, roots and root bark of *Berberis* species have been widely used in Ayurvedic, Homeopathic and ethno-medicines as raw materials or ingredients. In Ayurveda, it is traditionally used to cure various infections of eye, ear and mouth, to lose weight, to heal wounds quickly, to cure piles and hemorrhoids, to treat dysentery, indigestion, uterine and vaginal disorders as well as to treat snake or Scorpion bite as an antidote. In Iranian traditional medicine, it is used to cure jaundice, enlarged liver, enlarged spleen, eye sores, toothache, asthma and skin pigmentation, to dry unhealthy ulcers as well as to eliminate swelling and inflammation as orally and topically (13, 45, 46). *B. vulgaris* is also used as to treat scrobutor, Alzheimer’s disease, depression, diabetes, icterus, kidney stones, gout, rheumatism, and skin diseases (33, 47-49). In traditional medicine of Bulgaria and Eastern world, the extracts of the roots of different species from family Berberidaceae are used to treat rheumatoid arthritis and other chronic inflammatory diseases (50). Saranghara acclaims that decoction of barberry mixed with honey can be used to treat jaundice. A decoction of barberry and *Emblc myrobalan* combined with honey is prescribed to treat acrid urine or painful micturition from bilious (13).

**The properties of *B. vulgaris* according to recent studies**

Many researchers reported pharmacological effects of *B. vulgaris* (Table 2 and 3). *B. aristata* root extract caused decrease in glycemia and helped to regulate carbohydrate metabolism in diabetic rats (51). Moreover, the extract of *B. vulgaris* tree root is effective in treating and preventing the formation of stones in gastrointestinal tract (52). *B. croatica* Horvat is rich in barberry, phenol, and flavonol. The root extract of this plant can exert antimicrobial effects against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*, and *Candida albicans* (53). One of the main compounds of *B. integerrima* is berberine. Berberine can exert protective effects on central nervous system and help to treat the diseases of this system (54).

Moreover, this alkaloid can protect islets of Langerhans in diabetic mice and cause increase in insulin secretion, decrease in cholesterol and low-density lipoprotein, and increase in high-density lipoprotein (55). As with other fruits, *B. vulgaris* fruit contains salts and different vitamins including vitamin C. Ascorbic acid was found to exert positive effects on dementia progression in Alzheimer’s disease patients (56). In addition, the plasma levels of ascorbic acid were found to be lower in patients with dementia compared to the controls, representing the protective effect of ascorbic acid on the brain function and in preventing cognitive disorders (57). Moreover, ascorbic acid, a nature-based agent, has been reported to be effective in improving memory in patients and older animals (58).

Ascorbic acid has been reported to be effective in improving learning disabilities and memory disorders in several experimental models (59). The effect of the administration of aqueous and hydroalcoholic *B. vulgaris* extract on the rate of insulin secretion in islets of Langerhans in mice confirmed the *in vitro* antidiabetic effects in low concentrations of glycemia, and that affecting islets of Langerhans was a hypoglycemic mechanism of *B. vulgaris* (60). The useful effect of long-term consumption of processed *B. integerrima* has been confirmed on some of the components of metabolic syndrome (61). Moreover, this plant has morphine-like properties and is therefore effective in quitting
substance abuse. B. vulgaris fruit has been shown to have hypotensive effects in patients with type 2 diabetes (5). Besides that, scientific studies have confirmed the control of inflammatory markers in animal models through the use of B. vulgaris fruit (62).

Aqueous B. integerrima fruit extract can have a highly important role in lowering cholesterolemia and triglyceridemia in patients (63). The protective effects of B. vulgaris extract on carbon tetrachloride-induced cytotoxicity in liver demonstrated that this extract could prevent liver damage in mice (64). B. vulgaris antioxidant effect on oxidative systems such as liver cells oxidation, red blood cells hemolysis, and hemoglobin non-enzymatic glycosilation demonstrated that the highest inhibitory effect was exerted on glycosilation, and that lipid peroxidation was adequately inhibited in the presence of different concentrations of B. vulgaris (65). Oral use of aqueous B. vulgaris fruit extract was demonstrated to be effective on moderate Acne vulgaris in adolescents (66). Hydroalcoholic B. integerrima extract was reported to be effective in inhibiting the growth of E. coli and S. aureus (67).

A study on the protective effect of aqueous B. vulgaris extract in rat model of Parkinson’s disease demonstrated that the aqueous B. vulgaris extract could decrease the behavioral symptoms of this disease due probably to inhibiting ACE enzyme in brain tissue (68). The inhibition of some markers and the activation of some others by two-week oral use of B. vulgaris caused inhibition of T lymphocytes and prevented the progression of type 1 diabetes in mice (69). Use of B. vulgaris root extract alongside drinking water inhibited the deposition of calcium oxalate crystals in kidney tubules, improved oxidative stress in kidney and polyuria, and prevented weight loss in rats (70). B. integerrima is a rich source of antioxidants that can contribute significantly to promoting community health (31).

Aqueous B. vulgaris fruit extract caused a significant decrease in the liver enzymes and total bilirubin and an increase in total serum protein in mice with streptomycin-induced diabetes. It is therefore concluded that B. vulgaris fruit is likely to improve diabetes mellitus-induced liver damage in diabetic mice through modulating detoxifying enzymes and antioxidant factors (71). The optimal effects of B. integerrima extract have been confirmed on weight loss and decrease in systolic and diastolic blood pressure. If clinical trials are conducted with the populations of large sample size, the findings can be more definitely generalized to the whole community and this extract can be recommended to lose weight and lower blood pressure in patients with alcoholic fatty liver (72). Moreover, use of hydroalcoholic B. vulgaris extract can cause a considerable decrease in the lipid profile of diabetic rats (29).

**Table 1. Summary of metabolites in Berberis vulgaris**

| Disease | Type of study | Berberis species | Part of plant | Results | Reference |
|---------|--------------|-----------------|---------------|---------|-----------|
| Human prostate cancer cell lines | Experimental (Rat) | Berberis lycium | Root | Ammonia-dichloromethane extract showed a high therapeutic potential to target prostate cancer and its cancer stem cells. | (75) |
| Cancer | | | | Berberine and the butanolic extract inhibited the expression of the proto-oncogene cyclin D1 and induced the acetylation of α-tubulin. This correlated with the induction of apoptosis. The data demonstrate that berberine is a potent anti-neoplastic compound that acts via anti-proliferative and pro-apoptotic mechanisms independent of genotoxicity. Microscopic examinations of the TUNEL-positive apoptotic cells demonstrated a significant difference between cancer control and normal control group. Increasing concentration of B. vulgaris aqueous extract in cancerous treated groups showed considerable increase in TUNEL-positive cells compared with the cancer control group, and apoptotic | (77) |
| | | | | Ethanolic extract was observed to be efficient and the presence of alkaloids and flavonoids may be responsible for the observed anticancer effects. Methanolic extract induces a concentration-dependent inhibition of HT29 cells, with an IC50 of 1.8964 μg/ml after 72 hours of incubation. The fruit can reduce the activity of liver enzymes and inhibit the gene expression of alpha-fetoprotein in rats during hepatocarcinogenesis. Ammonia-dichloromethane extract showed a high therapeutic potential to target prostate cancer and its cancer stem cells. Berberine and the butanolic extract inhibited the expression of the proto-oncogene cyclin D1 and induced the acetylation of α-tubulin. This correlated with the induction of apoptosis. The data demonstrate that berberine is a potent anti-neoplastic compound that acts via anti-proliferative and pro-apoptotic mechanisms independent of genotoxicity. Microscopic examinations of the TUNEL-positive apoptotic cells demonstrated a significant difference between cancer control and normal control group. Increasing concentration of B. vulgaris aqueous extract in cancerous treated groups showed considerable increase in TUNEL-positive cells compared with the cancer control group, and apoptotic | (42) (73) (74) (75) (76) (77) |
| Category                        | Condition                                                                 | Test Model                                                                 | Plant/Compound                    | Part | Activity                                                                                                          | Reference |
|--------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------|-----------------------------------|------|------------------------------------------------------------------------------------------------------------------|-----------|
| Antihistaminic                 |                                                                           |                                                                            |                                   |      | cells increased with increase in *B. vulgaris* extract concentration in cancerous groups. The results indicated antihistaminic and anticholinergic activities of the extract, potentially competitive. | (5)       |
| Cardiovascular / Hypertension  |                                                                           |                                                                            |                                   |      | Aqueous extract has beneficial effects on both cardiovascular and neural systems, suggesting a potential use to treat hypertension, tachycardia, and some neurological disorders, such as epilepsy and convulsion. | (78)      |
| Gastrointestinal               |                                                                           |                                                                            |                                   |      | Aqueous extract has beneficial effects on both cardiovascular and neural systems, suggesting a potential use to treat hypertension, tachycardia, and some neurological disorders, such as epilepsy and convulsion. | (78)      |
| Epilepsy                       |                                                                           |                                                                            |                                   |      | It causes decrease in systolic blood pressure in the right ventricle.                                             | (79)      |
| Epilepsy                       |                                                                           |                                                                            |                                   |      | Aqueous extract has beneficial effects on both cardiovascular and neural systems, suggesting a potential use to treat hypertension, tachycardia, and some neurological disorders, such as epilepsy and convulsion. | (80)      |
| Fever / Antibacterial          |                                                                           |                                                                            |                                   |      | The onset of castor oil-induced diarrhea was delayed and the number of diarrheal episodes was reduced by the extract in a dose-dependent manner.                                                       | (82)      |
| Fever / Antibacterial          |                                                                           |                                                                            |                                   |      | *B. aristata* produces anti diarrheal effect through decreasing intestinal secretions and antispasmodic effect through inhibiting intestinal motility.                                                                                     | (83)      |
| Fever / Antibacterial          |                                                                           |                                                                            |                                   |      | *B. aristata* root was effective. The extract was more effective than the alkaloid berberine.                                                                                 | (84)      |
| Fever / Antibacterial          |                                                                           |                                                                            |                                   |      | *B. integrerrima* reduced systolic blood pressure in the right ventricle.                                                                                                 | (85)      |
| Fever / Antibacterial          |                                                                           |                                                                            |                                   |      | Significant hypoglycemic activity and hypolipidemic activity was exhibited by the methanolic extract.                                                                     | (86)      |
| Fever / Antibacterial          |                                                                           |                                                                            |                                   |      | The crude extract significantly prevented the increase in LDL, VLDL, total cholesterol, triglyceride, attherosclerotic index, and coronary risk index in high fat diet, cholesterol, fructose and olive oil-induced hyperlipidemic rat model. | (87)      |
| Fever / Antibacterial          |                                                                           |                                                                            |                                   |      | Blood glucose levels of the diabetic rats treated with aqueous extract decreased on the first day. This condition remained roughly constant for three weeks. Both extracts also declined                                                                             | (88)      |
| Diabetes                       |                                                                           |                                                                            |                                   |      | The amount of cholesterol, triglyceride, and LDL decreased significantly.                                                                                                  | (89)      |
| Diabetes                       |                                                                           |                                                                            |                                   |      | *B. lycium* treatment increased the levels of high density lipids.                                                                                                       | (90)      |
| Diabetes                       |                                                                           |                                                                            |                                   |      | The extracts also lowered the levels of cholesterol, triglycerides, LDL, VLDL, serum glutamic oxaloacetic transaminase, serum glutamic-pyruvic transaminase, and serum ALP in diabetic rats.         | (91)      |
| Diabetes                       |                                                                           |                                                                            |                                   |      | Blood glucose levels of the diabetic rats treated with aqueous extract decreased on the first day. This condition remained roughly constant for three weeks. Both extracts also declined                                                                             | (92)      |
Experimental (rat)  B. aristata  Root  The extract has strong potential to regulate biochemical parameters significantly.  (51)

Experimental (rat)  B. lyceum  Root  Oral administration of 50 mg/kg of the extract and berberine to normal and experimental diabetic rats caused a significant reduction in blood glucose levels from day 3 to day 7 of treatment. As well, significant effects were observed on the glucose tolerance, glycosylated hemoglobin, serum lipid profiles, and body weight of experimental animals.  (93)

Experimental (rat)  B. integrerrima  Root  Aqueous extract improves renal dysfunction in streptozotocin-induced diabetes in rats through controlling blood glucose and renal protective effects.  (94)

Experimental (rat)  B. integrerrima  Root  Aqueous extract has hypoglycemic, hypolipidemic, and antioxidant effects in streptozotocin-induced diabetes in rats.  (95)

Experimental (rat)  B. integrerrima  Root  Aqueous extract had a desirable effect on the testosterone level, blood glucose, and histological changes of testes during the course of diabetes.  (96)

Table 2. Summary of the findings on some species from genus Berberis most frequently used to treat different diseases

| Disease                      | Title of article                                      | Berberis species | Part of plant | Results                                                                                           | Reference |
|------------------------------|-------------------------------------------------------|------------------|---------------|---------------------------------------------------------------------------------------------------|-----------|
| Acne vulgaris                | Aqueous extract of dried fruit of Berberis vulgaris in acne vulgaris, a clinical trial | Berberis vulgaris | Fruit         | Oral aqueous extract of dried barberry is a safe, well-tolerated, and effective choice in teenagers with moderate to severe acne vulgaris | (97)      |
| Cardiovascular / Hypertension | The Effect of Berberis Vulgaris extract on blood pressure and weight of the patients suffered from Non-alcoholic fatty liver disease | B.vulgaris | Fruit        | Mean systolic and diastolic blood pressure was significant compared to control group.             | (72)      |
| Cardiovascular / Hypertension | Effect of processed Berberis vulgaris in apple vinegar on blood pressure and inflammatory markers in type 2 diabetic patients | B.vulgaris | Fruit Of B.vulgaris in apple vinegar | findings had shown processed B.vulgaris had no effect on systolic- and diastolic blood pressure but apple vinegar had positive effect on interleukin-6. Nevertheless, further investigations about B.vulgaris effect on blood pressure and inflammatory markers are necessary. | (98)      |
| Diabetes                     | Clinical trial (patients with diabetes type 2)        | Berberis         | Fruit         | The fruit had a significant reducing effect on serum glucose and decreased HbA1c levels during the 8 weeks of study. | (99)      |
| Diabetes                     | Clinical trial (type 2 diabetic patients)             | B.vulgaris       | Fruit         | Mean nutritional intake, anthropometric indices, hs CRP concentration, and systolic and diastolic blood pressure did not change in processed B. vulgaris. Also, interleukin-6 concentration did not change in processed B. vulgaris and control groups. | (98)      |
| Diabetes                     | The effects of Berberis vulgaris fruit extract on serum lipoproteins, apoB, apoA-I, homocysteine, glycemic control and total antioxidant capacity in type 2 diabetic patients | Berberis         | Fruit         | The intake of 3 g/d of B. vulgaris fruit extract for 3 months may have benefical effects on lipoproteins, apoproteins, glycemic control and total antioxidant capacity in type 2 diabetic patients. | (100)     |
| Lipid profile                | Clinical trial (dyslipidemic patients)                | Berberis aristata | Fruit       | B. aristata reduced total cholesterol, triglycerides, and LDL cholesterol and increased HDL cholesterol after three months. | (101)     |

Discussion

This study was conducted to investigate the phytochemical characteristics, the findings of the experimental studies and the clinical trials conducted on the most frequently used species of the plants from this genus in traditional medicine, focusing on B. vulgaris which is the most frequently used plant of this genus.

Because no single pattern has been used to refer to different species of barberries in the articles published in Persian language and the recently published works, the readers and examiners of the texts might become confused. For example, Mozaffarian, in "A Dictionary of Iranian Plant Names", classified the B. integrerrima and B. crataegina as black or seeded berbery (B). However, in several studies, B. vulgaris has been referred to as
black barberry (61-63). B. vulgaris has been considered to be the same as B. khorasanaica in some references and different from this plant in some others (73, 102). This can affect the interpretation of the findings and the conclusions drawn.

The fruits of most plants from family Berberidaceae are rich in antioxidants (51, 75, 76). Free radicals are the normal by-products of metabolism in the body, and can cause cell damage by bonding to other molecules and stimulating the growth of anomalous cells, or intervening in the function of normal cells such as nerve and brain cells (74, 77). However, in the presence of antioxidants, the effects of free radicals are neutralized and the damage due to them is minimized (78). Antioxidants therefore play a significant role in preventing a variety of diseases such as cancer and diabetes and hypertension(49, 103).

The results briefly indicate that B. vulgaris contains a large number of phytochemical materials including ascorbic acid, vitamin K, several triterpenoids, more than 10 phenolic compounds and more than 30 alkaloids. Therefore B. vulgaris may have antihypertensive, anti-cancer, anti-inflammatory, antioxidant, antibacterial, analgesic and anti-nociceptive and hepa-to-protective effects (15, 29, 79).

The fruits of most plants from Berberidaceae family have a sour taste which is due mainly to the presence of ascorbic acid or vitamin C. We can discuss vitamin C in these fruits with regard to affecting physiological functions of the body in both antioxidants and vitamins. As vitamin C, an antioxidant, enters into bloodstream, it neutralizes or minimizes the damage to the body's tissues due to the effect and destruction caused by chemicals (62).

This vitamin can protect the skin of human body against adverse effects of the sun ultraviolet radiation. Besides that, vitamin C improves the body's immunity and contributes to the increased strength of gums and teeth (80).

Collagen is a connective tissue which keeps the body parts together. Vitamin C is required to produce and maintain collagen tissue in the body (104).

This vitamin can prevent hypercholesterolemia and clot formation in blood vessels (81). Moreover, vitamin C facilitates iron absorption in gastrointestinal tract, and therefore people with anemia are recommended to use vitamin C alongside iron-containing foods and medications (82). This important vitamin that is found in the fruits of the plants from Berberidaceae family can be used to prevent osteoporosis and osteomalacia and to treat stroke and atherosclerosis (83, 84).

Plants are the richest sources of alkaloids, and alkaloids can cause strong physiological reactions with special effects in human beings. These compounds are particularly effective on nervous system(105, 106).

The aerial organs of the plants from Berberidaceae family contain several compounds that are effective in treating diseases. Alkaloids are a group of these compounds (85, 107). Alkaloids can exert strong physiological effects in the body of mammals, including human beings. Lack of alkaloids may cause various problems in the body of human being. For example, deficiency of phenylalanine, as a non-polar alkaloid, can lead to disturbed process of thyrosine production in converting levodopa in the brain to dopamine or noradrenaline to adrenaline. Phenylalanine deficiency can lead finally to certain disorders such as depression and declined pain tolerance (85, 86, 108).

**Conclusion**

In the light of use of different organs of B. vulgaris in traditional medicine and certain properties of these organs that were confirmed in the recent studies, it is possible to use them, especially fruit, to develop new drugs.

**Acknowledgment**

Hereby, we gratefully thank the Deputy of the Research and Technology of the Shahrekord University of Medical Sciences for providing financial to conduct this study.

**References**

1. Bahmani M, Zargaran A, Rafieian-Kopaei M, Saki K. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus in the Urmia, Northwest Iran. Asian Pac J Trop Med 2014; 7:S348-5354.
2. Calixto J. Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). Braz J Med Biol Res 2000; 33:179-189.
3. Fallah Huseini H, Zareei Mahmoudabady A, Mehrzam M, Alavian SM, Kianbakht S, Mehdizadeh M. The effects of taraxacum officinale L. and Berberis vulgaris L root extracts on carbon tetrachloride induced liver toxicity in rats. J Med Plan 2010; 9:45-52.
4. Hasani-Ranjbar S, Larijani B, Abdollahi M. A systematic review of Iranian medicinal plants useful in diabetes mellitus. Arch Med Sci 2008; 4:285-292.
5. Shamsa F, Ahmadiani A, Khoreshkarvar R. Antihistaminic and anticholinergic activity of barberry fruit (Berberis vulgaris) in the guinea-pig ileum. J Ethnopharmacol 1999; 64:161-166.
6. Alemardan A, Asadi W, Rezaei M, Tabrizi L, Mohammadi S. Cultivation of Iranian seedless barberry (Berberis integerrima ‘Bidaneh’): A medicinal shrub. Ind Crops Prod 2013; 50:276-287.
7. Hesami M, Alibaday S. Berberis use traditional Drbh. National Seminar on Natural Products and Medicinal Plants. J North Khorasan Univ Med Sci 2012; Exclusive Magazine Conference: p. 31.
8. Mozaffarian V. A Dictionary of Iranian Plant Names. Tehran-Iran: Farhang Moaser; 2007.
9. Ardestani SB, Sahari MA, Barzegar M, Abbasie S. Some physiochemical properties of Iranian native barberry fruits (abi and poloei): Berberis integerrima and Berberis vulgaris. J Food Pharm Sci 2013; 1:3.
10. Rahimi-Madiseh M, Gholami-Arjenaki M, Bahmani M, Mardani G, Farzan M, Rafieian-Kopaei M. Evaluation of minerals, phenolics and anti-radical activity of three species of Iranian berberis fruit. Derpharma Chemica. 2016; 8:191-197.

11. Zarghami Moghadam M. Barberry ecophysiology. Environ Iran 2011; 24:50-51.

12. Mokhber-Dezfuli N, Saeidnia S, Gohari AR, Kurepaz-Mahmoodabadi M. Phytochemistry and pharmacology of berberis species. Pharmacogn Rev 2014; 8:8.

13. Bhardwaj D, Kaushik N. Phytochemical and pharmacological studies in genus Berberis. Phytchem Rev 2012; 11:523-542.

14. Abd El-Wahab AE, Ghereeb DA, Sarhan EE, Abu-Serie MM, El Demellawy MA. In vitro biological assessment of Berberis vulgaris and its active constituent, berberine: antioxidants, anti-acetycholinesterase, anti-diabetic and anticancer effects. BMC Complement Altern Med 2013; 13:1.

15. Farhadi AK, Gavadaifir K, Farha A. Effects of Berberis Vulgaris fruit extract on blood cholesterol and triglyceride in hyperlipidemic patients. Koomeh, J Semman Unim Univ Med 2008; 9:211-216.

16. Rezaei M, Etahi A, Reim S, Fatahi R, Balandary A, Farrokhi N, et al. Molecular analysis of iranian seedless barberries via SSR. Sci Hortic 2011; 129: 702-709.

17. Roy S, Tyagi A, Shukla V, Kumar A, Singh UM, Chaudhary LB, et al. Universal plant DNA barcode loci may not work in complex groups: a case study with Indian Berberis species. Plos One 2010; 5:e1.3674.

18. Singh M, Srivastava S, Rawat A. Antimicrobial activities of Indian Berberis species. Fitoterapia 2007; 78:574-576.

19. Gahreman A. Flora of Iran. Tehran-Iran: Research institute of forests and rangelands; Vol. 7. 1987.

20. Mozaflarian V. Trees and Shrubs of Iran. Tehran-Iran: Farhang Moaser; 2005.

21. Mazandarani M, Ghasemi N, Bayat H. The second review and comparison of active ingredients in plant organs of Berberis vulgaris. J Plant Sci Res 2013; 8:59-17.

22. Khan T, Khan IA, Rehman A. Evaluation and detailing of taxonomic and historical perspectives on genus Berberis from Pakistan. J Bio & Env Sci 6:361-367.

23. Christenhusz JM, Byng JW. The number of known plants species in the world and its annual increase. Phytotaxa 2016; 261:201-217.

24. Landrum LR. Revision of Berberis (Berberidaceae) in Chile and adjacent southern Argentina. Ann Mo Bot Gard 1999; 79:834.

25. Laamech, J. Laamech J, El-Hilaly J, Fetoui H, Chbourou Y, Gouttaa H, Tahrroui A, Lyoussi B. Berberis vulgaris L. effects on oxidative stress and liver injury in lead-intoxicated mice. J Complement Integr Med 2017; 14. DOI: 10.1515/jcim-2015-0079

26. Nickol MG. Phylogeny and in florescences of Berberidaceae—a morphological survey, in Systematics and Evolution of the Ranunculiflorae. Springer; 1995.p. 527-340.

27. Ahrendt LWA. Berberis and Mahonia. Bot J Linn Soc 1961; 57:1-410. DOI: 10.1111/j.1095-8339.1961.tb00899.x

28. Sodagar N, Bahrami AR, Memariani F, Eftehadi H, Vaezi J, Khosravi AR. Bi osystematic study of the genus Berberis L(Berberidaceae) in Khorassan, NE Iran. Plant Syst Evol 2012; 298:193-203.

29. Madiseh MR, Heidarian E, Rafieian-kopaei M. Biochemical components of Berberis lycium fruit and its effects on lipid profile in diabetic rats. J HerbMed Pharmacol 2014; 3: 1.

30. Yin J, Hu R, Chen M, Tang J, Li F, Yang Y, et al. Effects of berberine on glucose metabolism in vitro. Metabolism 2002; 51:1439-1443.

31. Farhady Chitgar M, Varidy MJ, Varidy M. Evaluation of some phyaechanical properties of Berberis crataegi. 2012, Bojnord-Iran: Book of the National Conference of natural products and herbs.

32. Rajurkar NS, Pardeshi BM. Analysis of some herbal plants from India used in the control of diabetes mellitus by NAA and AAS techniques. Appl Rad Isot 1997; 48:1059-1062.

33. Arayne MS, Sultana N, Bahadur SS. The berberis story: Berberis vulgaris in therapeutics. Pak J Pharm Sci 2007; 20:83-92.

34. Zarei A, Changizi-Ashiyani S, Taheri S, Ramezani M. A quick overview on some aspects of endocrinological and therapeutic effects of Berberis vulgaris L. Aviceca J Phytomed 2015; 5: 485.

35. Hadaruga DI, Hadaruga NG, Bandur GN, Rivas A, Costescu C, Ordodi VL, et al. Berberis vulgaris extract/β cycloextrin nanoparticles synthesis and characterization. Rev Chim(Bucharest) 2010; 61:669-675.

36. Kong W, et al. Berberine is a novel cholesterol-lowering drug working through a unique mechanism distinct from statins. Nat Med 2004; 10:1344-1351.

37. Fatemi-Hassanabad Z, Jafarzadeh M, Tarhini A, Fatehi M. The antihypertensive and vasodilator effects of aqueous extract from Berberis vulgaris fruit on hypertensive rats. Phytother Res 2005; 19: 222-225.

38. Arayne MS, Sultana N, Bahadur SS. The berberis story: Berberis vulgaris in therapeutics. Pak J Pharm Sci 2007; 20:83-92.

39. Kupeli E, Kogar M, Yesilada E, Hinsu K, Basar C. A comparative study on the anti-inflammatory, antiinceptive and antipyretic effects of isoquinoline alkaloids from the roots of Turkish Berberis species. Life Sci 2002; 72:645-657.

40. Laferriere JE, Weber CE, Kohlhepp EA. Use and nutritional composition of some traditional Mountain Pima plant foods. J Ethnobiol 1991; 11:93-114.

41. Hunt AH. The role of vitamin C in wound healing. Br J Surg 1941; 28:436-461.

42. Pai K, Srilatha P, Suryakan K, Setty MM, Nayak PG, Rao CM, et al. Anticancer activity of Berberis aristata in Ehrlich ascites carcinoma-bearing mice: A preliminary study. Pharmacol Biol 2012; 50:270-277.

43. Carr AC, Frei B. Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. Am J Clin Nutr 1999; 69:1086-1107.

44. Boul S, Terezhalmi G. Vitamin C in health and disease. J Contemp Dent Pract 2004; 5:1-13.

45. Aghili M. Makhzan-al-Advia. Tehran: Tehran University of Medical Sciences; 2009.p.328.
with metabolic syndrome. Med J Tabriz Univ Med Sci Health Services 2009; 31:89-94.
63. Farhadi A, Gavadinfar K, Farhadi A. Effects of Berberis vulgaris fruit extract on blood cholesterol and triglyceride in hyperlipidemic patients. koomesh 2008; 9:211-216.
64. Hermeneue A, Popescu C, Ardelean A, Stan M, Hadaruna N, Mihali CV, et al. Hepatoprotective effects of Berberis vulgaris L. Extract/B. cycloxdextrin on carbon tetrachloride–induced acute toxicity in mice. Int J Mol Sci 2012; 13:9014-9034.
65. Esraghi A, Movahedian AA, Asgari S, Naderi GA, Badiee A. Antioxidant Effect of Ziziphus vulgaris, Portulaca oleracea, Berberis intergerma and gandelia tournefortti on lipid peroxidation, HB glycosylation and Red Blood Cell Hemolysis. J Med Plants 2011; 10:80-88.
66. Fouland RF. Aqueous Extract of dried fruit of Berberis vulgaris L. in Acne vulgaris, a clinical trial J Diet Suppl 2012; 9:253-61.
67. Meskhilab MH, Abdollahi A, Fasiti RM, Admani SJ, Moravej A, Hatami S. Antibacterial effects of hydro-alcoholic extracts of Ziziphus tenuior, Teucrium polium, Berberis concorde and Stachys inalate. koomesh J Semann Univ Med Sci 2010; 11:240-244.
68. Salar F, Ziai SA, Nasri S, Roghani M, Kalaminejad M. Neuproteective Effect of aqueous extract of Berberis vulgaris L. in a model of parkinson’s disease in rat. J Med Plants 2010; 4:24-33.
69. Cui G, Qin X, Zhang Y, Gong Z, Ge B, Zang YQ. Berberine differentially modulates the activities of ERK,p38 MAPKand JNK to suppress Th17 and Th1 cell differentiation in type 1 diabetic mice. J Biol chem 2009; 284:29420-29429.
70. Bashir S, Gilani AH, Siddiqui AA, Perv ez S, Khan SR, Sarfaraz NJ, et al. Berberis vulgaris root bark extract prevents hypoxaluracia induced urolithiasis in rats. Phytother Res 2010; 24:1250-1255.
71. Ashraf H, Zare S, Farnad N. The effect of aqueous extract of barberry fruit on liver damage in streptozotocin - induced diabetic rats. J Shahrekord Univ Med Sci 2013; 15:1-9.
72. SalehZadeh H, Ilou KashkoolI R, Najafi SS, HosseinM As MK, Hamed A, Kalateh Sadati A. The effect of Berberis vulgaris extract on blood pressure and Weight of the wPatients suffered from Nonalcoholic fatty liver disease. jgbfnm 2013; 10:21-27.
73. Das S, Das MK, Mazumder PM, Das S, Basu SP. Cytotoxic activity of methanolic extract of Berberis aristata DC on colon cancer. Global J Pharmacol 2009; 3:137-140.
74. Motalleb G, Hanachi P, Fauziah O, Asmah R. Effect of Berberis vulgaris fruit extract on alpha-fetoprotein gene expression and chemical carcinogen metabolizing enzymes activities in hepatocarcinogenesis rats. Iran J Cancer Prev 2012; 1:33-42.
75. El-Merahbi R. Berberis lihanthina Ehrenb extract shows anti-neoplastic effects on prostate cancer stem/progenitor cells. PloS One 2014; 9:112453.
76. Khan M, Giessrigl B, Vonach C, Madlener S, Prinz S, Herbageck I, et al. Berberine and a Berberis lycium extract inactivate Cdk25A and induce α-tubulin acetylation that correlate with HL-60 cell cycle inhibition and apoptosis. MUTAT RES-FUND MOL M 2010; 683:123-130.
77. Hanachi P, Othman F, Motalleb G. Effect of Berberis vulgaris aqueous extract on the apoptosis, sodium and potassium in hepatocarcinogenic rats. Iran J Basic Med Sci 2008; 11:62-69.
78. Fatehi M, Saleh TM, Fatehi-Hassanabad Z, Farrokhfali K, Jafarzadeh M, Davodi SA. A pharmaceutical study on Berberis vulgaris fruit extract. J Ethnopharmacol 2005; 102:46-52.
79. Alamgeer A, Akhtar MS, Jabeen Q, Akram M, Khan Hu, Karim S, et al. Antihypertensive activity of aqueous-methanol extract of Berberis orthobotrys Bien Ex Aitch in rats. Trop J Pharm Res 2013; 12:393-399.
80. Mahdavi N, Joukar S, Najafi-Pour H, Asadi-Shekari M. The promising effect of barberry (Zereshk) extract against experimental pulmonary microvascular remodeling and hypertension: A comparison with sildenafil. Pharm Biol 2015; 54: 1-7.
81. Yejilada E, Kupeli E. Berberis crataegina DC. Root exhibits potent anti-inflammatory, analgesic and frutifuge effects in mice and rats. J Ethnopharmacol 2002; 79: 237-248.
82. Joshi PV, Shirkhedkar AA, Prakash K, Maheshwari VL. Antidiarrheal activity, chemical and toxicity profile of Berberis aristata. Pharm Biol 2011; 49:94-100.
83. Shamkuwar P, Pawar D. Antidiarrhoeal and antispasmodic effect of Berberis aristata. Int J Pharm Phytochem Res 2013; 5:24-26.
84. Bhutada P, Mundhada Y, Bansod K, Dixit P, Umathe S, Mundhada M. Anticonvulsant activity of berberine, an isoquinoline alkaloid in mice. Epilepsy Behav 2010; 18:207-210.
85. Singh M, Srivastava S, Rawat R. Antimicrobial activities of Indian Berberis species. Fitoterapia 2009; 79:574-576.
86. Changizi Ashityani S, Zarei A, Taheri S, Rezaei A, Golshan M, Ghafarzadegan R. A Comparative Study of Hypolipidemic Activities of the Extracts of Melissa officinalis and Berberis vulgaris in Rats. J Med Plants 2013; 3:38-47.
87. Razaar FA, Khan RA, Feroz Z, Afroz S. Effect of Berberis aristata on lipid profile and coagulation parameters. African J Pharm Pharm 2011; 5:943-947.
88. Upwar N, Patel R, Waseem N, Mahobia NK. Hypoglycemic effect of methanolic extract of Berberis aristata DC stem on normal and streptozotocin induced diabetic rats. Int J Pharm Pharm Sci 2011; 3:222-224.
89. Ghufar A, Ahmad T, Mushqaq MN. Antihyperlipidemic effect of Berberis orthobotrys in hyperlipidemic animal models. Bangladesh J Pharmacol 2014; 9:377-382.
90. Ahmed M, Alamgeer A, Sharif T, Zabta C, Akbar A. Effect of Berberis lycium Royle on lipid profile in alloxa induced diabetic rabbits. Ethnobotan Leaflets 2009; 13: 702-708.
91. Mustafa KG, Ganai B, Akbar S, Dar M, Tantry M, Masood A. The extracts of Berberis lycium and diabetes mellitus in alloxa monohydrate induced diabetic rats. J Pharm Res 2011; 4:2570-2573.
92. Meliani N, Dib MEA, Allali H, Tabti B. Hypoglycaemic effect of Berberis vulgaris L in normal and streptozotocin-induced diabetic rats. Asian Pac J Trop Biomed 2011; 1:468-471.
93. Gulfraz M, Mehmood S, Ahmad A, Fatima N, Praveen Z, Williamson E. Comparison of the antidiabetic activity of Berberis lyceum root extract and berberine in alloxa-induced diabetic rats. Phytother Res 2008; 22:1208-1212.
94. Ashraf H, Heidari R, Nejati V, Ilkhanipoor M. Aqueous extract of Berberis integerrima root improves renal dysfunction in streptozotocin induced diabetic rats. Avicenna J Phytopharm 2012; 3:82-90.
95. Ashraf H, Heidari R, Nejati V, Ilkhanipoor M. Effects of aqueous extract of berberis integerrima root on some physiological parameters in streptozotocin-induced diabetic rats. Iran J Pharm Res 2013; 12:425-434.
96. Ashraf H, Khanesi F, Rafiee Raki F, Nejati V. Evaluation of aqueous extract of Berberis Integerrima root on the testis tissue and testosterone levels in streptozotocine (stz) induced diabetic rats. Qom Univ Med Sci J 2013; 7: 28-35.
97. Fouladi RF. Aqueous extract of dried fruit of Berberis vulgaris L. in acne vulgaris, a clinical trial. J Diet Suppl 2012; 9:253-261.
98. Golzarand M, Ebrahimi-Managhani M, Arefhosseini S, Asgarzadeh AA. Effect of processed Berberis vulgaris in apple vinegar on blood pressure and inflammatory markers in type 2 diabetic patients. J Diabetes Metab Dis 2008; 7:3.
99. Moaezzi Z, Qiuej D. Berberis fruit extract and biochemical parameters in patients with type II diabetes. Jundishapour J Nat Pharm Prod 2014; 9:2.
100. Shidfar F, Seyed Ebrahimi S, Hosseini S, Heydari I, Shidfar S, Hajhassani G. The effects of Berberis vulgaris fruit extract on serum lipoproteins, apoB, apoA-I, Shidfar F, Seyed Ebrahimi S, Hosseini S, Heydari I, Shidfar S, Hajhassani G. The effects of Berberis vulgaris fruit extract on serum lipoproteins, apoB, apoA-I, homocysteine, glycemic control and total antioxidant capacity in type 2 diabetic patients. Iran J Pharmacol Res 2012; 12:643-652.
101. Derosa G, Bonaventura A, Bianchi L, Romano D, D’Angelo A, Fogari E, et al. Berberis aristata/Silybum marianum fixed combination on lipid profile and insulin secretion in dyslipidemic patients. Exp Opin Biol Ther 2013; 13:1495-1506.
102. Imanshahidi M, Hosseinzaadeh H. Pharmacological and therapeutic effects of Berberis vulgaris and its active constituent, berberine. Phytother Res 2008; 22:999-1012.
103. Baradaran A, Rafieian-Kopaei M. Oxidative stress and hypertension: Possibility of hypertension therapy with antioxidants. J Res Med Sci 2014; 19:4.
104. Saleh Zadeh H, Iloun ishakkooliR R, Najafi S, Hosseini Asl M, A. H, Kalateh Sadati A. The effect of Berberis vulgaris extract on blood pressure and weight of the patients suffered from Non-alcoholic Fatty Liver Disease. Journal of Research Development in Nursing & Midwifery (jgbfm) 2013; 11:21-27.
105. Smith L, Culvenor C. Plant sources of hepatotoxic pyrrolizidine alkaloids. J Nat Prod 1981; 44: 129-152.
106. Kulkarni S, Dhir A. Berberine: a plant alkaloid with therapeutic potential for central nervous system disorders. Phytother Res 2010; 24:317-324.
107. Javadzadeh SM, Falah SR. Therapeutic application of different parts Berberis vulgaris. Int J Agric Crop Sci 2012; 4:404-408.
108. Torres R, Delle Monache F, Marinì-Bettolo G. Biogenetic relationships between lignans and alkaloids in Berberis genus. Lignans and berbamine from Berberis chilensis. Planta Med 1979; 37: 37-44.