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REVIEW



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Iranian plant *Eremurus persicus*: an overview of botany, traditional uses, phytochemistry and pharmacology

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ABSTRACT

Eremurus persicus (Jaub. & Spach) Boiss. commonly known as "Serish" is a valuable ornamental plant with culinary uses and also utilized in traditional medicine for treating Gastrointestinal diseases. This comprehensive study was performed to investigate the pharmacological and biological effects of *E. persicus* and the compounds identified and isolated from it in order to encourage researchers to study it further. Despite the few number of studies on the ethnopharmacology of the plant *E. persicus*, however studies conducted on either crude extracts, solvent fractions or isolated pure compounds from *E. persicus* a varied range of biological effects comprising antibacterial, anti-fungal, anti-diabetic and etc. have reported. Phytochemical analysis of different parts of *E. persicus* unveiled 52 phytochemicals. However, the toxicity of this plant and its ethnopharmacological claims should be thoroughly investigated.



ARTICLE HISTORY

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KEYWORDS

E. persicus; Serish; phytochemicals; pharmacological

1. Introduction

The species *Eremurus persicus* (Jaub. & Spach) Boiss. with a local name called "Serish", it belongs to the family Xanthorrhoeaceae (or Asphodelaceae) and the genus *Eremurus* (The taxonomical classification of *E. persicus* plant is presented in Table 1). This genus is one of the most important genus of the Xanthorrhoeaceae family, with nearly 50 species reported in from that at the world and seven species from that also in Iran. Natural habitats of *E. persicus* widely distributed in arid and semi-arid regions, rocky

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2 👄 M. BEIRANVAND AND F. BEIRANVAND

| Kingdom | Plantae |
|----------|---|
| Phylum | Tracheophyta |
| Class | Liliopsida |
| Order | Asparagales |
| Family | Xanthorrhoeaceae or Asphodelaceae |
| Genus | Eremurus |
| Species | Eremurus persicus (Jaub. & Spach) Boiss. |
| Synonyms | =Asphodelus persicus Jaub. & Spach |
| | Eremurus aucherianus Boiss. |
| | <i>Eremurus persicus</i> subsp. sikesarus (O.Fedtsch.) Al |
| | <i>Eremurus sikesarus</i> subsp. doubtful. |
| | <i>—Henningia aucheriana</i> (Boiss.) Boiss. |
| | =Henningia persica (Jaub. & Spach) Regel |
| | =Henningia sikesara (O.Fedtsch.) A.P.Khokhr. |

| Table 1. | Taxonomical | classification | of | Ε. | persicus. |
|----------|-------------|----------------|----|----|-----------|
|----------|-------------|----------------|----|----|-----------|

mountains, especially in central and western Asia countries such as Afghanistan, Pakistan, Iran, Iraq, Syria, Tajikistan, Lebanon, Turkey, India and China. This plant species is also found in large areas of Iran including the provinces of Isfahan, Sistan and Baluchestan, Kohgiluyeh and Boyer Ahmad, Markazi, Qom, Chaharmahal and Bakhtiari, Fars, Kerman, Yazd, Lorestan, Semnan, North Khorasan and Razavi Khorasan.

E. persicus is a perennial herbaceous plant and has characteristics such as elongated and narrow leaves, complex at the base, 30 to 70 cm long and 1 to 3 cm wide. The flowers are White color, inclined to pink, in the form of a cluster inflorescence, and the roots are swollen, thick, fleshy, and tuberous. The roots of this species are thick and highly brittle with a starfish-shaped structure which would be sticky adjacent to water. The flowering stems of this plant, which have beautiful inflorescences and a height of 1-2 meters, have economic value and are often sold as cut flowers in flower shops around the world. *Eremurus* species are important commercially as ornamental plants for landscaping and cut-flower markets. Also, due to their large and colorful floral spikes, *Eremurus* species are known in the international horticulture trade as "Foxtail Lily" or "Desert Candle" (Naderi et al. 2009; Hadizadeh et al. 2020).

The thin and elongated leaves of *E. persicus* are consumed as a vegetable in Central Asia, and in Iran, its cooked leaves are used along with rice as a traditional food. In traditional medicine, the leaves and root of the *E. persicus* plant are used to treat liver, stomach, constipation and diabetes disorders. *E. persicus* root is used in the alcohol production due to the presence of branched and long chain carbohydrates. Also, the root of this plant (serish) is a well-known glue of plant origin in Iran that has been used for centuries as natural glue in the textile, carpentry, binding and book restoration industries. People traditionally collected the roots, dried and powdered them, and mixed them with water to make glue. (Koohkesh et al. 2020). Also, Decoction and root Poultice of this plant has been used in the past to treat ulcers and scabies. Some other Medicinal traditional uses of *E. persicus* are also listed in Table 2. (Kamenetsky and Rabinowitch 1999; Mosaddegh et al. 2012; Safar et al. 2014; Batooli et al. 2015; Jahanbin and Beigi 2016; Salehi et al. 2017; Kohkesh et al. 2019).

2. Phytochemistry

Several categories of phytochemicals different have been identified and isolated of genus *Eremurus*, including terpenes, polyphenols, flavonoids, naphthoquinones,

| Plant part | Folk medicine use | Reference |
|--------------|--|----------------------------|
| Leaves | Diuretic | (Rajaei and Mohamadi 2012) |
| Seeds | Arteriosclerosis | (Zare et al. 2014) |
| Leaves | Jaundice, liver disorders, and infectious diseases | (Zare et al. 2014) |
| Leaves | Genitourinary and nutritional disorders | (Shahrokhi et al. 2014) |
| Aerial parts | Skin diseases caused by fungi infections | (Hashemi et al., 2014) |
| Roots | Inflammation-related diseases and skin disorders | (Gaggeri et al. 2015) |

Table 2. Medicinal traditional uses of E. persicus.

Table 3. Chemical constituents of E. persicus essential oil.

| Compound | Relative % | Compound | Relative % |
|---------------------------|------------------------|----------------------------|------------|
| α-Pinene | 6.89 ^a | Epizonarene | 0.03(tr) |
| β-Pinene | 0.09 | Germacrene-D | 0.57 |
| α-Terpinene | 0.03(^b tr) | α-Farnesene | 3.52 |
| Limonene | 16.25 | (E)-Octenyl cyclopentanone | 0.23 |
| 1,8-Cineol | 5.22 | (Z)-Nerolidol | 0.04(tr) |
| Benzene acetaldehyde | 8.51 | Apiole | 2.52 |
| Guaiacol | 0.52 | Oxopentadecanone | 0.02(tr) |
| Linalool | 7.93 | n-Heptadecane | 0.34 |
| n-Nonanal | 9.48 | 2-Pentandecanol | 0.44 |
| trans-Pinocarveol | 0.01(tr) | Farnesol | 0.04(tr) |
| trans-Verbenol | 0.08 | Octadecane | 0.55 |
| 3,7-Dimethyl-6-octen-3-ol | 0.01(tr) | 7-Hydroxycoumarin | 0.03(tr) |
| cis-Verbenol | 0.02(tr) | (Z,Z)-Farnesyl acetone | 2.44 |
| Nonadienol | 1.57 | n-Nonadecane | 3.54 |
| 1,3-Dimethoxybenzene | 0.01(tr) | 2-Heptadecanone | 0.02(tr) |
| p-Cymen-8-ol | 0.45 | Methyl hexadecanoate | 0.02(tr) |
| α-Terpineol | 0.02(tr) | lcosane | 0.59 |
| Limonene aldehyde | 0.01(tr) | (-)-Falcarinol | 0.65 |
| Tetradecane | 0.1 | Geranylgeraniol | 15.23 |
| Geranyl acetone | 9.12 | Manool | 0.02 (tr) |
| 10-epi-β-acoradiene | 0.5 | n-Octadecanol | 0.53 |

a major compounds are shown in bold; ^b tr: traces, concentration less than 0.05%.

coumarin derivatives, anthraquinones, etc (Zhu et al. 2014). Tables 3 and 4 show in detail the identified and isolated (in some cases) phytochemicals from different parts of the *E. persicus* plant. Also, Figures 1 and 2 the chemical structure of the most important phytochemicals in this plant species it has been shown.

2.1. Terpenes

A wide variety of terpenes and their oxygenated derivatives (terpenoids) have been detected in E. persicus which are discussed as follow.

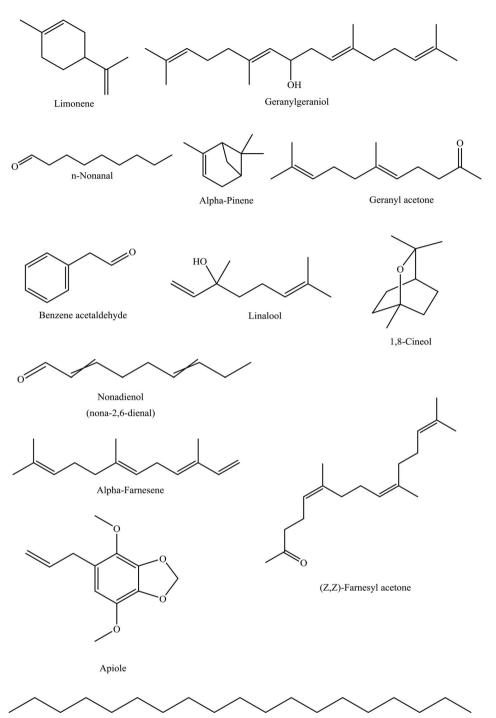
In a study conducted by Batooli et al. (2015) on the essential oil of various parts of *E. persicus* belonging to the Azaran region of Kashan. they reported that among the volatile compounds identified from the studied organs of this plant, 4.91% of the compounds The leaves and 3.80% of the compounds in the fruit, are monoterpenes, and 1.46% of the volatile compounds in the flower, 9.98% of the volatile compounds in the leaves and 15.55% of the volatile compounds in the fruit of this plant of monoterpenes oxygenated have formed. Also, only 0.66% of the flower components, 1.78% of the leaves and 1.09% of the fruit of this plant are Sesquiterpenes and 6.5% of the volatile compounds of the flower and 0.98% of the leaf essential oils of the plant from Sesquiterpenes oxygenated. In addition, among

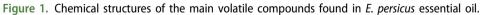
| Phytochemical | Extraction solvent(s) | Part used | Country (City) | Reference |
|--|---|------------------------------|------------------------------------|----------------------------------|
| Corchoionoside A | methanol–water 1:1, n-hexane, chloroform and ethyl acetate | Aerial parts | Iran (Fars) | (Mottaghipisheh et al., 2020) |
| 4-amino-4-carboxychroman- 2-one | methanol–water 1:1, n-hexane, chloroform and ethyl acetate | Aerial parts | Iran (Fars) | (Mottaghipisheh et al., 2020) |
| Isoorientin | methanol–water 1:1, n-hexane, chloroform and ethyl acetate | Aerial parts | Iran (Fars) | (Mottaghipisheh et al., 2020) |
| Ziganein 5-methyl ether | methanol–water 1:1, n-hexane, chloroform and ethyl acetate | Aerial parts | Iran (Fars) | (Mottaghipisheh et al., 2020) |
| Auraptene (coumarin derivative) | methanol–water 1:1, n-hexane, chloroform and ethyl acetate | Aerial parts | Iran (Fars) | (Mottaghipisheh et al., 2020) |
| Imperatorin (coumarin derivative) | methanol–water 1:1, n-hexane, chloroform and ethyl acetate | Aerial parts | Iran (Fars) | (Mottaghipisheh et al., 2020) |
| (R)- aloesaponol III 8-methyl ether | ethanol | Roots | lran (Isfahan) | (Martino et al., 2019) |
| Glucomannan | ethanol-water | Roots | lran (Isfahan) | (Jahanbin and Beigi, 2016) |
| 5,6,7-trimethoxy-coumarin | methanol | Flowering aerial parts | Iran (Isfahan) | (Asgarpanah et al., 2011) |
| 1, 5, 8- trihydroxy-3- methylanthraquinone (Helminthosporin) | methanol and ethyl acetate | Whole plant | Pakistan (Kirbi Kuch Ziarat) | (Khan et al., 2011) |
| 2-acetyl-1-hydroxy-8-methoxy- 3-methylnaphthalene | methanol and ethyl acetate | whole plant | Pakistan (Kirbi Kuch Ziarat) | (Khan et al., 2011) |

 Table 4. Isolation of secondary metabolites from E. persicus extracts

the volatile compounds identified in the leaf limb, 22.7% of the total identified compounds belonged to diterpenes. Comparison of monoterpene and sesquiterpene compounds in the essential oils of different organs of *E. persicus* showed that the percentage of monoterpenes in the essential oils of leaves and fruits was estimated between 14% and 19%, while in the essential oils of flowers, only 1.46% was obtained. However, the percentage of sesquiterpene of flower essential oil terpenes is estimated to be more than 6%. The amount of sesquiterpene of fruit and leaf has been obtained between 1 to 2.7%. Therefore, most of the monoterpene compounds of *E. persicus* essential oil were related to the leaf and fruit organs of the plant and the main sesquiterpene compounds of the essential oil of the plant were related to the flower organ (Batooli et al. 2015).

In another study conducted by Salehi et al. (2017) On essential oil of aerial parts (stems, leaves and flowers) of *E. persicus*. In total, 42 compounds were characterized by gas chromatography coupled to flame ionization (GC-FID) and gas chromatography coupled to mass spectrometry (GC-MS), representing 98.19% of the essential oil. In general, terpenes and their oxygenated derivatives (terpenoids) were the main class, with a relative abundance of 68.52%. Among them, the most abundant subclass was monoterpenes (46.13%). Moreover, the main individual constituents were limonene (16.25%), Geranylgeraniol (15.23%), n-Nonanal (9.48%), Geranyl acetone (9.12%), benzene acetaldehyde (8.51%), linalool (7.93%), α -Pinene (6.89%), and 1, 8-cineol (5.22%). The list of these compounds in Table 3 and the chemical structure of they main volatile compounds is shown in Figure 1 (Sharifi-Rad et al. 2018).





2.2. Polyphenols, flavonoids and naphthoquinones

Previous studies have reported that the genus *Eremurus* contains a wide range of polyphenols, flavonoids and naphthoquinones. In one of these studies on ethanolic extract

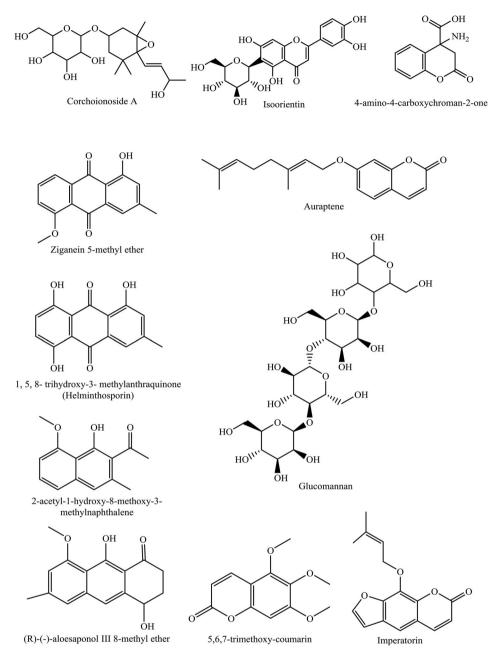


Figure 2. The chemical structures of the isolated phytochemicals from *E. persicus* extracts.

of *E. persicus* root, the presence of polyphenols, flavonoids and naphthoquinones were reported using thin layer chromatographic (TLC) analysis. Also, the amount of total phenolic contents in this study based on the method of measuring Folin-Ciocalteu's was expressed as 49.84% (Gaggeri et al. 2015). Recently, some polyphenols, such as Corchoionoside A (A rare glucoside aliphatic alcohol) and flavone C-glycoside isoorientin were identified and isolated from the methanolic-aqueous extract of *E. persicus* aerial parts (Table 4 and Figure 2) (Mottaghipisheh et al. 2020).

2.3. Coumarins

According to studies on *E. persicus*, the presence of compounds such as 5, 6, 7-trimethoxy-coumarin (Asgarpanah et al. 2011), 4-amino-4-carboxychroman-2-one, auraptene and imperatorin (Mottaghipisheh et al. 2020), which are derivatives of coumarins, at this plant has been proven (Table 4 and Figure 2).

2.4. Anthraquinones

Two anthraquinones have been identified and isolated in *E. persicus*: Helminthosporin is isolated from the whole plant by column chromatography and by TLC and NMR (nuclear magnetic resonance), were detected (Khan et al. 2011). Recently too, Ziganein 5-methyl ether has been isolated from the aerial parts of this plant species by flash chromatography and identified by TLC and NMR analysis (Table 4 and Figure 2) (Mottaghipisheh et al. 2020).

2.5. Miscellaneous compounds

In addition to the above-mentioned phytochemicals, some other chemical structures such as glucomannan (Jahanbin and Beigi 2016), 2-acetyl-1-hydroxy-8-methoxy-3-methylnaphthalene (Khan et al. 2011) and (R)- aloesaponol III 8-methyl ether are also isolated from the aqueous, methanolic and alcoholic extracts of *E. persicus* different parts (Table 4 and Figure 2) (Martino et al. 2019).

3. Pharmacological effects and biological activities

3.1. Antioxidant activity

Antioxidants are one of the most wonderful natural compounds in protecting humans against oxidative damage. Many plant-based antioxidants have been identified as freeradical scavengers (Ahmed et al. 2020). Many species of the genus Eremurus are known as an excellent source of natural antioxidants that have high antioxidant capacity (Tosun et al. 2012; Karadeniz et al. 2015; Tuzcu et al. 2017). Several studies have evaluated the antioxidant potential of E. persicus essential oil and extracts. Gaggeri et al. (2013) in a study on ethanolic extract of the root of this plant reported, the free radical scavenging activity of 2,2'-diphenyl-1-picrylhydrazyl (DPPH) by ethanolic extract of this plant at a dose of 250 μ g/ml 68% and EC₅₀ = 62.1 μ g/ml was estimated. In another study on the hydroalcoholic extract of E. persicus leaves, the inhibitory concentration of 50% from DPPH radicals, $IC_{50} = 79.80 \,\mu$ g/ml was evaluate. In both studies, the high antioxidant capacity of the plant extract was attributed to the high content of phenolic and flavonoid compounds and naphthoquinones (Beiranvand 2020). Also, in the study that was performed on Bioactive chemical compounds, the essential oil of the aerial parts of this plant, the IC_{50} value of the essential oil of the plant in relation to ascorbic acid and BHT was expressed as follows: ascorbic acid (0.48 g/L) <BHT (0.55 g/L) <E. persicus EO (6.20 g/L) (Salehi et al. 2017).

8 👄 M. BEIRANVAND AND F. BEIRANVAND

3.2. Antibacterial activity

Some species of the genus *Eremurus* have been shown to have antibacterial activity (Kanaani and Mohamadi 2015). The essential oil obtained from the aerial parts of *E. persicus* had antibacterial action against standard strains of *Staphylococcus aureus* (ATCC 6538) and *Escherichia coli* (ATCC 8739), so that dilutions of 1: 1 and 1: 2 zones of bacterial growth In *S. aureus* and *E. coli*, respectively, 12 and 10 mm have inhibited at 1: 1 dilution, 9 and 3 mm in 1: 2 dilution. This inhibitory effect is showed a relatively moderate effect of plant essential oil compared to gentamicin in inhibiting these bacteria (Salehi et al. 2017).

In investigation that by Hakemi Vala et al. (2011) on 4 Gram-positive bacteria strains and 5 Gram-negative bacterial strains were performed. Methanolic crude extract related to E. persicus flowering aerial parts, antibacterial action against *Staphylococcus aureus* (MIC 17.5 mg/ml), *Staphylococcus epidermidis* (MIC 15 mg/ml), *Bacillus cereus* (MIC 13.5 mg/ml), *Escherichia coli* (MIC 12.5 mg/ml), *Salmonella typhi* (MIC 14 mg/ml), *Shigella dysantriae* (MIC 32 mg/ml) showed. Also in a similar study (Ebrahimabadi et al. 2013) the antimicrobial activity of leaves and flowers of this plant were detected against 12 microorganisms including 3 fungi and 9 bacteria using disc diffusion and MIC test methods. Methanolic extract of the flowers showed weak effectiveness against *Staphylococcus aureus* and *Staphylococcus epidermidis* with inhibition zones of 9 mm and 10 mm and MIC values more than 1000 µg/ml, receptively. The leaves extract was also only weakly active against *Proteus vulgaris* with inhibition zone of 10 mm and MIC > 1000 µg/ml.

Recently too, In a study by Rahmani et al. (2021) done on the antimicrobial effect of ethanolic extract of *E. persicus* leaves in laboratory conditions, was observed that the MIC of ethanolic extract of *E. persicus* leaves on 12 strains of *staphylococcus aureus* between 5 to 10 ppm and also MBC on Staphylococcus aureus varies between 2.5 to 20 ppm.

3.3. Antiglycation (anti-diabetic) activity

The non-enzymatic reaction of sugar and protein is called glycation. This reaction does not take place under normal conditions in the body, but when the blood glucose is high for a long time, such as untreated diabetes, the glycation process occurs. Anti-glycation compounds can help reduce glycation-related diseases such as diabetes. A variety of natural compounds have been evaluated to test their anti-glycation properties (Dil et al. 2019). One of these compounds is 5, 6, 7-trimethoxy-coumarin, which has been identified and isolated from the methanolic extract of *E. persicus* aerial parts. 5, 6, 7-trimethoxy-coumarin is exhibited a good antiglycation activity. It was observed that this compound at 3 mM concentration showed 75% inhibition, while the standard inhibitor, rutin showed 83% inhibition (Asgarpanah et al. 2011).

In addition, the pharmacological effects of Corchoionoside A have not been studied so far; however, the presence of this type of compounds in the plant may contribute to the in vitro antiglycation activity of *E. persicus*, and could be related to the folk medicinal use of it as anti-diabetic remedy (Mottaghipisheh et al. 2020).

3.4. Antifungal and anti-leishmanial activities

E. persicus essential oil and extracts have significant antifungal and anti-leishmanial activity. In a study on the antifungal activity of *E. persicus* essential oil was reported, that the essential oil of this plant the greatest effect at minimum inhibitory concentration (MIC) on *Microsporum canis* and *Trichophyton rubrum* and minimum fungicidal concentration (MFC) on *Microsporum gypseum* and *Trichophyton rubrum* has (Salehi et al. 2017). Also in another study the anti-leishmanial potential of ethanolic extract and (R)-aloesaponol III 8-methyl ether isolated from ethanolic extract of *E. persicus* root by laboratory biological experiments, in particular, their anti-parasitic effects on *L. infantum* promastigotes have been investigated by MTT assay. The results of this study clearly have been showed that ethanolic extract had no effect on the survival of *L. infantum* promastigotes, while (R)-aloesaponol III 8-methyl ether showed an interesting anti-leishmaniosis activity with an IC₅₀ of 73 µg/ml. Moreover, this combination it was not toxic on macrophages at the concentration tested, thus representing a promising molecule against leishmania infections (Rossi et al. 2017).

3.5. Anti-inflammatory and anti-proliferative activities

Many plants have been experimented and investigated for anti-inflammatory activity and how they act to find new anti-inflammatory drugs (Nunes et al. 2020). Studies on ethanolic extract of E. persicus root in vitro have shown its anti-proliferative and antiinflammatory activity. Inhibitory activity of ethanolic extract of this plant species on human peripheral blood mononuclear cell (hPBMC) has clearly shown that ethanolic extract is able to inhibit phytohemagglutinin A (PHA) stimulated hPBMC proliferation. Particularly, ethanolic extract significantly have reduced the PHA-stimulated hPBMC proliferation in the concentration range 800 to $50 \,\mu$ g/ml. Also, the effect of ethanolic extract on the release of cytokines (TNF- α , IL-6 and IFN- γ) from PHA-stimulated hPBMC was also have evaluated. Interestingly, ethanolic extract did not affect the release of IL-6 and IFN- γ , while a significant effect (P < 0.05) had on TNF- α release. Particularly, PHA-induced TNF- α release was significantly reduced by the extract in the concentration range 200-800 μ g/ml (P < 0.05). The findings of these studies indicate that ethanolic extract of E. persicus root has an interesting in vitro anti-inflammatory effect, being effective in inhibiting the PHA-induced hPBMC proliferation as well as TNF- α release. Moreover, the observed inhibition of hPBMC proliferation is entirely due to anti-inflammatory properties of the extract and not to cytotoxic effect, as proved by cell viability experiments (Gaggeri et al. 2013, 2015).

3.6. Anticancer and cytotoxicity activities

So far, research has been done on the anti-cancer activity of many plants and the phytochemicals in them to prevent the progression and treatment of cancers (Lalitha et al. 2020). In the meantime, several articles have focused on the cytotoxic and anticancer activity of *E. persicus* essential oil and extract in vitro. In one of these studies, the cytotoxic effect of *E. persicus* methanolic extract on two cell lines HeLa (Human cervix carcinoma) and Caco-2 (Human colon carcinoma) have evaluated using the MTT assay. The results of this study have showed that the more concentration of extract in the cell culture the less OD (Optical density) was detected. It means, after increasing the concentration of methanolic extract the viability of cells were decreased. Similarly, both cell lines showed decrease in cell viability after the concentration of extract was increased and decrease in viability begins when 2.125 and 4.25 mg/ml of methanolic extract was added to Caco-2 and HeLa cells, respectively. On the other hand, some studies also have shown that the cytotoxic activity is related to the anthraquinones because it is shown that they are able to induce apoptosis (Hakemi Vala et al. 2011). Also In another study, the anti-cancer propertied of Helminthosporin was reported as a compound isolated from *E. persicus* extract (Khan et al. 2011).

Gaggeri et al. (2013, 2015) in their study on the effect of ethanolic extract of *E. persicus* root on cell viability, have showed that doses of 12.5, 25, 50, 100, 200, 400 and 800 ethanolic extracts on three tumor cell lines A549 (lung cancer), MCF-7 (breast cancer) and CaCo-2 and control cells were low and the cell viability was 98%, which indicates the absence of toxicity and any non-specific toxic effects or possible effects on cell growth. So that No difference in cell viability was observed between control cells and cells treated with the extract, even at the highest concentration.

Salehi et al. (2017) have evaluated the anti-cancer activity of essential oil of *E. persicus* on Hep-G2 (human hepatocellular carcinoma) and MCF-7 cell lines by MTT method. In this study, concentrations of 200, 250, 500, 1000 and 1500 ng/ml of essential oil were used. MTT results showed that In Hep-G2 cells, 200 ng/mL of essential oil decreased cell viability by 98% and 97% after 3 and 7 days, respectively, compared to untreated cells (P < 0.05).

3.7. Anticholinesterase and anti-tyrosinase activities

Anti-acetylcholinesterase (AChE) activity has been confirmed as a therapeutic solution for Alzheimer's disease in some plants, including *E. persicus* in two studies. In one of these studies, which have performed on methanolic extract of different parts of *E. persicus*, methanolic extract of flowers and fruits of this plant did not have an inhibitory effect on AChE activity, while methanolic extract of aerial parts of *E. persicus* was about 7% showed an inhibitory effect on AChE activity (Gholamhoseinian et al. 2009). In 2017, Salehi et al. have determined the activity of AChE in the essential oil of aerial parts (stems, leaves and flowers) of *E. persicus* using Ellman's spectrophotometric method. In this study, AChE activity of *E. persicus* essential oil was relatively moderate ($IC_{50} = 95.37 \mu g/mL$) compared to galanthamine as a standard drug.

Melanin is responsible for pigmentation of skin and hair and it protects the skin from the harmful effects of UV radiation; however, its abnormal production by increasing the activity of the enzyme Tyrosinase may lead to different diseases such as hyper-pigmentation or vitiligo. On the other hand, extracts of various plants such as *E. persicus* have been shown to be effective in regulating and reducing the activity of this enzyme. Gholamhoseinian and Razmi (2012) have shown that methanolic extracts of aerial parts and flowers of *E. persicus* can inhibit Tyrosinase enzyme by 21% and 5%, respectively. Also, Ahmed et al. (2011) have investigated the inhibitory effect of *E. persicus* root ethanolic extract on fungal tyrosinase. In this study, serial doses (from

750 to 32 mg/mL) of the extract were used and Arbutin was used as standard. The results of this study showed that the plant extract at a dose of 750 mg/mL has a maximum inhibitory effect of 80.3% on enzyme activity.

3.8. Gastroprotective (anti-ulcer) activity

Recently, researchers are trying to find new anti-ulcer drugs to protect the gastrointestinal tract, including the stomach (Beiranvand and Bahramikia 2020). Herbal medicines have a long history of treatment and prevention of gastric ulcers and they have shown this in experimental studies (Zakaria et al. 2014). Recently too, in a study by Beiranvand (2020) on the hydroalcoholic extract of E. persicus leaves. It has been reported that pretreatment of rats with doses of 250 and 500 mg/kg of this plant extract increased glutathione, tissue nitrogen oxide and catalase activity in comparison with the normal group. It is therefore believed that this plant strengthens the antioxidant defense system of the stomach. On the other hand, the hydroalcoholic extract of this plant, while reducing ROS, malondialdehyde, protein carbonyl and serum nitric oxide compared with the positive control group, has tried to reduce oxidative stress and thus prevent stomach damage. Also, the microscopic and macroscopic findings of this study have confirmed the anti-ulcer effect of this plant. In this study, the anti-ulcer activity of *E. persicus* was attributed to phenolic, flavonoid and coumarin derivatives. Of course, many studies have shown the anti-ulcer activity of naphthoquinones (Goel et al. 1987), polyphenols and a number of terpenes and terpenoids compounds.

3.9. Other pharmacological properties

One of the medicinal uses of *E. persicus* leaf is its use as a toothache spray that relieves the pain of a damaged tooth (Faridi et al. 2015). Some sources have also reported that leaves of *E. persicus* to treat inflammation and joint pain it is placed on wounds, bruises and burns (Amin et al. 2016).

4. Safety and toxicity

There are very few studies in which the toxicological aspects of Species of the genus *Eremurus* and their secondary metabolites have been assessed. However, a study by Mushtaq et al. (2014) on the acute toxicity of one species of the genus *Eremurus* showed that the ethyl acetate extract, methanolic and aqueous extracts of this species were safe up to 2000 mg/kg of body weight in Wistar strain albino rats weighing 190–220 g, and approximate median lethal dose (LD₅₀) is more than 2000 mg/kg is. Also, it is important to point out that the name of the genus *Eremurus* and also the species *E. persicus* are not poisonous among plants, which this promises the safety of this plant species [https://ucanr.edu/sites/poisonous_safe_plants/]. However, there is currently no study on the toxicity of *E. persicus*, and in vitro and in vivo studies are needed to consider whether the plant is completely safe and harmless.

5. Conclusion and future perspectives

The purpose of this review is to provide information on the botany, traditional applications, phytochemicals, pharmacology, toxicity and safety of *E. persicus*, which includes literature published over the last two decades. Most of the reported research on extracts from different parts of the plant shows a diverse range of pharmacological and biological propensities. In the study conducted during this review, we found that more than 52 phytochemicals were identified and isolated from different parts of E. persicus. On the other hand, phytochemical studies have shown that most of these secondary compounds belong to terpenes and terpenoids, phenolic compounds, coumarins and anthraquinones. Among these identified phytochemicals, only a few of them have been purified from the plant itself, that they have shown significant biological and pharmacological effects, especially antiglycation, anti-leishmaniosis and anti-cancer activities. But, so far no clinical studies have been performed to demonstrate the pharmacological effects of E. persicus on humans, and only one in vivo study showing the anti-ulcer effect of *E. persicus* crude extract on gastric ulcer induced by ethanol in rats' shows, has been reported. Therefore, according good medicinal capacity of this plant we suggest that in studies in vivo of future, anti-diabetic properties, liver diseases and constipation of this plant be checked. Also be done a comprehensive study on the safety and toxicity properties of this plant, to determine the possible side effects or toxicity of the extracts this plant and its active compounds for use in laboratory conditions, be clarified in vivo and even in subsequent clinical trials.

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