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Review Article

# A Short Review of *Allium jesdianum* Boiss. & Buhse (Amaryllidaceae)

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## Abstract

*Allium jesdianum* Boiss. & Buhse (Bon-e-Sorkh or Yazdi onion in Persian) is one of Iran's important endemic and threatened plants belonging to the genus *Allium*. It grows at high altitudes (1800–2600 m) in Zagros Mountains, where locals use the bulbs and aerial parts of the plant to treat colds, stomachaches, rheumatic pains, moisture diseases, and kidney problems. There is little research that highlights the chemical composition and biological activities of this medicinal herb. This review outlines the available literature on morphological characteristics, chemical composition, and medicinal uses of the *A. jesdianum*. Google Scholar, PubMed, Scopus, Web of Science, and local databases were searched to find relevant articles published in these databases from 1996 to 2023. Various climatic and environmental factors can affect the chemical composition of *A. jesdianum*. Bon-e-Sorkh possesses several medicinally significant activities such as antioxidant, anti-inflammatory, analgesic, antidiabetic, antibacterial, antifungal, anti-hepatic, anti-nephrotoxicity, anticancer, anti-Alzheimer's, antiplatelet, anti-anxiolytic, nephrolithiasis, protoscolicidal, and anti-toxicity activities. Investigators should complete further research to prove or confirm the results of previous studies reported in this paper by conducting more *in vitro* studies, and then *in vivo* as well as clinical studies if the results are promising.

**Keywords:** *A. jesdianum*, Medicinal herb, Endophytes, Phytochemicals, Pharmaceutical preparations

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## Introduction

The genus *Allium* L. (Amaryllidaceae) comprises one of the groups of petaloid monocotyledons characterized by a remarkable degree of diversity with currently more than 1,000 accepted species (1–2) and is widely found across the Holarctic area from the dry subtropics to the boreal zone (3). The major center of diversity of this genus is in the southwest and Central Asia and a minor one is in North America. It has bulbs enclosed in membranous tunics, free or almost free tepals, and a usual subgynobasic style (2). *Allium* genus is comprised of several economically significant species, including onions (*Allium cepa* L.), garlic (*Allium sativum* L.), leek (*Allium porrum* L.), chives (*Allium schoenoprasum* L.), and shallots (*Allium ascalonicum* L.) cultivated as vegetables or spices, as well as species used as herbal crops used traditional medicines and ornamental plants (3).

In traditional medicine, *Allium* species have been used to prevent and treat diseases such as diabetes, arthritis, colds, flu, cough, headache, hemorrhage, asthma,

atherosclerosis, and inflammatory diseases (4). Previous studies have shown that *Allium* species can have various biological effects such as antimicrobial, anti-inflammatory, antiplatelet, anti-hypertension, anti-diabetic, scavenging activity, cytotoxic effect, and anti-cancer effects (5). Phytochemical studies showed that *Allium* species are a rich source of organosulfur, antioxidants, and numerous phenolic compounds (4, 6).

*Allium jesdianum* Boiss. & Buhse (Bon-e-Sorkh or Yazdi onion in Persian) is a significant endemic, threatened, and underutilized herbal species of Iran (7). It is found in high altitudes (1800–2600 m) of Zagros Mountains, and native people of this region use the bulbs and aerial parts of the plant to treat colds, digestive system pains, rheumatic pain, moisture diseases, and kidney problems (8–9). Esmaeili *et al*. (10) reported that endophytes grow in several regions of the *A. jesdianum*, including stem, leaf, onion, and flower. Endophytes are the fungi or bacteria that exist in a plant in a symbiotic relationship. They are potent producers of bioactive compounds and secondary metabolites with potential uses in different fields, including agriculture, pharmaceuticals, environmental cleaning, and the food industry (10–11). Although several laboratory studies have been conducted on *A. jesdianum*, there is not much information about it. This review article was conducted on the medicinal plant *A. jesdianum* focusing on its medicinal activities.

## Materials and Methods

Google Scholar, PubMed, Scopus, Web of Science, and local databases were searched to find relevant articles published in these databases from 1996 to 2023. Additional sources were identified by cross-references. Search terms included *A. jesdianum*, *A. jesdianum*, Bon-e-Sorkh, Yazdi onion, *Allium*, taxonomy, morphology, chemical compound, chemical composition, phytochemical, therapeutic, pharmacological, and biological activity.

## Results and Discussion

**Systematics, Geographical Distribution, and Botanical Description**

*Allium jesdianum* belongs to kingdom Plantae, subkingdom Tracheobionta, clade Angiosperms, clade Monocots, super-division Spermatophyta, order Lillales, family Alliaceae, subfamily Allioideae, class Monocotyledons, sub-class Liliidae, genus *Allium*, subgenus *Melanocrommyum*, section *Procerallium*, and subsection *Costatae* (12–13). This medicinal plant is distributed in several provinces of Iran, including Lorestan, Kerman, Kohgiluyeh and Boyer-Ahmad, and Yazd provinces on shady montane gorges or arable land under trees (13–15).

Its bulbs are depressed globose, 1.5–5 cm in diam., 1.5–3.5 cm long, outer tunics smooth and membranous. Its scape is slightly flexuous, terete, green, basally red flushed, 25-50 (80) cm long, and (3) 4–8 (10) mm in diam. Its leaves are 2–6, lamina lanceolate or narrowly lanceolate, green with glaucous bloom, recurved, margin smooth, 30–40 (60) cm long, and (8) 18–25 (30) mm width. Sheath leaf is hyaline and tender. Spathe is fine membranous, brownish, split into 1–2 ovate-triangular parts, and veins. Inflorescences are spherical, medium dense, numerous flowers, 4–8 cm in diameter. Pedicel is thick, straight, stiff filamentous, brown to purple, finally green, and semi-glossy. The flowers are cup-shaped and star-shaped. Tepals are long lanceolate-triangular, patent and claw-like incurved, pinkish-carmine with narrow darker median vein, 8–10 (13) mm long, and 1–1.5 (2) mm width. Filaments are as long as tepals, subulate, slightly wider and converging at base, first pinkish, and then carmine. The upper part is first clear white, then purplish. Anthers are long ovoid, carmine, c. 2 mm long and 1 mm broad. Pollen is grayish yellow. Ovary is shortly stipitate, depressed globose or shortly pear-shaped triangular with 3 longitudinal grooves, surface tuberculate, green, 3–3.5 mm long and in diam. Style is ± thread-like, whitish finally pink and 5–9 mm long. Stigma is undivided, whitish. Capsule is stipitate depressed-globose triangular with 3 broad grooves, widely opening, valves rather broadly elliptical, shortly and broadly notched at the apex, with a broad longitudinal furrow, greenish yellow-brown, 6–7 mm long and c. 8 mm in diameter. Seeds are 1–2 per locule, flat ovoid-globose, ± angled, surface finely reticulate lacunose, dull black, 3–3.5 mm long, 2.5–3 mm wide, and c. 2 mm thick (Figure 1) (13, 16).

**Chemical Composition**

*Allium jesdianum* is collected from nature or cultivated for the production of essential oil and extract.

**Figure 1.** *A. jesdianum* Boiss. & Buhse (photo by Kalantari *et al.* 2018, published by Pharmaceutical Sciences).

A few authors have explored the composition of the essential oil and extract of *A. jesdianum* (e.g., 14–15, 17–18), and found high variability in the chemical composition. The variability was found to be dependent on the variety of ecotypes, plant growth stage, and environmental conditions. Amiri (14) examined the composition of the essential oil in natural individuals of *A. jesdianum* from Sefid Kooh located in Lorestan province by Gc and GC/MS, and the main compounds were dimethyl trisulfide (22.34%), hexadecanoic acid (19.03%), phytol (12.82%), disulfide methyl-1-ethyl (9.25%), pentacosane (8.03 %), and curzerene (7.62%). Askari *et al*. (15) studied essential oil of aerial parts from *A. jesdianum* collected in May from the Chamkhani area at Kohgiluyeh and Boyer-Ahmad province, southwest of Iran. The authors identified 54 compounds by Gc and GC/MS, where the most abundant compounds were hexadecanoic acid (18.34%), neral (13.74%), dimethyl trisulfide (12.15%), caryophyllene oxide (8.05%), gereninal (5.25%), borneol (3.31%), trans-propenyl propyl disulfide (3.17%), geranyl acetate (2.74%) and β-caryophyllene (2.65%). Falahi *et al*. (17) studied the dried flower extract of *A. jesdianum* collected from nature in Rimale, Sefid Kooh, Kala Kooh of Lorestan province. Their analysis of the chemical composition revealed many monoterpenes, sesquiterpenes, and nonterpene compounds (alcohols, esters, ketones, aldehydes, and phenols). The authors identified 48 compounds by GC/MS, and the main compounds were dimethyl trisulfide (48.85%), thymol (5.89%), linalool (3.62%), pulegone (3.6%), nonanal (3.22%), bornyl acetate (2.59%), tetradecane (2.28%), β-Ionone (1.81%), carvacrol (1.3%), pentadecane (1.21%), and heptanal (1.15%). Ramak *et al*. (18) compared essential oil compositions, some metabolites (soluble sugar, starch, proteins, vitamin C), and nutrients (N, P, K, Fe, Cu, Zn, and Mn) among three wild and cultivated ecotypes of *A. jesdianum* in Lorestan province. The results showed that dimethyl trisulfide, dipropyl trisulfide, di-2-propenyl tetrasulfide, hexadecanoic acid, and pentacosane were the significant components of the *A. jesdianum* essential oil. Moreover, the percentage of the essential oil components significantly differed among wild and cultivated ecotypes. They observed that the amount and quality of the essential oil, nutrients, and metabolites in planted populations were better than in wild populations. Thus, the authors concluded that planting this plant in organic conditions increases the chemical compounds, nutrients, and metabolites in this plant. Furthermore, in a phytochemical analysis of the fresh bulbs of *A. jesdianum*, Mimaki *et al*. (19) identified four steroidal glycosides, (22*S*)- cholest-5-ene-1*β*,3*β*,16*β*,22-tetrol 1,16-di-*O*-*β*-D-glucopyranoside (1), (22*S*)-cholest-5-ene-1*β*,3*β*,16*β*,22-tetrol 1-*O*-α-L-rhamnopyranosyl 16-*O*-*β*-D-glucopyranoside (2), (25*R*)-5α-spirostane-2α,3*β*-diol 3-*O*-{*O*-*β*-D-glucopyranosyl-(1→2)-*O*-[*β*-D-xylopyranosyl-(1→3)]-*O*-*β*-D-glucopyranosyl-(1→4)-*β*-D-galactopyranoside} (F-gitonin) (3), and (25*R*)-5α-spirostane-2α,3*β*,6α-triol 3-*O*-{*O*-*β*-D-glucopyranosyl-(1→2)-*O*-[*β*-D-xylopyranosyl-(1→3)]-*O*-*β*-D-glucopyranosyl-(1→4)-*β*-D-galactopyranoside} (4). Finally, using computational methods (DMol3 and Monti Carlo (MC) simulations) to determine the inhibition potentials for corrosion, chemical reactivates, and adsorption behaviors, Wazzan (20) showed that three phytochemicals present in *A. jesdianum* (AJ) flower, including α-linolenic acid, palmitic acid, and 1-ecosanol had effective corrosion-resistant materials for Fe, Al, and Cu (20). The four main chemical components of *A. jesdianum* have been presented in Figure 2.

**Biological Activity**

Pharmacological studies have shown that *A. jesdianum* can have various biological effects ranging from

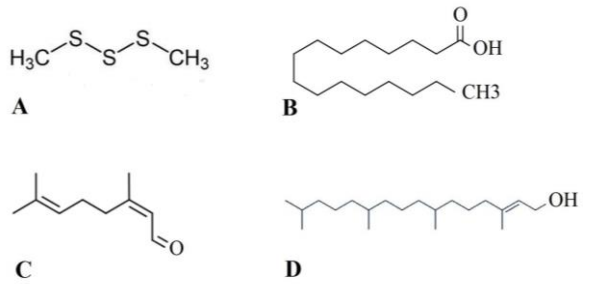


**Figure 2.** The major components of *A. jesdianum*. A: Dimethyl trisulfide, B: Hexadecanoic acid, C: Neral, D: Phytol.

antioxidant (8, 18), anti-inflammatory (21), analgesic (22), antidiabetic (23), antibacterial (8, 10, 14, 24–25), antifungal (26–28), anti-hepatic (29–32), anti-nephrotoxicity (33), anticancer (6, 19, 34–36), anti-Alzheimer's (37), antiplatelet (38), anti-anxiolytic (39), nephrolithiasis (40), protoscolicidal (41), and anti-toxicity effects (42). An overview of *in vivo* and *in vitro* studies of *A. jesdianum* based on its therapeutic efficacy has been shown in Table 1 (after references).

**Antioxidant Activity**

Antioxidant activity is a suitable instance of a useful advantage that plant extracts can provide. Plants have a combination of natural antioxidants that protect and maintain their physical and metabolic integrity. Several of these extracts and compounds from herbs can be candidates for mediating the aftermaths of the aging process on the skin by restricting the biochemical consequences of oxidation (43). Ghasemi Pirbalouti (8) studied the antioxidant and antibacterial effects of ethanolic extracts from bulbs and leaves of different populations of *A. jesdianum*. Antioxidant and antibacterial activities were evaluated using DPPH and the serial dilution test, respectively. The results showed that the total phenolic content in the ethanolic extracts of the leaves and bulbs of *A. jesdianum* ranged from 27.83 to 36.03 and 80.31 to 98.23 mg GAE/g extract. He found that the leaf extract had more antioxidant and antibacterial effects than the bulb extract. Ramak *et al*. (18) showed that antioxidant activity in planted populations is better than in wild populations.

**Anti-inflammatory Activity**

Several diseases are characterized by inflammation, which is a defense response aimed at the termination of noxious agents. Recognition of drugs that can decrease inflammation in glial cells is one of the essential contemporary subjects (44). The effect of *A. jesdianum* extract and essential oil on COX-1 and COX-2 was tested in fresh human blood at various concentrations ranging from 0.5–6 mg/ml and 0–100 mg/ml, respectively (21). Solvents, dimethyl sulfoxide (DMSO) and phosphate-buffered saline (PBS) were used as controls to compare the effect of the extract or essential oil, and the percentage of COX-1 and COX-2 enzyme activities was measured by the percentage of paroduction of TXB2 and PGE2, respectively. They found that the essential oil and extract of *A. jesdianum* inhibited the COX-1 enzyme activity more than the COX-2 enzyme activity, and also inhibited platelet aggregation, as did non-steroidal anti-inflammatory drugs (NSAIDs).

**Analgesic Activity**

Pain is an increasing problem worldwide. It has been indicated that 20% of adults suffer from pain throughout the world, and 10% are recently diagnosed with chronic pain each year (45). Analgesics are medications that stop or relieve the feeling of pain that accompanies many pathologic conditions (46). Khaksarian *et al*. (22) investigated the analgesic effects of the *A. jesdianum* plant using the tail flick and hot-plate methods. In this study, the opioid receptor antagonist naloxone was used as a pretreatment. The results showed that the intraperitoneal injection of the hydro-ethanolic extract of *A. jesdianum* could have analgesic effects, which are reversed by naloxone. The authors noted that the analgesic effects of *A. jesdianum* extracts were associated with drugs that affected the opioid system and that these effects could be reversed with one of the morphine antagonists, naloxone.

**Antidiabetic Activity**

Alaee *et al*. (23) investigated the effects of *A. jesdianum* hydro-alcoholic extract on diabetic nephropathy, using 24 rats divided into four groups, with six rats in each group, including a normal rats group and three diabetic rats groups. The normal group did not receive *A. jesdianum* extract. One of the groups of diabetic rats was not given any extract, but two groups were given the extract at doses of 250 mg/kg and 500 mg/kg body weight/day, respectively, for 42 days. Diabetes was induced using streptozotocin at a dose of 55 mg/kg. Alaee and colleagues found that *A. jesdianum* could

improve blood glucose (FBG), blood urea nitrogen (BUN), blood creatinine (Cr), albumin, and oxidative stress (increased superoxide dismutase activity and decreased malondialdehyde) in the kidney tissue compared with the diabetic group. They also indicated that the benefits of *A. jesdianum* were dose-dependent. Thus, the authors concluded that *A. jesdianum,* given for 42 days, has anti-diabetic and anti-inflammatory properties in diabetic rats and can be used as adjunctive therapy in treating diabetes.

**Antibacterial Activity**

Many studies have been conducted to investigate the effects of the *A. jesdianum* essential oil and extract on Gram-positive and Gram-negative bacteria and various fungi. Amiri (14) investigated the effects of essential oil and different extracts, including aqueous, ethanolic, methanolic, and etheric extracts, from *A. jesdianum* on bacterial pathogens, gram negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, and *Shigella flexneri*) and the gram positive bacteria (*Staphylococcus aureus, S. epidermidis*, and *S. saprophyticus*). The gentamicin antibiotic was used to compare the antibacterial effects of different extracts of *A. jesdianum*. It was revealed that the ethanolic extract had the greatest antibacterial effect. Gholami *et al*. (24) investigated the effect of the methanolic and aqueous extracts of *A. jesdianum* on bacterial pathogens, including the Gram-negative bacteria (*P. aeruginosa*, *E. coli*, *Acinetobacter baumannii*, *Enterobacter cloacae*), and the Gram-positive bacteria (*S. aureus*, *Streptococcus pyogenes*, *S. mutans*, *Enterococcus faecalis*). Antibacterial impacts of the extracts on the studied bacteria in comparison with gentamicin were examined using two methods, i.e. the broth microdilution and agar-well diffusion methods. It was observed that the ethanolic and aqueous extracts had beneficial effects on all the examined bacteria except *E. faecalis*. Ghasemi Pirbalouti (8) investigated the effect of the ethanol extract of *A. jesdianum* leaves and bulbs on the Gram-positive bacteria (*Bacillus cereus* and *Listeria monocytogenes*) and the Gram-negative bacteria (*Proteus vulgaris* and *Salmonella typhimurium*). It was concluded that ethanol extracts of *A. jesdianum* leaves and bulbs had moderate to good degrees of inhibitory activity against the examined bacteria. Esmaeili *et al*. (10) investigated the effects of endophytes isolated from various parts of *A. jesdianum* on bacterial pathogens, including *E. coli* and *S. aureus*, and pathogenic fungi, including *Candida albicans*, and *Trichophyton mentagrophytes*, using the drip method via chloroform, and secretory metabolite tests. Eleven bacterial endophytes were obtained from various parts of the plant, including stems, leaves, bulbs, and flowers. They found that only 4 out of 11 isolated endophytes had antibacterial activity against *Trichophyton mentagrophytes*, and metabolites secreted by endophytes had antimicrobial activity only against *S. aureus* and *Candida albicans*. The authors noted that *A. jesdianum*, with its antibacterial properties, could be a source of important antibacterial agents in agriculture and medicine. Ekrami *et al*. (25) compared the characteristics of nanoliposome (NLP)-loaded salep mucilage-based bionanocomposite films containing free and encapsulated *A. jesdianum* essential oil (AEO). The authors suggested that as an innovative sustained-release system, NLP/AEO could have the ability to produce antimicrobial food packaging based on salep mucilage to extend the shelf life of perishable foods.

**Antifungal Activity**

Using disk diffusion and broth macrodilution methods, Naeini *et al*. (26) investigated the antifungal activity of amphotericin B, nystatin and the hydro-alcoholic extract of *A. jesdianum* against *C. albicans*. Furthermore, they explored the effect of the aqueous extract of *A. jesdianum* (at doses 0.5, 1, 5, and 10 µg/mL) on macrophage viability and nitric oxide (NO) production using microculture tetrazolium (MTT) and nitrite assays (Griess test), respectively. The results showed that *A. jesdianum*, nystatin, and amphotericin B inhibition zone values against *C. albicans* were 8, 16, and 28 mm, respectively. They determined that the minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) of *A. jesdianum* were 330 µg/mL and 663 µg/mL, respectively. Naeini *et al*. found that the macrophage viability indices decreased after the treatment with all concentrations of aqueous extract from *A. jesdianum* (especially at 5 and 10 mg/mL), and higher amounts of nitric oxide were produced at lower concentrations, including 0.5 mg/mL (79.4 µM) and 1 mg/mL (77.6 µM) in comparison with the control group. They

concluded that the extract of *A. jesdianum* had anti-*C. albicans* and nitric oxide stimulating effects *in vitro*. The effect of the *A. jesdianum* hydro-ethanolic extract on vulvovaginal candidiasis (VVC) infection caused by fluconazole-resistant *C. glabrata* was investigated using vaginal samples from 28 women diagnosed with VVC and 8 healthy subjects (27). The results revealed that the hydro-ethanolic extract of *A. jesdianum* had remarkable antifungal activity, and the hydro-ethanolic extract had a $MIC_{90}$ of 3 mg/ml against *C. glabrata* isolated from VVC patients and healthy women. According to the authors, the use of *A. jesdianum* extract could be a remedy for the treatment of VVC infection caused by fluconazole-resistant *Candida* spp. Using 20 bald patients with suspected dermatophytosis of scalp, Sarlak *et al*. (28) examined the effects of *Allium hirtifolium* Boiss. and *A. jesdianum* extracts against the keratinase activity of *T. mentagrophytes*. The *T. mentagrophytes* isolates were grown on a selective medium containing keratin to detect keratinase production. They reported that the highest decreases in keratinase activity were observed at the dilution values of 50 mg/ml and 100 mg/ml of aqueous and ethanolic extracts, respectively.

**Anti-Hepatic Activity**

Kalantari *et al*. (29) examined the hepatoprotective impact of the hydro-alcoholic extract of *A. jesdianum* on injured liver induced by bromobenzene (BB), using 35 rats divided into five groups with seven rats in each group. The control group was given normal saline along with olive oil. Groups 2–4 were given *A. jesdianum* extract (500, 1000, and 2000 mg/kg) plus BB for five days. And the fifth group was given a BB (460 mg/kg). Then, each group was given hexobarbital sodium (25 mg/kg) on the fifth day. They recorded how long all the rats slept. The authors examined alanine aminotransferase (ALT), aspartate aminotransferase (AST), reduced glutathione (GSH), malondialdehyde (MDA), and histopathological changes using blood and tissue biomarkers. Congestion, severe fat changes, pyknotic nuclei, necrosis, disorderly sinusoidal spaces, and ballooning degeneration were observed in the group treated with BB. This study showed that BB could significantly increase sleep duration, ALT, AST, and MDA levels, and decreased the GSH level compared with the control group. However, *A. jesdianum* extract at doses 1000 and 2000 mg/kg showed a significant alter in all the studied biochemical parameters. Moreover, the 2000 mg/kg dose showed notable improvement in histopathological examination. Kalantari *et al*. concluded that the use of the hydro-alcoholic extract of *A. jesdianum* could prevent BB-induced hepatotoxicity by improving blood and tissue parameters and histopathological changes in the liver tissue. In a similar study, the protective effects of *A. jesdianum* extract against liver oxidative stress were investigated in male rata treated with carbon tetrachloride (CCl4) (30). The 42 male rats were divided into 6 groups. Groups 1 and 2 received normal saline and olive oil, respectively. Group 3 received a single dose of CCl4 (1 ml/kg). Groups 4, 5, and 6 were treated with *Allium* extract 500 mg/kg, 1000 mg/kg, 2000 mg/kg, and a single dose of CCl4 (1 ml/kg), respectively. In the CCl4-treated group, Kalantari *et al*. observed that CCl4 remarkably increased serum levels of aspartate aminotransferase, alanine aminotransferase and lipid peroxidation, while it reduced catalase activity and glutathione level, and also caused inflammation, coagulative necrosis, degeneration of hepatocytes, fatty change, and dilated sinusoids in liver tissue. However, the administration of *A. jesdianum* at all doses noticeably changed all the investigated biochemical parameters induced by CCl4. They suggested that *A. jesdianum* extract ameliorates CCl4-induced hepatotoxicity by increasing antioxidant activity and inhibiting oxidative stress. Sohrabinezhad *et al*. (31) investigated the effects of *A. jesdianum* extract at doses of 50, 100, and 200 mg/kg against acetaminophen (APAP)-induced liver dysfunction in male rats. They found that the safe dose of *A. jesdianum* extract was 50–100 mg/kg, while high doses of *A. jesdianum* extract (200 mg/kg) increased alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) blood levels. They stated that *A. jesdianum* extract could reduce liver damage by decreasing oxidative markers (LPO and NO). Moreover, it could reactivate the antioxidant thiol system, thus improving the oxidative/antioxidative balance in the liver. Jalili *et al*. (32) evaluated the potential therapeutic impacts of *A. jesdianum* against hepatocyte degeneration, inflammation, apoptotic changes, and oxidative injuries induced by Mercuric chloride (MC) administration. In this study, the 64 rats were randomly divided into eight

groups (n=8). The control group received normal saline. A single dose of MC (50 mg/kg) was given to the second group. The third to fifth groups were given 500, 1000, and 2000 µg/ml doses of *A. jesdianum* extract, respectively for a week. The sixth to eighth groups received a single dose of MC (50 mg/kg) to induce liver injury, followed by the administration of *A. jesdianum* 500, 1000, and 2000 µg/ml, respectively for a week. They examined nitrite oxide, lipid peroxidation (LP) levels, and the ferric-reducing ability of plasma (FRAP) to evaluate the intracellular antioxidant index. Expression levels of apoptotic genes (p53, Bcl2, and Bax) and cytokines involved in inflammatory bowel disease were evaluated by real-time PCR and ELISA, respectively. The activity of liver enzymes was also measured according to the biochemical method of Reitman and Frankel. Light and fluorescent microscope methods were used to evaluate the hepatocyte diameter (HD), central hepatic vein (CHV), and apoptosis cell index. The authors stated that *A. jesdianum* reduced hepatotoxicity caused by MC administration by increasing the antioxidant defense and regeneration of histopathological alterations (reduction of reactive oxygen species, inflammatory cytokines, cell apoptosis, and expression of p53 and Bax genes). Jalili *et al*. suggested that *A. jesdianum* could be considered as an alternative drug against oxidative damage induced by toxic materials.

**Anti-Nephrotoxicity**

Kalantari *et al*. (33) investigated the effect of *A. jesdianum* in the therapy of nephrotoxicity caused by carbon tetrachloride (CCl4). In this study, forty-two rats were randomly divided into six groups (n=7). The first group received normal saline (control group). The second group received olive oil for five days (sham group). The 3$^{rd}$, 4$^{th}$ and 5$^{th}$ groups received 500 mg/kg, 1000 mg/kg, and 2000 mg/kg of *A. jesdianum* extract respectively for five consecutive days, and on the fifth day an hour after the oral administration of *A. jesdianum* extract, received the single dose of CCl4 (1 ml/kg). The 6$^{th}$ group received a dose (1 ml/Kg) of carbon tetrachloride (CCl4 group). Serum creatinine and blood urea nitrogen in serum, and malondialdehyde, catalase (CAT), glutathione, and reactive oxygen species (ROS) in the kidney tissue were examined. Kalantari *et al*. observed significantly increased level of MDA, Cr, BUN, and ROS levels and decreased levels of in CAT and GSH in the blood of the CCl4 group compared with the control group. In contrast, all the studied items changed significantly in pretreatment *A. jesdianum* extract compared with the CCl4 group. Furthermore, the administration of *A. jesdianum* extract ameliorated changes in the kidney tissue induced by CCl4. The authors noted that using the hydro-alcoholic extract of *A. jesdianum* could prevent nephrotoxicity caused by CCl4 through scavenging free radicals.

**Anticancer Activity**

Alidadi *et al*. (6) investigated cell survival, colony numbers, flow cytometry, oxidative stress, and gene expression in order to examine the toxic impacts of the *A. jesdianum* hydro-alcoholic extract on the growth of HT-29 human colorectal cancer cell line at concentrations 25, 50, and 100 $\mu$g/ml for 48 hours. The survival rate of HT-29 cells decreased within 48 hours after treatment with different concentrations of *A. jesdianum* extract, but the colony numbers were significantly reduced when treated with 50 or 100 µg/ml. The results showed that *A. jesdianum* extract could enhance necrosis by regulating the expression of necroptosis-related genes such as RIPK1, RIPK3, and MLKL in a concentration-dependent manner. Moreover, *A. jesdianum* extract dose-dependently increased MDA content and (ROS), and decreased antioxidant enzymes in HT-29 cells. The authors concluded that *A. jesdianum* extract inhibits the growth of HT-29 cells by inducing oxidative stress and activating necroptosis signaling pathways. In a similar study, Alidadi *et al*. (34) considered the anti-cancer activity of *A. jesdianum* extract loaded on microemulsions on colon cancer cells (HT-29). The authors found that *A. jesdianum* extract (AJE) loaded into microemulsion (AJE-ME) at the dose of 50 µM/ml could remarkably reduce the survival percentage and colony formation of HT-29 cells compared with the free AJE by suppressing autophagy (increased mTOR gene expression and decreased expression of autophagy-related genes such as Beclin1 and Atg5) and activating necroptosis (promoted expression of necroptosis-related genes such as RIP3 and MLKL). Using cyclophosphamide drug, Dorosti *et al.* (35) evaluated the anticancer activity of the methanolic extract of *A. jesdianum* and *Nectaroscordeum coelzi* against HeLa

and K562 cell lines. Dorosti *et al*. showed that the methanolic extract of *A. jesdianum* had cytotoxic effects against HeLa and K562 cell lines, and this cytotoxic activity was more than cyclophosphamide. Rashidi *et al*. (36) evaluated the impact of *A. jesdianum* (AJ) hydroalcoholic extract on glioblastoma multiforme cells. This study treated the cell line with the extract for 24, 48, and 72 hr. Cell viability was evaluated using trypan blue staining, MTT assay, and lactate dehydrogenase activity measurement. Tumor invasion potential was evaluated by cell migration, invasion, and adhesion tests. Real-time PCR was operated to evaluate the shifts in the expression pattern of genes implicated in cancer invasion. This study showed that *A. jesdianum* extract therapy could decrease cell survival, cell migration, invasion and adhesion potential, and the expression of metalloproteinases 2 and 9 in cells. They concluded that *A. jesdianum* could exhibit beneficial anti-cancer activity in glioblastoma multiforme cells. Mimaki *et al*. (19) investigated the anticancer activity of several steroidal glycosides of fresh bulbs from *A. jesdianum* against HL-60 human promyelocytic leukemia cells. Dorosti *et al*. indicated that steroidal glycoside, (25R)-5α-spirostane-2α,3β-diol 3-O-{O-β-D-glucopyranosyl-(1→2)-O-[β-D-xylopyranosyl-(1→3)]-O-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside} (F-gitonin) in the fresh bulbs of *A. jesdianum* had cytotoxic activity against several malignant tumor cells with an $IC_{50}$ value of 1.5 µg/ml.

**Anti-Alzheimer's Disease**

Kamranfar *et al*. (37) evaluated the protective effects of *A. jesdianum* extract on cognitive dysfunction, mitochondrial/cellular, and genetic parameters in a streptozotocin-induced Alzheimer's disease (AD) rat model. A single dose of streptozotocin (STZ) (3 mg/kg) was injected into rats to induce Alzheimer's disease. Fourteen days after model induction, *A. jesdianum* extract (100, 200, 400 mg/kg/day) and donepezil (5 mg/kg/day) were given as treatment with an oral tube. They examined cognitive function, mitochondrial toxicity parameters comprised of succinate dehydrogenase activity, mitochondrial ROS formation, MMP decline, mitochondrial swelling and efflux of cytochrome c in various parts of the rat brain, miR-330, miR-132, Bax, and Bcl-2 genes expression in isolated rat brain neurons using RT-qPCR analysis. They observed that STZ injection led to high expression of the Bax gene and low expression of miR-330, miR-132, and Bcl-2 genes, but *A. jesdianum* reversed the expression of miRNAs and genes in favor of enhancing AD and decreasing neuronal apoptosis. Moreover, *A. jesdianum* extract could significantly reduce STZ-induced cognitive dysfunction and mitochondrial upstream toxic events. Therefore, they concluded that *A. jesdianum* could prevent the effects of STZ-induced Alzheimer's disease in animal models through free radical scavenging, improving mitochondrial function, and miRNA overexpression, as an efficient drug for AD treatment.

**Antiplatelet Activity**

Using adenosine diphosphate (ADP) and arachidonic acid (AA) as platelet aggregation inducers, Lorigooini *et al*. (38) examined the antiplatelet aggregation impact of some *Allium* species, including *A. jesdianum*, *A. ampeloprasum* L., *A. atroviolaceum* Boiss., *A. haemanthoides* Boiss. & Reut. ex Regel, *A. hirtifolium*, *A. shelkovnikovii* Grossh., and *A. vavillovi* Popov & Vved. The results showed that *Allium* extracts could inhibit *in vitro* platelet aggregation induced by AA and ADP. The authors concluded that the dietary intake of *Allium* might be efficient in preventing cardiovascular disease. Moreover, they suggested that *Allium* species extracts are good candidates for further *in vitro* and *in vivo* studies to find potential lead compounds for antiplatelet aggregation.

**Anti-Anxiolytic Activity**

Mousavi *et al*. (39) evaluated the anxiolytic and antidepressant effects of *A. jesdianum* hydro-alcoholic extract at doses 500, 1000, and 2000 mg/kg compared with diazepam at a dose of 5 mg/kg and fluoxetine at a dose of 10 mg/kg in mice. The results indicated that *A. jesdianum* had anxiolytic and antidepressant activities as diazepam and fluoxetine.

**Nephrolithiasis**

Vahdani *et al*. (40) examined the effect of the hydrophilic extract of *A. jesdianum* on ethylene glycol-induced kidney stones in male Wistar rats. In this study, 44 rats were divided into four groups with 11 rats in each group, including the normal rats group (without receiving 1% ethylene glycol), the ethylene glycol rats group (receiving 1% ethylene glycol), and two preventive rat groups (in addition to 1% ethylene glycol, receiving daily 1g/kg and 2g/kg of *A. jesdianum*

extract respectively for 30 days). The authors stated that the hydrophilic extract of *A. jesdianum* could be effective in preventing calcium oxalate stones in rats. However, its effects on urinary and blood parameters were insufficient for kidney stones.

**Protoscolicidal Activity**

Ghorbanipour *et al.* (41) investigated *in vitro* protoscolicidal effects of aqueous, alcoholic and hydroalcoholic extracts of *A. jesdianum* against protoscoleces of *Echinococcus granulosus*. The authors showed that100 µl/ml aqueous extract of *A. jesdianum* (63.90 min) could inactivate 100% of protoscoleces after 30 min of exposure. The authors noted that aqueous extracts of *A. jesdianum* could inactive protoscoleces of hydatid cysts.

**Anti-Toxicity**

Nowadays, the release of pesticides into aquatic habitats is one of the main environmental problems threatening the health of the environments and organisms involved. Naserabad *et al.* (42) investigated the protective effects of *A. jesdianum* essential oil (AJEO) on growth, immunity, and biochemical as well as antioxidant indicators in rainbow trout (*Oncorhynchus mykiss*) exposed to cypermethrin. Rainbow trout specimens were fed 0, 0.5, 1, and 1.5% AJEO for 60 days. Subsequently, the fish were exposed to 12.5% $LC_{50}$ of cypermethrin for 14 days. This study showed that growth indices and digestive enzyme activity (lipase and protease) improved greatly in the experimental treatments compared with the control group and decreased dietary conversion ratio. Furthermore, fish fed with the essential oil exhibited better oxidative shapes and antioxidant enzymes and were well-performing when exposed to cypermethrin. The fish showed higher levels of serum biochemical parameters (total protein, globulin, albumin), serum and mucus immune parameters, i.e. lysozyme (LYZ) and immunoglobulin (Ig), protease, and alternative complement activity (ACH50) compared with the control treatment. Furthermore, the fish fed the AJEO diet showed lower levels of lipid peroxidation, metabolic enzymes such as alanine aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and lactate dehydrogenase, and also cortisol as well as glucose contents compared with the control group. Altogether, this study showed that adding AJEO to the diet of rainbow trout led to enhanced digestion, nutrient absorption, and water quality, and augmented growth, antioxidant activity, and immune response. Thus, this diet could ease many harmful effects of toxin exposure (particularly cypermethrin) in rainbow trout.

## Conclusion

In this review, the pharmacological activities of the essential oil and extract of *A. jesdianum*, a folk medicinal plant indigenous to Iran, were comprehensively stated. Based on the results of the studies mentioned above, Bon-e-Sorkh has a wide range of beneficial activities, including antioxidant, anti-inflammatory, analgesic, anti-diabetic, antibacterial, antifungal, anti-hepatic, anti-nephrotoxicity, anticancer, anti-Alzheimer's, antiplatelet, anti-anxiolytic, nephrolithiasis, protoscolicidal, and anti-toxicity activities. Researchers should conduct further research to confirm the findings of previous studies mentioned in this article by conducting *in vitro*, *in vivo*, and clinical studies if the results are promising. Moreover, most of the observed works have been performed using crude extract or essential oil, and very few pure molecules have been separated from this plant. Thus, future studies are required to investigate new molecules from this plant and explore their medicinal and biological effects. This study will guide us to a better insight into the phytochemistry of this plant, thereby leading to more promising information for the design of drug products. Hopefully, this article will encourage more research teams to profoundly investigate the chemical composition of this species and the molecular mechanisms implicated in these observed pharmacological activities.

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## Conflict of Interest

The authors declare that they have no conflict of

interest.

## Founding

None

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Table 1: Thee overview of *in vivo* and *in vitro* studies of *A. jesdianum* based on its therapeutic efficacy.

| Year | Aim of the Study | Subject | Model | | Ref. |
|---|---|---|---|---|---|
| 2019 | Ghasemi Pirbalouti studied the antioxidant activity of ethanolic extracts from bulbs and leaves of different populations of *A. jesdianum*. | - | *In vitro* | The leaf extract had more antioxidant activity than the bulb extract. | (8) |
| 2020 | Ramak *et al*. antioxidant activity among three wild and cultivated ecotypes of *A. jesdianum* in Lorestan province. | - | *In vitro* | Antioxidant activity in planted populations is better than in wild populations. | (18) |
| 2017 | Khaksarian *et al*. tested the anti-inflammatory activity of *A. jesdianum* on platelet aggregation and COX-1 and COX-2 in fresh human blood at various concentrations ranging from 0.5–6 mg/ml and 0–100 mg/ml, respectively. | Human | *In vitro* | The essential oil and extract of *A. jesdianum* inhibited the COX-1 enzyme activity more than the COX-2 enzyme activity, and also inhibited platelet aggregation, as did non-steroidal anti-inflammatory drugs (NSAIDs). | (21) |
| 2008 | Khaksarian *et al*. investigated the analgesic effects of the hydro-ethanolic extract of *A. jesdianum* plant using the opioid receptor antagonist naloxone as a pretreatment. | Mice | *In vivo* | The intraperitoneal injection of the hydro-ethanolic extract of *A. jesdianum* has analgesic effects, which are reversed by naloxone. | (22) |
| 2021 | Alaee *et al*. investigated the effects of *A. jesdianum* hydro-alcoholic extract on diabetic nephropathy using streptozotocin at a dose of 55 mg/kg. | Mice | *In vivo* | *A. jesdianum* given for 42 days has anti-diabetic and anti-inflammatory properties in diabetic rats and can be used as adjunctive therapy in the treatment of diabetes. | (23) |
| 2019 | Ghasemi Pirbalouti investigated the effect of ethanol extract of *A. jesdianum* leaves and bulbs against the gram-positive bacteria | *B. cereus*, *L. monocytogenes*, *P. vulgaris*, and *S. typhimurium* | *In vitro* | Ethanol extracts of *A. jesdianum* leaves and bulbs had moderate to good inhibitory activity against the bacteria studied. | (8) |

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| 2007 | Using the gentamicin antibiotic, Amiri investigated the effects of essential oil and different extracts, including aqueous, ethanolic, methanolic, and etheric extracts, from *A. jesdianum* on bacterial pathogens. | *E. coli*, *P. aeruginosa*, *S. typhi*, *S. flexneri*, *S. aureus*, and *S. epidermidis* | *In vitro* | Ethanolic extract has the most antibacterial effect. | (14) |
| 2016 | Using the gentamicin antibiotic, Gholami *et al*. investigated the effect of the methanolic and aqueous extracts from *A. jesdianum* on bacterial pathogens. | *P. aeruginosa*, *E. coli*, *A. baumannii*, *E. cloacae*, *S. aureus*, *S. pyogenes*, *S. mutans*, and *E. faecalis* | *In vitro* | Ethanolic and aqueous extracts had a good effect on all examined bacteria, except *Enterococcus faecalis* | (24) |
| 2021 | Esmaeili *et al*. investigated the effects of endophytes isolated from various parts of *A. jesdianum* on bacterial and fungi pathogens. | *E. coli*, *S. aureus*, *C. albicans*, and *T. mentagrophytes* | *In vitro* | Several isolated endophytes had antibacterial activity against *Trichophyton mentagrophytes*, and metabolites secreted by endophytes had antimicrobial activity only against *Staphylococcus aureus* and *Candida albicans*. | (10) |
| 2022 | Ekrami *et al*. compared the properties of nanoliposome (NLP)-loaded salep mucilage-based bionanocomposite films containing free and encapsulated *A. jesdianum* essential oil (AEO). | - | *In vitro* | NLP/AEO has the potential to produce antimicrobial food packaging based on salep mucilage to extend the shelf life of perishable foods. | (25) |
| 2020 | Using disk diffusion and broth macrodilution methods, Naeini *et al*. performed the antifungal activity of amphotericin B, nystatin, and hydro-alcoholic extract of *A. jesdianum* against fungi pathogen. | *Candida albicans* | *In vitro* | The results showed that the inhibition zone values of *A. jesdianum*, nystatin, and amphotericin B against *Candida albicans* were 8, 16, and 28 mm respectively, and the minimum inhibitory concentration and minimum fungicidal concentration of *A. jesdianum* were 330 µg/ml and 663 µg/ml, | |

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| | | | | respectively. | |
| 2017 | Using vaginal samples from 28 women diagnosed with VVC and 8 healthy subjects individuals, Shahrokh *et al.* investigated the effect of *A. jesdianum* hydro-ethanolic extract on vulvovaginal candidiasis (VVC) infection caused by fluconazole-resistant *Candida glabrata*. | Human | *In vitro* | The hydro-ethanolic extract of *A. jesdianum* has good antifungal activity, and hydro-ethanolic extract has a $MIC_{90}$ of 3 mg/ml against *Candida glabrata* isolated from VVC patients and healthy women. | (27) |
| 2022 | Using 20 bald patients with suspected dermatophytosis of scalp, Sarlak *et al*. examined effects of aqueous and ethanolic extracts from *Allium hirtifolium* Boiss. and *A. jesdianum* extracts against the keratinase activity of *Trichophyton mentagrophytes*. | Human | *In vitro* | The highest decrease in keratinase activity was observed at the dilution values of 50 mg/ml and 100 mg/ml of aqueous and ethanolic extracts, respectively. | (28) |
| 2018 | Kalantari *et al*. evaluated the hepatoprotective effect of hydro-alcoholic extract of *A. jesdianum* on injured liver induced by bromobenzene. | Mice | *In vivo* | Use of hydro-alcoholic extract of *A. jesdianum* can prevent BB-induced hepatotoxicity by improving blood and tissue parameters and histopathological changes in liver tissue. | (29) |
| 2018 | Kalantari *et al*. investigated the protective effects of *A. jesdianum* extract against liver oxidative stress treated with carbon tetrachloride. | Mice | *In vivo* | *A. jesdianum* extract ameliorates CCl4-induced hepatotoxicity by increasing antioxidant activity and inhibiting oxidative stress. | (30) |
| 2019 | Sohrabinezhad *et al*. investigated the effects of *A. jesdianum* extract at doses of 50, 100, and 200 mg/kg against acetaminophen (APAP)-induced liver dysfunction. | Mice | *In vivo* | *A. jesdianum* extract reduces liver damage by reducing oxidative markers (LPO and NO) and reactivates the antioxidant thiol system, thus improving the oxidative/antioxidative balance in the liver. | (31) |
| 2020 | Jalili *et al*. evaluated the probable therapeutic effects of *A. jesdianum* against hepatocyte degeneration, inflammation, apoptotic changes, and oxidative injuries | Mice | *In vivo* | *A. jesdianum* reduced hepatotoxicity caused by MC administration by increasing antioxidant defense and regeneration of | (32) |

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| | induced by Mercuric chloride administration. | | | histopathological alterations (reduction of reactive oxygen species, inflammatory cytokines, cell apoptosis, and expression of p53 and Bax genes). | |
| 2018 | Kalantari *et al*. investigated the effect of *A. jesdianum* in the therapy of nephrotoxicity induced by carbon tetrachloride. | Mice | *In vivo* | Use of the hydro-alcoholic extract of *A. jesdianum* could prevent nephrotoxicity induced by CCl4 through scavenging free radicals. | (33) |
| 2021 | Alidadi *et al*. examined cell survival, colony numbers, flow cytometry, oxidative stress, and gene expression to evaluate the toxic impacts of the *A. jesdianum* hydro-alcoholic extract on the growth of HT-29 human colorectal cancer cell line at concentrations 25, 50, and 100 $\mu$g/ml for 48 hours. | Human | *In vitro* | *A. jesdianum* extract inhibits the growth of HT-29 cells by inducing oxidative stress and activating necroptosis signaling pathways. | (6) |
| 2022 | Alidadi *et al*. considered anti-cancer activity of *A. jesdianum* extract loaded on microemulsions on colon cancer cells (HT-29). | Human | *In vitro* | *A. jesdianum* extract (AJE) loaded into microemulsion at the dose of 50 µM/ml significantly diminished the survival percentage and colony formation of HT-29 cells compared to the free AJE by suppressing autophagy and activating necroptosis. | (34) |
| 2017 | Using cyclophosphamide drug, Dorosti *et al.* evaluated anticancer activity of methanolic extract from *A. jesdianum* and *Nectaroscordeum coelzi* against HeLa and K562 cell lines. | Human | *In vitro* | Dorosti and colleagues showed that methanolic extract of *A. jesdianum* has cytotoxic effects against HeLa and K562 cell lines, and this cytotoxic activity was more than cyclophosphamide. | (35) |
| 2022 | Rashidi *et al*. evaluated the effect of *A. jesdianum* hydroalcoholic extract on glioblastoma multiforme cells. | Human | *In vitro* | *A. jesdianum* showed good anti-cancer activity in glioblastoma multiforme cells. | (36) |

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| 1999 | Mimaki *et al*. evaluated anticancer activity of several steroidal glycosides of fresh bulbs from *A. jesdianum* against HL-60 human promyelocytic leukemia cells. | Human | *In vitro* | The steroidal glycoside, (25R)-5α-spirostane-2α,3β-diol 3-O-{O-β-D-glucopyranosyl-(1→2)-O-[β-D-xylopyranosyl-(1→3)]-O-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside} (F-gitonin), in the fresh bulbs of *A. jesdianum* has cytotoxic activity against several malignant tumor cells with an $IC_{50}$ value of 1.5 µg/ml. | (19) |
| - | Kamranfar *et al*. evaluated the protective effects of *A. jesdianum* extract on cognitive dysfunction, mitochondrial/cellular, and genetic parameters in the streptozotocin-induced Alzheimer's disease | Mice | *In vivo* | *A. jesdianum* can prevent the effects of STZ-induced Alzheimer's disease in animal model through free radical scavenging, improving mitochondrial function, and miRNA overexpression, as a good drug for AD treatment | (37) |
| 2015 | Using adenosine diphosphate (ADP) and arachidonic acid (AA) as platelet aggregation inducers, Lorigooini *et al*. evaluated the antiplatelet aggregation effect of some *Allium* species, including *A. jesdianum*, *A. ampeloprasum*, *A. atroviolaceum*, *A. haemanthoides*, *A. hirtifolium*, *A. shelkovnikovii*, and *A. vavillovi*. | Human | *In vitro* | *Allium* species extracts are good candidates for further *in vitro* and *in vivo* studies to find potential lead compounds for antiplatelet aggregation. | (38) |
| 2017 | Mousavi *et al*. evaluated the anxiolytic and antidepressant effects of *A. jesdianum* hydro-alcoholic extract at doses 500, 1000, and 2000 mg/kg compared to diazepam at a dose of 5 mg/kg and fluoxetine at a dose of 10 mg/kg. | Mice | *In vivo* | *A. jesdianum* has anxiolytic and antidepressant activities as diazepam and fluoxetine. | (39) |
| 2013 | Vahdani *et al*. studied the effect of the hydrophilic extract of *A. jesdianum* on ethylene glycol-induced kidney stones. | Mice | *In vivo* | The hydrophilic extract of *A. jesdianum* had some benefit in preventing calcium oxalate stones in rats, but the effect on urinary and | (40) |

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| | | | | blood parameters was insufficient for kidney stones. | |
| 2023 | Ghorbanipour *et al.* investigated protoscolicidal effects of aqueous, alcoholic and hydroalcoholic extracts of *A. jesdianum* against protoscolece. | *Echinococcus granulosus* | *In vitro* | Aqueous extracts of *A. jesdianum* could inactive protoscoleces of hydatid cysts. | (42) |
| - | Naserabad *et al.* investigated the protective effects of *A. jesdianum* essential oil (AJEO) on growth, immunity, and biochemical and antioxidant indicators in Rainbow trout (Oncorhynchus mykiss) exposed to cypermethrin. | Rainbow trout | *In vivo* | Adding AJEO to the diet of Rainbow trout enhances digestion and nutrient absorption, enhances water quality, and augments growth, antioxidant activity, and immune response. | (41) |