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THE PHARMACOLOGICAL IMPORTANCE OF *ASPARAGUS OFFICINALIS* - A REVIEW

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ABSTRACT

Asparagus officinalis contained steroid saponins including asparagosides A, B, D, F, G, H, I, the bitter steroid saponins, amino acids, fructans (asparagose and asparagosine), ferulic acid, minerals, vitamins and flavonoids. It exerts anticancer, antimicrobial, antioxidant, hypolipidemic, antidiabetic and many other effects. This paper will highlight the chemical constituents and the pharmacological effects of *Asparagus officinalis*.

Keywords: *Asparagus officinalis*, pharmacology, chemical constituents.

INTRODUCTION

Plant derivates had been employed by population to prevent different kind of diseases for centuries. The knowledge of plant properties was acquired by ancient civilization that passed down from generation to generation until today. *Asparagus officinalis* contained steroid saponins including asparagosides A, B, D, F, G, H, I, the bitter steroid saponins, amino acids, fructans (asparagose and asparagosine), ferulic acid, minerals, vitamins and flavonoids. It exerts anticancer, antimicrobial, antioxidant, hypolipidemic, antidiabetic and many other effects. This paper will highlight the chemical constituents and the pharmacological effects of *Asparagus officinalis.*

Synonyms

Asparagus caspius Hohen.*; Asparagus longifolius* Fisch. ex Steud.*; Asparagus officinalis var. caspius (*Hohen.*)* Asch. & Graebn.*; Asparagus officinalis subsp. officinalis ; Asparagus polyphyllus* Steven ex Ledeb [1].

Taxonomical Classification

Kingdom: plantae
Division: tracheophyta
Subdivision: spermatophytina
Class: magnoliopsida
Superorder: lilianae
Order: asparagales
Family: asparagaceae (also placed in: lamiaceae)
Subfamily: asparagoideae
Genus: asparagus
Species: *Asparagus officinalis* [2].

Common names

Arabic: Ehlilaj aswad, Helion, Dhagboth, Akla, al theeb; Chinese: Shi diao bai; English: Asparagus, Garden asparagus, White asparagus, Sparrow grass and Common asparagus; German: Spargel; French: Asperge; Italian: Asparagio; Japanese: Oranda-kiji-kakushi; Portuguese: Espargo; Spanish: Espárrago, Esparraguera, and Swedish: Sparris [1].

Description

It is perennial herb. Rootstock creeping, thick, tuberously swollen, short-jointed. Height: 60–150 cm (24–60 in.). Stem many-branched, 2–6 needle-like shoots in whorls. Flower: Perianth regular (actinomorphic), whitish–greenish yellow, 4–6 mm (0.16–0.24 in.) wide, fused, 6-lobed. Male flowers' perianth narrowly campanulate, female and bisexual flowers almost spherical. Stamens 6. Gynoecium fused, single-styled. Flowers solitary or in pairs–whorls of a few flowers in leaf axils. Leaves: Rudimentary, scale-like. Axillary shoots needle-like, whorled. Fruit: Round, initially green, when ripe orange, 6–10 mm (0.24–0.4 in.) wide berry [3-4].

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Distribution

The plant was distributed in Central and Southern Europe, the Middle East, Western Siberia and Northern Africa. It was cultivated in many places [1]. It was now distributed in: Algeria, Morocco, Tunisia (Africa); Afghanistan, Iran, Iraq, Lebanon, Syria, Turkey, Armenia, Azerbaijan, Georgia, Russian Federation, Kazakhstan, Mongolia and China (Asia); Denmark, Austria, Belgium, Czechoslovakia, Germany, Hungary, Netherlands, Poland, Switzerland, Belarus, Moldova, Ukraine, Albania, Bulgaria, Former Yugoslavia, Greece, Italy, Romania, France, Portugal, Spain, Finland, Norway, Sweden, Estonia, Latvia and Lithuania (Europe) ; USA and Canada (Northern America); Bolivia, Ecuador, Argentina and Uruguay (Southern America) ; as well as Australia and New Zealand [1].

Traditional uses

Traditionally, the roots were used for non-specific inflammatory diseases of the efferent urinary tract and for prevention of kidney and bladder stones (irrigation therapy), dropsy, rheumatic conditions, liver disease, bronchial asthma and gout. In Chinese medicine, the root was also used to treat irritable cough, coughing with blood, dry mouth and throat, and constipation [1]. Part used: The herb, rhizome and root were used medicinally [1].

Chemical constituents

Asparagus officinalis contained steroid saponins including asparagosides A, B, D, F, G, H, I, the bitter steroid saponins, amino acids, fructans (asparagose and asparagosine), ferulic acid and flavonoids (quercetin, rutin hyperoside, and isoquercitrin) [1-3]. Among 23 commonly consumed vegetables, the highest antioxidant activity based on dry weight was seen in asparagus [8]. The most abundant known flavonoid in asparagus is rutin [9], it represented 60-80% of the total phenolic content of purple and green asparagus extracts (10). It was observed that rutin in green spears of 12 asparagus hybrid lines, ranging from 0.015 to 0.45% of fresh weight. The level of rutin varies with asparagus genotype as well as the tissue location. For instance, rutin has been found to be more abundant at the upper portions of the spears, while the bottoms of asparagus contain a very small quantity of rutin (less than 0.01% of fresh weight from three lines of sampled asparagus) [11].

Shao *et al.,* isolated two oligofurostanosides from the seeds of *Asparagus officinalis*, and their structures characterized as 3-O-[alpha-L-rhamnopyranosyl-(1-->2)- (alpha-L-rhamnopyranosyl-(1-->4))-beta-D-glucopyranosyl]-26-O-[beta- D- gluco pyranosyl] -(25R) -22 alpha-methoxyfurost-5-ene-3 beta,26-diol(methyl protodioscin) and its corresponding 22 alpha-hydroxy analogue (protodioscin) [12].

New asparagusic acid anti-*S*-oxide methyl ester and asparagusic acid syn-*S*-oxide methyl ester, a new acetylenic compound, 2-hydroxyasparenyn {3‘,4‘-*trans*-2-hydroxy-1-methoxy-4- [5-(4-methoxyphenoxy) -3-penten -1-ynyl] - benzene}, as well as eleven known compounds, asparenyn, asparenyol, (±)-1-monopalmitin, ferulic acid, 1,3-*O*-di-*p*-coumaroylglycerol, 1-*O*-feruloyl-3-*O*-*p*-coumaroylglycerol, blumenol C, (±)-epipinoresinol, linoleic acid, 1,3-*O*-diferuloylglycerol, and 1,2-*O*-diferuloylglycerol, were isolated from an ethyl acetate-soluble fraction of the methanol extract of the aerial parts of *Asparagus officinalis* [13].

Two major anthocyanins (A1 and A2) were also isolated from peels of the spears of *Asparagus officinalis*. A1 was identified as cyanidin 3-[3"-(O-beta-d-gluco pyranosyl)-6"-(O-alpha-l-rhamnopyranosyl)-O-beta-d-glucopyranoside], whereas A2 was cyanidin 3-rutinoside, which was widely distributed in higher plants. Oxygen radical absorbance capacity assays proved their high antioxidant activities [14].

Sun *et al.,* isolated a new steroidal saponin, yamogenin II, with a unique aglycone moiety, and a structure of (25S)-spirostan-5-ene-3*β*-ol-3-*O*-*α*-L-rhamnopyranosyl-(1,2)-[*α*-L-rhamno pyranosyl- (1,4)]-*β*-D-glucopyranoside from the dried stems of *Asparagus officinalis* [15]. Furthermore, more saponins were isolated from the plant included (25R)-furost-5-en-3β,22,26-triol-3-O-[α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside] -26-O-β-D-glucopyranoside, (25R)-furostane-3β,22,26-triol-3-O-[α- L-rhamnopyranosyl- (1→4) -β-D-glucopyranoside] -26-O-β-D-glucopy ranoside, and (25S)-furostane-3β,22,26-triol-3-O- [α-L-rhamno pyranosyl-(1→4)-β-D-glucopyranoside]-26-O-β-D-glucopyranoside, and 3-O-[{α-L-rhamnopyranosyl-(1→2)} {α-L-rhamnopyranosyl-(1→4)}-β-D-glucopyranosyl]-(25S)-spirost-5-ene-3β-ol. They were identified as key bitter compounds in the edible spears of *Asparagus officinalis*, they showed human bitter recognition thresholds between 10.9 and 199.7 μmol/l (water) [16].

Many carotenoid pigments were isolated from the ripe and unripe fruits of *Asparagus officinalis*, these included capsanthin, capsorubin, capsanthin 5, 6-epoxide, antheraxanthin, violaxanthin, neoxanthin, mutatoxanthin epimers, zeaxanthin, lutein, β-cryptoxanthin, β-carotene, and some cis [17].

Nutritional analysis showed that the plant contained water 93.5 %, total protein 1.91%, fat 0.16%, carbohydrates 2.04%, total dietary fiber 1.31% total nitrogen 0.31% [18].

The amino acid and mineral contents were found to be much higher in the leaves than the shoots. The following amino acids were founds in the young shoots and leaves (mg /Kg) respectively: aspartic acid 921.17 and 4369.47 , asparagine 653.68 and 6967.50, threonine 61.21 and 611.20, serine 112.67 and 845.45, glutamic

acid 501.35 and 2933.77, proline undetectable in both, glycine 87.41 and 744.80, alanine 143.53 and 919.58, valine 113.80 and 835.70, isoleucine 65.82 and 574.49, leucine 106.94 and 995.94, tyrosine undetectable and 416.76, phenylalanine 95.54 and 517.61, histidine 190.16 and 590.94, lysine 40.85 and 1009.01, arginine 62.11 and 933.21, cysteine 108.19 and 347.14, methionine undetectable and 145.71, tryptophan undetectable and 227.21. Minerals detected in the young shoots and leaves were included respectively (mg /Kg): calcium 45.2 and 139, phosphorus 96.1 and 501.6, potassium 251.3 and 2574.8, iron 2.7 and 8.5, sodium 120.7 and 281.6. Young shoots and leaves also contained protein 3000 and 20200, carbohydrate 2600 and 31600, vitamin B2 0.16 and 0.45 mg/kg respectively [19].

PHARMACOLOGICAL EFFECTS

Antidiabetic effects

Streptozotocin-induced diabetic rats were treated with a methanolic extract of *Asparagus officinalis* seeds (250 and 500 mg/kg per day) or glibenclamide for 28 days. Treatment of the diabetic rats with the *Asparagus officinalis* extract at doses of 250 and 500 mg/kg suppressed the elevated blood glucose in a dose- and time-dependent manner. The 500 mg/kg, but not 250 mg/kg, dose significantly improved serum insulin levels in the diabetic rats. The insulin: glucose ratio was significantly increased at both doses in the *A. officinalis*-treated rats. Both qualitative and quantitative improvements in β-cell function were found in the islets of the *A. officinalis*-treated rats. The extract showed potent antioxidant activity in an *in vitro* assay and also improved the total antioxidant status *in vivo*. In most cases, the efficacy of *A. officinalis* (500 mg/kg) was very similar to a standard anti-diabetic drug, glibenclamide [20].

The hypoglycaemic effect of the aqueous extract of asparagus by-product (AEA) was also evaluated in a streptozotocin (STZ)-induced diabetic rat model. Continuous administration of AEA for 21 days significantly decreased fasting serum glucose and triglyceride levels but markedly increased body weight and hepatic glycogen level in diabetic rats. In an oral glucose tolerance test, both the blood glucose level measured at 30, 60 and 120 min after glucose loading and the area under the glucose curve showed a significant decrease after AEA treatment [21].

Anticancer, antioxidant and hypolipidemic effects

The plant exerted anticancer effects, the anticancer activity of *Asparagus officinalis* may be occurred via: (1) an antimutagenic effect – preventing genetic mutations which can directly precede the earliest stages of cancer development.(2) the promotion of (cellular phase II detoxifying enzymes) which (facilitate the removal of drugs and xenobiotic compounds) that are carcinogenic and supporting overall liver function. (3) synergistically enhancing the antioxidant activity of other plant foods. (4) the inhibition of chronic inflammation (cycooxygenase-2 suppression) which is thought to play a role in tumor development. (5) the promotion of healthier digestion and immune function [6].

Asparagus saponins inhibited the growth of HepG2 cells in a dose-dependent manner. The median inhibitory concentration (IC_{50}) was 101.15 mg/l at 72 hours exposure. The apoptosis morphology at 72 hours of treatment was obvious, showing cell protuberance, concentrated cytoplasm, and apoptotic bodies. The apoptotic rates at 72 hours were 30.9%, 51.7%, and 62.1% (for saponin concentrations of 50, 100 and 200 mg/l respectively). Treatment with Asparagus saponins for 24 hours increased the intracellular level of reactive oxygen species and Ca^{2+}, lowered the pH, activated intracellular mitochondrial permeability transition pore, and decreased membrane potential in a dose-dependent manner. Treatment also increased the activity of caspase-9 and caspase-3, down-regulated the expression of Bcl2, up-regulated the expression of Bax, and induced release of CytC and activation of caspase-3[22].

The crude saponins from the shoots (edible part) of asparagus were found to have antitumor activity. The asparagus crude saponins inhibited the growth of human leukemia HL-60 cells in culture and macromolecular synthesis in a dose and time dependent manner. The asparagus crude saponins at 75–100μg/ml range were cytostatic. Its concentrations greater than 200 μg/ml were cytocidal to HL-60 cells. The asparagus crude saponins at 6 μg/ml concentration inhibited the synthesis of DNA, RNA and protein in HL-60 cells by 41, 5, and 4% respectively, and at 50 μg/ml by 84, 68 and 59% respectively. The inhibitory effect of asparagus crude saponins on DNA synthesis was irreversible [23].

Shao *et al*., isolated two oligofurostanosides from the seeds of *Asparagus officinalis* with cytotoxic activity. They inhibited the growth of human leukemia HL-60 cells in culture and macromolecular synthesis in a dose-dependent manner. The inhibitory effect on DNA synthesis was found to be irreversible [12].

Treatment of HepG2 human hepatoma cells with the leaf extract of *Asparagus officinalis* suppressed more than 70% of the intensity of hydrogen peroxide (1mM)-stimulated DCF fluorescence, a marker of reactive oxygen species. Cellular toxicities induced by treatment with hydrogen peroxide, ethanol, or tetrachloride carbon were also significantly alleviated in response to treatment with the extracts of *A. officinalis* leaves and shoots. Additionally, the activities of 2 key enzymes that metabolize ethanol, alcohol dehydrogenase and aldehyde dehydrogenase, were upregulated by more than 2-fold in response to treatment with the leaf- and shoot extracts [19].

Saponins from old stems of asparagus (SSA) exerted potential inhibitory activity on tumour growth and metastasis. SSA suppressed cell viability of breast, colon and pancreatic cancers in a concentration-dependent manner, with half-maximum inhibitory concentrations ranging from 809.42 to 1829.96 µg/ml. However, SSA was more functional in blocking cell migration and invasion as compared with its cytotoxic effect, with an effective inhibitory concentration of 400 µg/ml. A mechanistic study showed that SSA markedly increased the activities of Cdc42 and Rac1 and decreased the activity of RhoA in cancer cells [24].

One new (Sarsasapogenin O) and seven known steroids were isolated from the roots of *Asparagus officinalis* L. These compounds together with nine steroids which were previously isolated from this plant, were tested for cytotoxic activity. Among them, eight compounds displayed significant cytotoxicities against human A2780, HO-8910, Eca-109, MGC-803, CNE, LTEP-a-2, KB and mouse L1210 tumor cells [25].

The antioxidant activity of asparagus juice was analyzed by 2,2‘-diphenyl-l-picrylhydrazyl and 2,2‘-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) methods. The enzymes, with the exception of pectinase from *Rhizopus* sp., contained rutinase, which hydrolyzed rutin to quercetin. Asparagus juice treated with viscozyme had the highest quercetin content without exhibiting a significant increase in the antioxidant activity. For a pectinase from *Aspergillus niger*, the antioxidant activity of asparagus juice was markedly reduced [7].

Sakaguchi *et al.*, found that anthocyanins A1 and A2 isolated from the spears of *Asparagus officinalis* were acting as antioxidants [6]. The potential effect of different concentrations of freeze-dried *Asparagus officinalis* (500, 250, and 125 mg/Kg of body weight/day) was evaluated on oxidative status and lipid profile in rats fed a cholesterol-rich diet. After five weeks of treatment, doses of 250 and 500 mg/Kg of asparagus were significantly reduced total cholesterol and LDL cholesterol levels. Atherogenic index was also significantly reduced in a dose-dependent manner by administrating freeze-dried asparagus. A beneficial effect was observed in the HDL cholesterol levels in asparagus-fed groups, although the increase was not significant. Consumption of asparagus also improved antioxidant status (superoxide dismutase and catalase enzymes), and protected against lipid peroxidation [26].

The antioxidant effects of *Asparagus officinalis* was investigated using superoxide dismutase, erythrocyte haemolysis and 2,2- diphenyl-1-picrylhydrazil free radical scavenging methods. The highest antioxidant capacity was obtained from the *in vivo* grown plant extract followed by *in vitro* grown plant extract in all three examined assays [27].

The hypolipidemic effect of *n*-butanol extract from asparagus by-products was evaluated in mice fed a high-fat diet. Asparagus butanol extract significantly decreased the levels of body weight gain, serum total cholesterol and low density lipoprotein cholesterol; it dramatically increased the high density lipoprotein level when administered at three different doses (40, 80 or 160 mg/kg bw) for 8 weeks in hyperlipidemic mice. In addition, asparagus butanol extract decreased the levels of alanine transaminase, aspartate transaminase and alkaline phosphatase in serum. Superoxide dismutase activity and the total antioxidation capacity were evidently increased; in addition, the malondialdehyde level and the distribution of lipid droplets were reduced in liver cells of asparagus butanol extract -treated mice [28-29].

Antimicrobial effects

The antibacterial potential of the ethanolic extracts of *in vitro* grown *A. officinalis* as well as ethanolic extract of undifferentiated callus cells of *A. officinalis* were studied using the paper disc diffusion method against two gram-negative pathogenic bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and two gram-positive pathogenic bacteria (*Staphylococcus aureus* and *Bacillus cereus*) . Antibacterial effect recorded only for callus extract (100 mg/ml) against *Bacillus cerus*. The rest of the extracts showed no antimicrobial activity in the same concentration against any of the tested pathogenic bacteria [27].

However Naema *et al*., found that aqueous extract of *Asparagus officinalis* showed a wide zone of inhibition when tested against *E. coli* growth in a concentration of 5% [30].

The saponin fraction of the *Asparagus officinalis* exerted antifungal activity [31-32].

Effect on colitis

The effects of cooked whole asparagus and its purified bioactive, rutin, were studied on colitis symptoms and disease progression in mice. C57BL/6 mice were fed a basal diet supplemented with 2% asparagus or 0.025% rutin for 3 weeks. Colitis was induced by 2% dextran sodium sulfate in drinking water for 7 days. Asparagus diet was determined to contain higher antioxidant capacities than rutin diet through antioxidant assays. During active colitis, consumption of asparagus alleviated some clinical symptoms (stool consistency, stool blood, and spleen hypertrophy) of colitis. In recovery, asparagus-fed mice were improving in terms of regenerating crypts, surface epithelial, and goblet cells, potentially due to its rutin content [33].

Other pharmacological effects

Asparagus officinalis increased the clearance rate of charcoal particles and the weight of immune organs in mice, it exerted antifatigue effects, enhanced anoxia tolerance, induced analgesia and improved memory, as

well as decreased the contents of lipid peroxide in plasma, liver and brain of the animal [34].

Jang *et al.*, examined *Asparagus officinalis* for its inhibitory effects against both cyclooxygenase-1 and -2. They found that linoleic acid was the most active compound [13].

The protecting effect of asparagus on the rat liver injured by CCl_4 (5%) poured into the stomach was investigated in rats. Compared with control, the contents of serum glutamic-pyruvic transaminase (SGPT) and malondialdehyde (MDA) were lower, and the content of liver superoxide dismutase (SOD) was higher in asparagus treated group [35].

Aqueous extract of *Asparagus officinalis* caused relaxation of spontaneous contractions of isolated smooth muscle of rabbit jejunum [14]. *Asparagus officinalis* also induced diuretic effects [36].

Contraindications and adverse effects

No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. Because of the irritating effect of saponin, the drug should not be administered in the presence of kidney diseases. In the case of reduced cardiac and/or kidney function, irrigation therapy should not be attempted. The berries were considered poisonous [5].

Dosage

Root: 3-5g powder [37]. A typical single dose is 800 mg of the plant. The cut rhizome was used as teas for internal use [5].

CONCLUSION

Asparagus officinalis is a plant with wide range of chemical constituents which exerted many pharmacological effects. There is a great promise for development of novel drugs from *Asparagus officinalis* to treat human diseases as a result of its effectiveness and safety.

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