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Review

Pharmacologic and medicinal properties of *Allium hirtifolium* Boiss

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Allium hirtifolium **is known as wild garlic and it grows wild just in Iran.** ***A. hirtifolium*** **extracts are important areas in drug development with numerous pharmacological activities. For a long time,** ***A. hirtifolium*** **has been used in traditional medicine for treatment of hypertension, rheumatoid, inflammation, and also wounds healing.** ***A. hirtifolium*** **has recently been shown to have antibacterial, antifungal, antioxidant, and anticancer activities. Saponins, sapogenins, sulphur containing compounds (thiosulfinates) and flavonoids are phytochemical compounds which are reported from this plant. Due to the easy propagation and collection of the plant and also remarkable biological activities, this plant has become both medicine and food in Iran. This paper presents comprehensive analyzed information on the botanical, chemical, and pharmacological aspects of** ***A. hirtifolium.***

Key words: *Allium hirtifolium*, Alliaceae, wild garlic, pharmacology.

INTRODUCTION

Allium hirtifolium Boiss. commonly known as wild garlic is endemic to Iran and grows wild in rocky slopes and fields at around 1,500 to 2,500 m high. It belongs to Alliaceae family in the order of Asparagales. *Allium* is the largest genus in this family and it comprises more than 600 species worldwide. *A. hirtifolium* has been known as “Moosir” in Iran and it is distributed in West, North-West and Central parts of Iran, especially in the Zagros Mountains (Amin et al., 2012). The main traditional usage of this plant is consuming it as spice in different foods. *A. hirtifolium* (Figure 1) grows from corms, 3 to 6 cm in diameter, which has blackish, paper-like tunics (Figure 2). The 4 to 6 basal leaves are broad, green to grayish green in color, and variably hairy. The leaves are normally withered by the time the bulb flowers. Flowers are borne on stems which are 60 to 150 cm tall and are arranged in an umbel. The umbels are some 8 to 12 cm in diameter, relatively small as compared to the tall stems, hence, the description 'drumstick allium'. Individual flowers, of which there are many, are a typical allium shape, with a superior ovary and six petals of a lilac to purple color, around 2.5 to 5 cm long (Ebrahimia et al., 2009). *A. hirtifolium* has been long used as spices and also medicine. The corms are widely used as flavor agent, preparation of pickles and in folk medicine as carminative and expectorant. They are used in Iranian traditional medicine for treating diabetes, arthritis, colds and flu, stress, fever, coughs, headache, hemorrhoids, asthma, arteriosclerosis, and cancer (Jellin et al., 2000). *A. hirtifolium* corms have been widely used for relief of rheumatic and inflammatory disorders (Jafarian et al., 2003).

A number of chemical constituents such as saponins, sapogenins, sulphur containing compounds (thiosulfinates) and flavonoids including quercetin and kaempferol have been identified in the plant (Kazemi et al., 2010). Disulphide and trisulphide compounds are amongst the most important compounds existing in *A. hirtifolium* (Rose et al., 2005). Allicin (diallyl thiosulfinate) has been isolated and identified in *A. hirtifolium* and was responsible for the remarkable potentials of this plant, especially the antibacterial, antifungal and antiparasite activities (Figure 3). Alliin was found to be the stable precursor that was converted to allicin by the action of alliinase (Ghodrati Azadi et al., 2008).

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Figure 1. *Allium hirtifolium* Boiss (Wild Garlic).

Figure 2. *A. hirtifolium* corms.

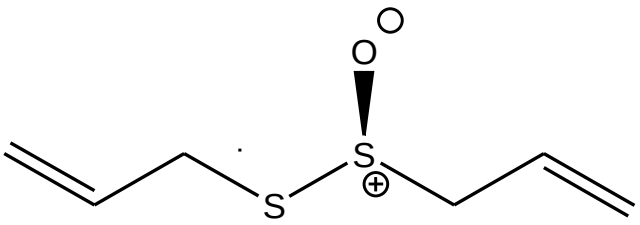

Figure 3. Structure of Allicin.

From current pharmaceutical studies, additional pharmaceutical applications of *A. hirtifolium* have revealed antibacterial, antifungal (Amin et al., 2012), antioxidant (Souri et al., 2008), anticancer (Ghodrati Azadi et al., 2009), antileishmania (Amanzadeh et al., 2006), immune system regulating, anti-trichomonas (Jafarian et al., 2003; Taran et al., 2006) and hepatoprotective (Kazemi et al., 2010) effects.

Since review and systemic analysis of chemistry, pharmacology and medicinal properties of *A. hirtifolium* have not been reported, we prompted to provide the currently available information on traditional and local knowledge, ethno biological and ethno medicinal issues and pharmacological studies on this useful plant. The aim of this paper is to introduce *A. hirtifolium* as a potent medicinal plant by highlighting its traditional applications as well as the recent findings for novel pharmacological and clinical applications.

Chemical composition

The commonly known phytochemical compounds identified in *A. hirtifolium* are saponins, sapogenins, sulphur containing compounds (thiosulfinates) and flavonoids including shallomin, quercetin and kaempferol (Kazemi et al., 2010; Amin and Kapadnis, 2005). The most important biological compounds from *A. hirtifolium* are alliin, alliinase, allicin, *S*-allyl-cysteine (SAC), diallyldisulphide (DADS), diallyltrisulphide (DATS), and methylallyltrisuphide (Ghodrati Azadi et al., 2009). Allicin is a precursor of several sulfides that are responsible for the flavour, odour and pharmacological properties of *A. hirtifolium* (Jafarian et al., 2003). Research has shown that both the corm and the flower of shallot contain a high density of glycosidic flavonols (Fattorusso et al., 2002; Barile et al., 2005).

Linolenic, linoleic, palmitic, palmitoleic, stearic and oleic acids have been identified in *A. hirtifolium* oil (Ebrahimi et al., 2008). Six new furostanol and spirostanol saponins, named hirtifoliosides A1/A2 (1a/1b), B (2), C1/C2 (3a/3b), and D (4) along with three known spirostanol saponins, alliogenin 3-O-β-D-glucopyranoside, gitogenin 3-O-β-D-glucopyranosyl-(1→4)-O-β-D-glucopyranoside, and agapanthagenin 3-O-β-D-glucopyranoside have been isolated from *A. hirtifolium* flowers. Kaempferol 3-O-β-D-rhamnopyranosyl-(1→2)-glucopyranoside, kaempferol 3-O-β-D-glucopyranosyl-(1→4)-glucopyranoside, kaempferol 3-O-glucopyranoside and kaempferol 7-O-glucopyranoside are flavonol glycosides characterized in both flowers and corms with high concentrations (Barile et al., 2005).

Potential of *Allium* species in phytotherapies

Antibacterial, antifungal, antiviral, antiprotozoal, and antihelmintic properties of *Allium* genus have been reported (Ariga and Seki, 2006; Ankri and Mirelman, 1999; Taran et al., 2006). Investigations conducted on *Allium* spp. show that the plants have wide and diverse biological activities including antidiabetic, antiatherosclerotic, antithrombotic, antihypertensive, antihyperlipidemic, anti-inflammatory, antioxidant, etc (Nencini et al., 2007). It is believed that *Alliums* can be used for treatment of diabetes, arthritis, colds and flu, stress, fever, coughs, headache, hemorrhoids, asthma, arteriosclerosis, cancer, rheumatic and inflammatory disorders (Eidi et al., 2006; Lawson, 1996; Bordia et al., 1997; Kojuri and Vosoughi, 2007; Hirsch et al., 2000). In the invading organisms and microorganisms, *Allium* genus extracts were shown to decrease the oxygen uptake, reduce the growth of the organism, inhibit the synthesis of lipids, proteins, and nucleic acids and damage the membranes (Borek, 2001; Dirsch and Kiemer, 1998).

Allicin, the most important compound found in *Allium* spp., was reported to possess diverse biological actions. It has been found that it inhibits lipid peroxidation and scavenges OH and free radicals (Borek, 2001; Lawson and Hughes, 1992). Garlic consumption reduces the risk of cancer, as its extract blocks effectively induced tumors in skin, breast, uterine cervix, and colon (Oommen and Anto, 2004; Vainio and Weiderpass, 2006). Aqueous garlic extract might exert its chemopreventive effect by inducing apoptosis (Balasenthil and Rao, 2002). Many organosulfur compounds, the major active principles in garlic, inhibit the proliferation of cancer cells, and some of them cause apoptosis in tumor cells of different tissue origin (Kwon and Moon, 2005; Arditti and Rabinkov, 2005). Hence, apoptosis could be a potential general mechanism providing a mechanistic basis for the anticarcinogenic activities of individual garlic components, although, the actual mechanism is not known (Thatte and Bagadey, 2000). *A. hirtifolium* belongs to the same biological genus as *Allium sativum* (garlic) and other onions. Therefore, such properties could also be related to this plant.

Anti bacterial and antifungal effects

In vitro studies have shown that the crude extract of *A. hirtifolium* corms has antimicrobial properties against a

variety of pathogenic bacteria, such as *Pseudomonas aeruginosa* (Abdou et al., 1972). *In vivo* investigations showed that 40 mg/ml of the topically applied aqueous extract was useful in the recovery of rats from burn injuries (Amin et al., 2005). After autoclaving, the crude aqueous extract of *A. hirtifolium* surprisingly could maintain its antimicrobial activity against both Gram negative and Gram positive bacteria strains including *Staphylococcus aureus*, *Listeria monocytogenes*, *Bacillus cereus*, *A. fumicans*, *Serratia marcescens*, *Escherichia coli*, *P. aeruginosa*, *Salmonella typhi*, *Salmonella paratyphi* A, *Proteus mirabilis*, and *Shigella* species, with a minimum inhibitory concentration (MIC) ranging from 5 to 20 µg/ml (Amin et al., 2005). The active compound responsible for the antimicrobial properties is a flavonoid named shallomin (Amin and Kapadnis, 2005).

The crude extract of *A. hirtifolium* also showed fungistatic and fungicidal activity against pathogenic fungi, including *Microsporum gypseum*, *Aureobasidium pullulans*, *Trichophyton mentagrophyte*, *Trichophyton rubrum*, *Fusarium oxysporum*, *Saccharomyces cerevisiae*, *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus fumigates* and *Candida albicans* with a MIC range of 0.15 to 20 mg/ml (Amin et al., 2005). Therefore, this ancient plant is a potential source for the treatment of bacterial and fungal infections and has a unique property not commonly found in current antibacterial and antifungal agents (Amin et al., 2012).

Antiprotozoal activities

A. hirtifolium hydroalcoholic and dichloromethane extracts inhibited the growth of *Trichomonas vaginalis* at low concentrations (MIC values = 10 and 5 µg/ml, respectively) and in short times. *T. vaginalis* infection is a sexually transmitted infection causing vaginitis and acute inflammatory disease of the genital mucosa.

Aqueous extract of *A. hirtifolium* also exhibited significant inhibition activity on *Leishmania infantum* growth with dose of 0.2 mg/ml (Amanzadeh et al., 2006). This activity is related to the presence of sulfide components including allicin, ajoene and other organosulfides which are contained in these extracts (Taran et al., 2006). It has been suggested that microorganism cells are more affected than human cells, because they do not have intracellular thiol content adequate to counterbalance the thiol oxidation by allicin and allicin-derived products. Ajoene has been shown to inhibit phosphatidyl choline synthesis in some protozoan (Harris et al., 2001; Foster and Tyler, 1999).

Hepatoprotective properties

Treating rats with hydroalcoholic extract of *A. hirtifolium* could protect liver cells against oxidant effects of alloxan and it could consequently cause a significant reduction in serum concentration of alkaline phosphatase (ALP), alanine transaminase (ALT), and aspartate transaminase (AST). Biochemical results confirm the usefulness of *A. hirtifolium* extract in decreasing the destructive effects of alloxan on liver tissue and hence on reducing the enzymes' leak into cytosol, which is possibly a result of herbal antioxidant compounds including flavonoids (Kazemi et al., 2010). *A. hirtifolium* contains effective compounds including active sulphur compounds, to which *A. hirtifolium*'s usefulness may be associated. –SH groups of sulphur compounds oxidize the lipid synthesizing enzymes, and hence reduce or inhibit lipid synthesis. Moreover, these compounds oxidize NADPH to nicotinamide adenine dinucleotide phosphate (NADP), and since NADPH provides the hydrogen necessary during lipid synthesis stages, they inhibit lipid synthesis (Augusti, 1977). Sulphur compounds also increase the activity of 7-alpha hydroxylase enzyme, and therefore, increase the conversion of cholesterol into bile acids (Stephan et al., 1987). So, hydroalcoholic extract of *A. hirtifolium* can possibly decrease plasma liver enzymes levels through the reduction of liver cell damage, and also, through hypoglycemic and hypolipidemic activities and preventing fatty liver formation (Kazemi et al., 2010).

Wound healing activity

The wound healing activity of hydroalcoholic extract of *A. hirtifolium* on full-skin-thickness wounds has been evaluated. One day after creation of wounds, the gel form solution of *A. hirtifolium* extract that was applied to the experimental wounds at 100 mg/kg topically. Wounds were daily treated for 12 days. The results showed that *A. hirtifolium* could accelerate wound healing by increasing the rate of epithelialisation. Thus, it is concluded that *A. hirtifolium* extract may be clinically effective in management of open wounds treatment (Ghodrati Azadi et al., 2011).

Anticancer properties

A. hirtifolium hydroalcoholic extract has shown a significant decrease in cancer cells population in Hela and MCF-7 cancerous cell lines by the dose of 44 µg/ml without any effect on the normal L-929 cell. Allyl sulfides, found in *A. hirtifolium* posses anticancer properties as shown by their ability to suppress tumor proliferation *in vitro* (Milner, 1996; Singh et al., 1996). Anti-cancer effect was greater for chloroform fraction. Allicin was quantified in the amount of 3.4 mg/g in this fraction. In 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay, the statistical analysis indicated that *A. hirtifolium* chloroformic extract significantly inhibited the proliferation of HeLa and MCF-7 cells. But this inhibition

could not occur in non-tumor L929 cells (Ghodrati Azadi et al., 2009).

Interestingly, the *A. hirtifolium* extract affected the tumor cells much stronger than pure allicin. *A. hirtifolium* could inhibit proliferation of tumor cell lines in a dose dependent manner. The inhibitory effect on tumor cell lines was 25 times stronger than that in normal cells (Ghodrati Azadi et al., 2008). As the data clearly indicate, a series of antimitotic agents would be synthesized based on purified components of *A. hirtifolium* extracts which would not affect normal cells, but stop the tumor cells in cancer patients (Ghodrati Azadi et al., 2009).

Immunomodulatory effects

The immune system is involved in the etiology, as well as pathophysiologic mechanisms of many diseases. Modulation of the immune responses to alleviate various diseases has been of interest for many years. Medicinal plants are a rich source of substances which are claimed to induce paraimmunity which is the non-specific immunomodulation of essentially granulocytes, macrophages, natural killer cells and complement functions (Sharififar et al., 2009).

Both hydroalcoholic extracts and polyphenolic fractions of *A. hirtifolium* decreased acquired immunity response in a dose dependent manner. The immunomodulatory activities of *A. hirtifolium* could depend on various chemical compounds, above all, on sulphur-containing compounds like allicin and polyphenolic compounds like flavonoids (Jafarian et al., 2003). Sulphur-containing compounds may interfere with the function of the gamma-glutamyl cycle as well as inhibitors of some of the enzymes having a SH-groups at the active site. Recently, these compounds were found to inhibit the tumor cell metastasis in experimental animals, which may be partially due to the immunostimulation of stem cells (Kuttan, 2000).

Conclusion

The objective of this review has been to show the recent advances in the exploration of *A. hirtifolium* as phytotherapy and to illustrate its potential as a therapeutic agent. With the current information, it is evident that *A. hirtifolium* has pharmacological functions including antibacterial, antifungal, antileishmania, anticancer, antioxidant properties as well as wound healing effect. As the current information shows, sulphur containing compounds (thiosulfinates), especially allicin might be useful in the development of new drugs to treat various diseases. However, the present results suggest a possibility that sulphuric compounds can be further developed as a potential disease-curing remedy. It must be kept in mind that clinicians should remain cautious until more definitive studies demonstrate the safety, quality and efficacy of *A. hirtifolium*. For these reasons, extensive pharmacological and chemical experiments, together with human metabolism will be a focus for future studies. Conclusively, this paper emphasizes the potential of *A. hirtifolium* to be employed in new therapeutic drugs and provide the basis for future research on the application of transitional medicinal plants.

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