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Phytochemistry and Pharmacology of *Athyrium* or fern

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Abstract: *Athyrium* or fern comes under family *Athyriaceae*. *Athyrium* contains phytochemicals which are beneficial for health. Traditionally it has been used by several tribal species in India and Abroad for medicinal purpose. *Athyrium* plant extract has shown promising pharmacological activities as antibacterial, antioxidant, anti HIV agent.

Keywords: *Athyrium*, fern, phytochemicals, pharmacological activities

Introduction:

Athyrium or fern belongs to the family *Athyriaceae*. It is a genus comprising more than two hundred species. These are terrestrial or epiphytic plants with mostly erect or sometimes with creeping or ascending rhizomes. The phytochemical and biological properties of the plant *Athyrium* have not been explored in adequate amount therefore scientific knowledge of their chemical constituent is limited.

Phytochemical constituents of *Athyrium*

Presence of different classes of natural compounds such as flavonoids, phenols, alkaloids, steroids, triterpenes and polysaccharides attribute to the great medicinal potency of *Athyrium* plants¹. In addition, *Athyrium* plants have been shown to contain nutrients, such as protein, carbohydrates, fats, antioxidants and vitamins, which benefit health in many ways.¹ The strong superoxide radical scavenging and reducing power of *Athyrium* genus have been attributed to its polysaccharides.^{2,3}

Traditional Medicinal uses of *Athyrium*

Athyrium species have been used in traditional medicine systems in different parts of the world. For instance, *A. filix-femina* (L.) Roth has been used along with honey to cure cough in Diano valley (Province of Salerno, Campania region, Italy),⁴ while its decoction has been used as an antiparasitic and anthelmintic agent.^{8,9} In Iran, the rhizome is also used as an antiparasitic and anthelmintic.⁷ The Rajasthan Bheels (a tribe from India) used the rhizome of *A. pectinatum* (Wall. ex Mett., T. Moore) as a strong anthelmintic.^{13,15} The people of Mymensing district of Bangladesh used fresh leaf juice of *A. asperum* in children as an anthelmintic and carminative.¹⁴ According to T. Moore in Maharashtra (India), fronds and rhizome of *A. hohenackerianum* are used as decoction against rheumatic pain as well as an anthelmintic.¹⁰ In addition, the rhizome paste has been used against scorpion bite.¹⁰ *A. falcatum* Bedd. has been used by the people of Madhya Pradesh (India) as an anthelmintic.¹¹ The people of Palani Hills (Western Ghats of South India) used its fronds and roots in their traditional medicine practices. For instance, the young fronds were consumed to treat internal ailments such as cancer and the roots consumed as an anthelmintic.⁶ *A. lanceum* roots are used to overcome pain, specifically breast pain during child birth. It is also used as a lactating agent and the dried powder when applied to sores is found to be useful.⁶ Moreover, it has been used as an anti-inflammatory herb for the treatment of ascariasis in Malaysia.¹² In New Guinea, *Athyrium* is used to treat sores.⁵ AMC has also been used in traditional Chinese medicine for its antioxidant properties.¹⁶⁻¹⁸ Lady Fern (*Athyrium filix-femina*) used for mothers with intestinal fevers and to prevent water breaking.

Pharmacological activities of *Athyrium*

Several extracts from ferns exhibited remarkable antioxidant capacity, comparable to vitamin C, making them good food preservatives. It is also used as antibacterial,⁷ antiparasitic,⁷⁻⁹ anthelmintic⁶⁻¹⁵ and diuretic agent.^{6,16-18} *Athyrium* plant species have also exhibited a promising effect on the inhibition of cell proliferation and stimulated apoptosis in the human liver cancer cell line (HepG2).¹⁹

Antimicrobial Activity

A. filix-femina (L.) Roth had good antimicrobial activity in acetone extract for both Gram-negative and Gram-positive bacteria with zones of inhibition of 7-20 mm diameter against *Escherichia coli* and *Bacillus megaterium*.¹⁹ *A. filix-femina* extract showed low antimicrobial activity with inhibition zone of 7-8 mm extract against *Staphylococcus aureus* and *Enterococcus faecalis* and a minimum inhibitory concentration (MIC) value of 600 mg/mL against *Bacillus cereus* and *Saccharomyces cerevisiae*.²⁰ However, the methanol extracts obtained from rhizome and leaves of *A. filix-femina* were found to have strong antibacterial potential against *E. coli*, *S. aureus*, and *B. megaterium* with MIC value ranging from 8 to 32 mg/mL.^{7, 21}

Parihar et al.^{22, 23} showed that the leaf extract of *A. pectinatum* inhibited the growth of *Salmonella arizonae*, but did not inhibit the growth of *E. coli* or *Salmonella typhi*. Aqueous and alcoholic extracts of *A. pectinatum* were found effective against *E. coli*, *S. arizonae*, *S. typhi* and *S. aureus*.^{22, 23}

Antioxidant activity

Liu et al.¹⁷ reported that the antioxidant activity of AMC is related to the amount of peptides, present in the form of polysaccharide peptide complexes. This study suggested that the molecular weight and sulfate content of AMC polysaccharides played very important roles on antioxidant activity¹⁷. Moreover, Yuan et al.²⁴ found that the presence of sulfate, acetyl or phosphate could enhance the antioxidant activity of polysaccharide in vitro. Similarly, Behera et al.²⁵ found that polysaccharides having small polysaccharide/peptide ratios showed higher scavenging activities. Chen et al.²⁶ also suggested that the mechanism of antioxidant action of polysaccharides might be linked to the supply of hydrogen from the polysaccharide peptide complexes, or the combination of the complexes with the radical ions, where the reaction was then terminated. Ferrous ions are considered the most important pro-oxidants in food systems:²⁷ so the chelating effect on ferrous ions is widely used to evaluate antioxidant activity. Liu et al.¹⁷ reported high chelating effect on ferrous ions of the AMC polysaccharides. As Liu et al.¹⁷ noticed, the chelating power could be related to the sulfate contents of the AMC polysaccharides. Sulfated poly-saccharides are often involved in many biological activities in animal cells, such as cell recognition, cell adhesion or regulation of receptor functions, which are of interest in medicine²⁸. Qi et al.²⁹ also observed that the higher the sulfate content of a polysaccharide, the stronger the antioxidant activity and anti-hyperlipidemic activity. The hydroethanolic extract of the dried aerial parts of AMC, defatted with petroleum ether and purified using an AB-8 macroporous resin, showed significant DPPH, ABTS, *OH scavenging activity and ferric reducing power with EC 50 of 15.0, 4.6, 48.0 and 13.2 mg/mL, respectively¹⁷. The extract also protected protein oxidation in a dose-dependent manner at concentration of 5-100 mg/mL¹⁷. Besides protein fragmentation, the oxidation of arginine, threonine, lysine and proline may also generate carbonyl derivatives considered to be a marker of ROS-mediated protein oxidation³⁰. Similarly, AMC purified extract in the range of 5-100 mg/mL efficiently inhibited 2,20-azobis (2-amidinopropane) dihydrochloride (AAPH) -induced oxidation of albumin from bovine serum (BSA) carbonyl in a dose dependent manner. In addition, AMC also inhibited lipid peroxidation in a dose dependent

manner and had the greatest cellular antioxidant activity, with cellular antioxidant activity values of 88.1 µmquercetin equivalents per g extract. AMC had powerful protective effects on biological macromolecules including proteins and lipids, indicating their potential use in the chemoprevention of diseases related to ROS. Sheng et al.¹⁶ also reported that the n-butanol fraction of the methanol extract of AMC exhibited strong superoxide anion scavenging capacity and strong reducing power. In another study, Sheng and Sun³¹ degraded AMC rhizomes by using hydrogen peroxide and ascorbic acid mixtures to obtain four low molecular polysaccharides derivatives. Their results showed that high molecular weight polysaccharides showed prominent reducing power and DPPH activity, whereas low molecular weight polysaccharides exhibited relatively stronger free-radical scavenging activity³¹. Total sugar and sulfate content could affect the scavenging capability of the samples against superoxide radicals³¹. Wang et al.³² found over-sulfated fucoidan, a sulfated polysaccharide found mainly in various species of brown algae and brown seaweed, had much greater antioxidant activity than fucoidan itself.

The oxidative stress theory of aging is based on the hypothesis that age-associated functional losses are due to the accumulation of ROS induced damages. Anti-aging effects of AMC have been reported and linked to its polysaccharide content and could thus be used as a promising adjuvant agent for aging prevention³³.

Anti-HIV activity

Mimhina et al.³⁴ isolated three sulfolipids from the pteridophyte *A. niponicum* (Mett.) Hance that were evaluated on human immunodeficiency virus (HIV). The sulfolipids at 6 µg/mL were found to significantly inhibit the activities of both calf DNA polymerase a (pol. a) and rat DNA polymerase b (pol. b). Calf thymus terminal deoxynucleotidyltransferase was inhibited moderately by the sulfolipids. The sulfolipids appear to be selective inhibitors of the mammalian DNA polymerases in vitro. Sulfolipids also inhibited the mammalian pol. a, pol. b, and HIV-RT in a concentration-dependent manner; IC₅₀ for inhibition of pol. a and pol. b was 1.5 and 3 µg/mL respectively, and almost complete inhibition (more than 90%) was achieved at 6 and 8 µg/mL, respectively. The sulfolipids were slightly more effective on pol. a than pol. b³⁴.

Conclusion:

In this chapter we discussed the phytochemical and pharmacological profile of the plant *Athyrium* or fern. Although several species of the plant are known in Chhattisgarh yet only few of them have been investigated for their phytochemical constituents and biological activities. Other species of the *Athyrium* genus require a thorough investigation to reveal their actual real clinical value.

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