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Phytochemical and pharmacological potential of *Artemisia absinthium Linn.* and *Artemisia asiatica* Nakai : A Review

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ABSTRACT

A world health organization survey indicated that about 75-80% of the world's populations rely on non-conventional medicine, mainly of herbal sources, in their primary healthcare. There has been an explosion of scientific information concerning plants, crude plant extracts and various substances from plants as medicinal agents during last 30-40 years. Although herbal medicine has existed since the dawn of time, our knowledge of how plants actually affect human physiology remains largely unexplored. Numbers of plants are claiming various medicinal uses and many researches are going on in this view. They are believed to be much safer and proved elixir in the treatment of various ailments. The genus *Artemisia* consists of about 500 species, occurring throughout the world. Among the different species of *Artemisia*, *A. absinthium* and *A. asiatica* have a vast range of biological activities including cytotoxic, antihepatotoxic, antibacterial, antifungal, antioxidant, antimalarial etc. Terpenoids, flavonoids, coumarins, caffeoylquinic acids, sterols and acetylenes constitute major classes of phytoconstituents of the genus *Artemisia*. The present review comprises the phytochemical, ethnopharmacological and pharmacological reports of *A. absinthium* and *A. asiatica*. The future scopes of these plants have been emphasized with a view to isolate bioactive moieties which could be used for multifarious biological activities.

Keywords: *Artemisia absinthium*, *Artemisia asiatica*, Antioxidant, Antimicrobial, Terpenoids

INTRODUCTION

Plants play a vital role in maintaining human health and contribute towards improvement of human life. They are important components of medicines, cosmetics, dyes, beverages etc. Plants have been one of the important sources of medicines even since the dawn of human civilization. In spite of tremendous development in the field of allopathy during the 20th century, plants still remain one of the major sources of drug in the modern as well as traditional system of medicine throughout the world. Over 60% of all pharmaceuticals are plant-based [1]. Plants are considered as state-of-art chemical laboratories capable of biosynthesizing number of biomolecules of different chemical classes. Many of these are proved to be precursors for development of other drugs [2]. India is one of the most medico-culturally diverse countries in the world where the medicinal plant sector is part of a time-honored tradition that is respected even today. Ethno-botanical and ethno-pharmacological studies on such plants continue to attract investigators throughout the world. In current scenario, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems [3]. The present review emphasizes the traditional uses, phytochemistry and therapeutic potential of *A. absinthium* and *A. asiatica*. Through this review, authors hope to attract the attention of natural product researchers throughout the world to focus on the unexplored potential of *Artemisia* species.

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The Genus *Artemisia*

The genus *Artemisia* belongs to a useful group of aromatic and medicinal plants. It is one of the largest and most widely distributed genera of the family Astraceae. It is a heterogenous genus, consisting over 450 diverse species distributed mainly in the temperate zone of Asia, Europe and North America. These species are perennial, biennial and annual herbs or small shrubs [4-7].

Ethnopharmacology

A. absinthium has been traditionally used as an anthelmintic, antiseptic, antispasmodic, febrifuge, stomachic, cardiac stimulant, for the restoration of declining mental function and inflammation of the liver, and to improve memory [8-11]. Traditional Chinese medicine practitioners use the plant for treating acute bacillary dysentery, cancers and neurodegenerative diseases [12-15].

Extracts of the whole herb of *A. asiatica* have been used in

traditional oriental medicine for the treatment of inflammation, cancer, infections and ulcerogenic diseases [16-19].

Phytochemistry

Exhaustive literature survey on phytochemical reports of *A. absinthium* and *A. asiatica* reveals that they comprise mainly terpenoids, flavonoids, coumarins, polyphenolics, caffeoylquinic acids, sterols and acetylenes. Both species are rich in terpenoids. Table-1 summarizes the phytoconstituents of *A. absinthium* and *A. asiatica*.

Pharmacological Reports

A. absinthium

Khattak et al. [43] reported that hexane-, chloroform-, and water-soluble extracts of *A. absinthium* exhibit antipyretic activity against subcutaneous yeast injections in rabbits. No toxic effects were documented for the plant extract at doses up to 1.6 g/kg. The essential oils distilled from the aerial parts of *A. absinthium* inhibited *in vitro* growth of *Candida albicans* and *Saccharomyces cerevisiae* var. chevalieri [22]. 5,6,3',5'-tetramethoxy 7,4'-hydroxyflavone, a flavone isolated from *A. absinthium* has been reported to exhibit *in vitro* anti-inflammatory activity as evidenced by inhibition of cyclo-oxygenase-2 (COX-2), prostaglandin (E-2 and PGE-2) and nitric oxide in lipopolysaccharide-stimulated RAW 264.7 cells [31]. *A. absinthium* has been studied for cognitive enhancement because of its nicotinic and muscarinic receptor activity (IC 50 concentration of less than 1 mg/mL) in homogenates of human cerebral cortical membranes [44]. The intoxicating effects of thujone were believed to activate receptors responsible for marijuana intoxication; however, thujone exhibited low affinity for rat cannabinoid receptors [45]. Methanol extract of *A. absinthium* enhanced neurite outgrowth induced by nerve growth factor and PC12D cells [46]. Free-radical scavenging activity of *A. absinthium* extracts has been reported [47]. The antioxidative activity was tested by measuring their ability to scavenge stable 2,2-diphenyl-1-picrylhydrazyl free radical and reactive hydroxyl radical during the Fenton reaction trapped by 5,5-dimethyl-1-pyrroline-N-oxide, using electron spin resonance spectroscopy. Aqueous methanolic extract of *A. absinthium* exhibited hepatoprotective effect against acetaminophen- and carbon tetrachloride-induced hepatic damage [12]. Recently it has been reported that crude aqueous extract and crude ethanolic extract of the aerial parts of *A. absinthium* exhibit anthelmintic activity in comparison to albendazole against the gastrointestinal nematodes of sheep [48]. Valdes et al. [49] reported that ethanol extract of *A. absinthium* exhibit antiprotozoal potential against *Trypanosoma brucei*, *Trypanosoma cruzi*, *Leishmania infantum* and *Plasmodium falciparum*; and antifungal activity against *Microsporum canis* and *Candida albicans.* Methanol extract of the aerial parts of *A. absinthium* at a dose of 300 mg/kg found effective against a trichinellosis (*Trichinella spiralis*) in rats [50]. Artemisetin isolated from *A. absinthium* exhibited marked antitumor activity against melanoma B16, but only weakly retarded growth of *Pliss lymphosarcoma* [51]. Chronic use of *A. absinthium* has been reported to have some neurotoxic effect due to presence of thujone and its derivatives [52].

A. asiatica

Ryu et al. [53] reported that DA-9601, a standardized extract of *A. asiatica* (10, 30, or 100 mg/kg, intragastrically) exhibit hepatoprotective effect on liver damage induced by acetaminophen and carbon tetrachloride. In another study, DA-9601(10% for 15 week) exhibited chemopreventive effects against azoxymethane-initiated and dextran sulfate sodium-promoted mouse colon carcinogenesis. In addition, DA-9601 treatment also suppressed the expression of COX-2 and inducible nitric oxide synthetase as well as nuclear factor (NF)-kappa-B DNA binding in the colonic tissues [18]. Moreover, DA-9601 also reported to suppress the airway allergic inflammation via regulation of various cellular molecules expressed by MAP kinases/NF-Kappa-B pathway [54]. Artemisolide, as NF-kappa-B inhibitor, isolated from *A. asiatica* inhibited NF-kappa-B transcriptional activity in lipopolysaccharide-stimulated macrophages RAW 264.7 (IC 50 value 5.8 µM) [17]. DA-9601 has been reported to inhibit increased susceptibility of ethanol-treated gastric mucosa to naproxen [55].

Eupatilin (5,7-dihydroxy-3,4,6-trimethoxyflavone), a pharmacologically active ingredient isolated from *A. asiatica*, has been evaluated for apoptosis-inducing capability in cultured human promyelocytic leukemia (HL-60) cells. Eupatilin exhibited concentration-dependent inhibitory effects on viability and DNA synthesis capability of HL-60 cells [16]. Park et al. [56] reported that pre-treatment of *A. asiatica* extract (30 or 100 mg/kg), significantly attenuate gastric injury against alcohol-induced damage in gastric mucosa of rats, by significantly decreasing lipid peroxidation, preventing glutathione depletion, and inhibiting cytochrome 2E1 ethanol-metabolizing enzyme.

Table 1: Phytoconstituents of *A. absinthium* and *A. asiatica*.

Species	Phytoconstituents
A. absinthium	**Essential oil** containing chamazulene, nuciferol butanoate, nuciferol propionate, caryophyllene oxide, phellandrene, pinene, azulene [20], (Z)-thujone , (E)-thujone [5,11], myrcene, trans-sabinyl acetate [21], cis- and trans-epoxyocymenes, chrysanthenyl acetate [20,22], thujyl alcohol, nerol, isothujyl acetate [23], prochamazulenogen [24], ß-pinene, hydrocarbon monoterpenes [25], sabinene, 1,8-cineole, *Artemisia* ketone, linalool, trans-verbenol, carvone, curcumene, neryl butyrate, neryl 2-methylbutanoate, neryl 3-methylbutanoate [26], **sesquiterpene lactones** arabsin, artabin, ketopelenolide, santonin related lactones [27]; **tannins** [28]; **carotenoids**; **lignans** [29]; **glucosides** absinthin, anabsinthin [30]; **phenolic compounds** [5], **flavonoid** 5,6,3',5'-tetramethoxy 7,4'-hydroxyflavone [31], 5-hydroxy-3,3',4',6,7-pentamethoxyflavone [32], artemitin, rutin, glycosides of quercetin [33], chlorogenic, caffeic acids [33]; **bitter principles** artamarin, artamaridin, artamaridinin, artamarinin [34]; Quebrachitol [35]; 24-zeta-Ethylcholesta-7,22-Dien-3-ß-ol [36].
A. asiatica	**Essential oil** containing terpene and a terpene alcohol [37], 1,8-cineole, selin-11-en-4-a-ol, monoterpene alcohols [38], camphor, borneol, bornyl acetate [5,39]; **flavone** eupatilin (5,7-dihydroxy-3',4', 6-trimethoxyflavone) [40,41]; **alkaloids** [42]; artemisolide [17].

The ethanol extract of *A. asiatica* has been reported to inhibit inflammatory activation of mouse microglial cells as determined by the production of nitric oxide and the expression of inducible nitric oxide synthase and inflammatory cytokine. The extract also protected nerve growth factor-differentiated PC12 cells against microglial cytotoxicity [19]. The essential oil 1,8-cineole and selin-11-en-4a-ol, and monoterpene alcohol fraction isolated from *A. asiatica* exhibited antibacterial and antifungal activity against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Candida albicans, Rhodotorula rubra* and *Aspergillus fumigatus*. The monoterpene alcohol fraction showed the highest antibacterial activity [38]. 4,5-dihydroxy-3',6,7-trimethoxyflavone isolated from *A. asiatica* has been reported to reduce micromolecular amyloid-ß protein-induced oxidative cell stress in PC12 cells [57].

DISCUSSION AND CONCLUSION

Since the beginning of the human civilization, man utilizes native and exotic plants for healing purposes, whose knowledge is transmitted by oral tradition through the generations. Despite the arrival of the industry, in many countries, the majority of the population does not have access to medicines, thus making use of home preparations to cure various health problems. The considerations made on the health of all the people of the world during the declaration of Alma-Ata in 1978, was the milestone that made the World Health Organization (WHO) stress the need, to develop the medicinal plants in the world in the therapeutic scope. Presently, there are different programs supported by WHO, which integrate several preventive and therapeutic aspects of the diseases.

The present review emphasizes the phytochemical, ethnopharmacological, pharmacological reports and toxicological information on *A. absinthium* and *A. asiatica*. Terpenoids, flavonoids, coumarins, caffeoylquinic acids and sterols constitute major classes of phytoconstituents of the genus *Artemisia*. Both *A. absinthium* and *A. asiatica* are rich in terpenoids. *A. absinthium* has been reported to have a broad spectrum of inhibitory activity against a variety of microorganisms due to presence of essential oil [22]. 5,6,3',5'-tetramethoxy 7,4'-hydroxyflavone, a flavone isolated from *A. absinthium* has been reported to exhibit *in vitro* anti-inflammatory activity [31]. *A. absinthium* has been studied for cognitive enhancement because of its nicotinic and muscarinic receptor activity in homogenates of human cerebral cortical membranes. Methanol extract of *A. absinthium* enhanced neurite outgrowth induced by nerve growth factor and PC12D cells [46]. In addition, free-radical scavenging activity of *A. absinthium* extracts has been reported [47].

DA-9601, a standardized extract of *A. asiatica* exhibits hepatoprotective and chemopreventive effect [53]. The essential oil 1,8-cineole and selin-11-en-4a-ol, and monoterpene alcohol fraction isolated from *A. asiatica* exhibited antibacterial and antifungal activity [54]. The ethanol extract of *A. asiatica* has been reported to exhibit anti-inflammatory activity. Eupatilin a pharmacologically active ingredient isolated from *A. asiatica*, has been evaluated for apoptosis-inducing capability in cultured human HL-60 cells [16].

Despite a long tradition of use of *A. absinthium* and *A. asiatica* for treatment of various ailments, little pharmacological work has been carried out to prove their traditional claims especially in central nervous system (CNS) disorders. Keeping in view the traditional, sporadic phytochemical and pharmacological reports, low toxicity, these species seem to hold great potential for in depth investigation for various biological activities, especially their effects on CNS.

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