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Potentialities of Artemisia Annua

***Sandhya S, Vinod K.R, Chaitanya R.S.N.A.K.K, Narender Prasad D**

Nalanda college of Pharmacy,Hyderabad Main Road Nalgonda-508001, Andhra Pradesh.

Abstract

Artemisia annua an annual wormwood is relatively unexplored in the Indian subcontinent but highly potential plant. It is mainly constituted with artemesinin an endoperoxide having a sesquiterpene lactone.It is reported to have effective treatment in skin diseases, malaria, various carcinoma conditions, haemorrhoids, leishmaniasis and viral infections. This article gives an in-depth view of the plant, its distribution, active constituents and pharmacological uses.

Keywords: Artemisisnin, artesunate, artether, anti-neoplastic, anti-leishmaniacidal, carcinoma

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Introduction

Artemisia annua otherwise known as sweet or annual wormwood is an aromatic annual herb (known as quingho in China), native to Asia especially China[1]. It contain Artemisinin an endoperoxide consisting of sesquiterpene lactone[2,3]. In India this herb is being cultivated only on an experimental basis. It is being cropped on a large scale in China, Vietnam, Turkey, Iran, Afghanistan and Australia[4]. In Europe and America this plant was identified in wild forest conditions[5]. Around 400 species of genus Artemisia have been identified out of which many have been screened. A. annua and A. apiacea was found to have artemisinin. The former was found to have maximum yield and later to have minimum. The active constituents were reported to have effective treatment in skin diseases, malaria, various carcinoma conditions, haemorrhoids, leishmaniasis and viral infections.

Morphology and floral botany

Artemisia belongs to the tribe Anthemidae of the Asteroidea, a subfamily of the Asteraceae. This is a large shrub often reaching more than 2 m in height; usually single stemmed with alternate branches. The aromatic leaves are deeply dissected and range from 2.5 – 5 cm in length. Leaves and flowers contain both 10 celled biseriate trichomes and 5 cell filamentous trichomes. The nodding flowers are greenish yellow having glandular trichomes which contain artemisinin as well as aromatic volatile oils[6].

Chemistry and Pharmacology

It is reported that artemisinin was first isolated in pure form in 1972 and its structure was determined in the year 1979[7]. It was identified in leaves, small green stems, buds, flowers and leaves. It was found that when mevalonic acid was added as a precursor yield of artemisinin was increased by 2 %. Semi synthetic derivatives include artemether, arteether, artesunate. Sixteen related sesquiterpenes has been isolated from ariel parts and reported by Zamal *et al*.In the year 1993 it was reported in Phytochemistry that a bisnorsesquiterpene and norannuic acid was isolated[8]. Essential oils are the other research area of interest in cosmetics and perfume industry. Major components in the oil were reported as artemesia ketone, isoartemesia ketone, 1, 8-cineole and camphor[9]. Artemisinin as such exhibits poor bioavailability because of its physical properties and therefore its semi synthetic derivatives are preferred. It has been reported by Oliver Burk *et al*, that artemisinin induces cytochrome P450 expression by activating PXR (pregnane X receptor) and/or CAR (constitutive adrostane receptor). Further more artemisinin acts as a ligand of both nuclear receptors, because it modulates the interaction of the receptors with coregulators[10]. The fact that Artemisinin's direct anti neoplastic effects closely resembles that of high dose of IV vitamin C is intriguing.

Artemisinin is available as α-β arteether injection 150mg/2ml IM having biological half life greater than 20 hours, metabolised and eliminated by the liver.

WHO currently recommends the following therapeutic options in the treatment of malaria.artemether, artesunate + maodiaquine, artesunate+sulphdoxine/pyremethamine, artesunate + mefloquine, amodiquine+sulphaodxine-pyrimethamine. Pharmacodynamic activity of artemisinin was reported to be altered when given in combination with thiabendazole or curcumin or doxycycline. Activity is based on a usual mode of action resulting in the production of alkylation of malarial specific proteins[11]. Pharmacokinetic studies on artemisinin reveal an unusual time dependency during a seven day oral daily regimen of 500mg in ten healthy male Vietnamese adults. AUC was decreased to 34% by day four with a further decrease by day seven to only 24% of values obtained after the first day of administration. This could be due to auto inductive effect on drug metabolism[12].

Significant cytotoxic activity of artemisinin was reported by Zheng *et al* in 1994[13]. Artemisinin has been shown to promote apoptosis (programmed cell death).In laboratory studies ,it reduced the expression of VEGF in tumour cells and inhibited nuclear factor κ-B an important activator in cancer development and progression .Artesunate, a semi synthetic derivative of artemisinin, inhibited angiogenesis in various laboratory and animal studies[14]. It has been recently reported that the treatment of proliferative cervical disorders such as cervical cancer and cervical dysplasia, and virus infections by administering artemisinin and related compounds. The virus infections include human papillomavirus (HPV), human T-lymphotropic virus type 1(HTLV-1), herpes virus, SV-40 like virus, hepatitis virus, human immunodeficiency virus (HIV), adenovirus and influenza virus[15].

Artemisinin has promising anti-leishmanial activity that is mediated by programmed cell death .The anti-leishmanial activity was seen in both promastigotes, with IC50 values of 160 and 22 μM, respectively. This activity was mediated via apoptosis as evidenced by externalization of phosphatidylserine, loss of mitochondrial membrane potential, *in situ* labelling of DNA fragments [16].

A coumarin, scopoletin from A. annua is reported to show good anti in flammatory activity[17].The flavonoid fisetin was found to be non-peptide angiotensin converting enzyme inhibitor[18].It has been reported that artemesinin has plant growth inhibitory activity with

potential herbicidal action[19]. Artemisinic acid a precursor for semi synthetic artemisinin is found to be a good antibacterial[20].

Discussion

Artemisia annua appears to be a resource of various active constituents with wide range to biological activity. The drug is extensively used as antimalarial, anticancer, anti-viral etc.But since it activates PXR and CAR resulting in the induction of *CYP3A4* and *MDR1* it has a higher risk of potential drug interactions than anticipated previously. This aromatic annual herb is yet to be explored in our Indian subcontinent.

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