

Therapeutic Activities of *Artemisia Herba-Alba* and *Rosmarinus Officinalis* against Microbial Infection: A Review

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Abstract: Natural products are still major potential sources of innovative therapeutic agents for various conditions, including infectious diseases as they represent an unmet source of chemical diversity. This study was conducted to determine the anti-trypanosomal properties of *Artemisia herba-alba* and *Rosmarinus officinalis* in vivo settings. We have reviewed previous studies in the literature, which support the therapeutic activity of these plants and the data suggest that *A. herba-alba* as well as *R. officinalis* have anti-trypanosomal activities, and reinforce the use of this plant as an alternative remedy for microbial infection in traditional medicine.

Keywords: *Artemisia herba-alba*, *Rosmarinus officinalis*, anti-trypanosomal properties

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I. Introduction

Artemisia herba-alba, commonly known as white wormwood or desert wormwood, is a grayish strongly aromatic dwarf shrub native to the Northern Africa, Arabian Peninsula, South Western Europe, and Western Asia. It is believed that *Artemisia. spp* serves as an important source of biological compounds for insecticides and fungicides, antibacterial and allelopathic products (Chauhan et al. 2010). Similarly, Rosemary (*Rosmarinus officinalis*) is a woody and perennial herb belonging to the family *lamiaceae* with pleasant smelling that grows wildly in several regions (Ozacan et al. 2008). There is evidence that later plant possess a large number of pharmacological properties (Pereira et al. 2005; Nabekuraa et al. 2010). These include hepatoprotective (Sotelo et al. 2002; Akrou et al., 2012), antibacterial (Del Campo et al. 2000), antithrombotic (Yamamoto et al. 2005), antiulcerogenic (Dias et al. 2000), diuretic (Haloui et al. 2000), antidiabetic (Bakirel et al. 2008), antioxidant (Bakirel et al. 2008), antinoceptive (González-Trujano et al. 2007), anti-inflammatory (Altinier et al. 2007), and anti-depressant activity (Heinrich et al. 2006). Hence, this review paper highlights the therapeutic properties of *A. herba alba* and *R. officinalis* and their potentiality as an alternative options in the market.

II. *Artemisia herba-Alba*

1.1. Description and Ecology

Artemisia herba-alba plant belongs to the composite family comprising about 400 species. The plant grows commonly in the steppes of North Africa (Libya, Morocco, and Algeria), Egypt, and Spain, deserts of Sinai, Middle-East and Northwestern Himalayas of India. It is a dwarf shrub fast growing in arid and warm climates and muddy areas. The flowering time starts from September to December and basically develops at the end of the summer with many basal, erect, and leafy stems covered by woolly hairs. The species vary and are of morphologically different from each other depending on their geographical, environmental and climatic conditions. The plant is green to light green in color, with strong roots. The order is variable depending on the origin: herbal, aromatic green odor with a burning freshness.

1.2. Pharmacological properties

The plant has long been described to be used in folk herbal medicine around the globe for the purpose of treatment, and prevention of number of diseases (Vermin et al., 1995). During the past two decades, many pharmacological studies conducted in different geographical regions have reported the significance of this plant in the traditional medicine. This includes anti-helminthic, colds, cough, gastric disturbances, worms, diarrhea, abdominal cramps, human and livestock wounds. Plants growing in Middle East possess spasmolytic activity and antibiotic properties against a wide range of microorganisms.

1.3. Antidiabetic effect of *A. herba-alba*

Artemisia species which belongs to the family *Asteraceae*, are reported to possess antidiabetic effects and have been used in many countries of North Africa, Middle East and Europe as a herbal medicine for treatment of diabetes, high blood pressure and gastrointestinal ailments (Mossa 1985; Al-Shamaony et al. 1994; Subramoniam et al. 1996) and *Teucrium* species (*Fam: Lamiaceae*) (Suleiman et al. 1988; Gharaibeh et al. 1988; Iriadam et al. 2006). A previous study published in the data base has demonstrated the aqueous extract of *A. herba-alba* caused significant decline in glucose levels in the serum of both normoglycaemic and alloxanized rabbits (Twajj& Al-Badr 1988). Moreover, other studies have confirmed that the extract of this plant had a clear preventive effect on the appearance and development of insulin resistance without affecting body weight (Hamza et al. 2010). Similar result has been reported by Al-Shamaony et al. (1994). In the later study, the aqueous extract of the aerial parts of *A. herba-alba* caused significant fall in plasma glucose level and prevented a significant elevation of glycosylated hemoglobin level without any bodyweight loss in diabetic animals. These results, however, appear to be in agreement with those reported by other researchers (Khlifi et al. 2013).

1.4. Antiparasitic activity of *A. herba-alba*

Numerous studies have reported extensively the anti-trypanosomal properties of *Artemisia .spp.* (Endalkachew et al. 2010). In earlier study, the methanol and crude extracts of *Artemisia absinthium* showed comparable effects on the growth inhibition of *T.b.brucei* in *invitro* models. Compared to the rest of *Artemisia* species extracts, methanol and dichloromethane extracts from *A. absinthium* showed significant anti-trypanosomal activities. Despite the presence of difficulties in terms of comparison within the parts of the plant, the methanol extract of the aerial part was found to be the best extract against trypanosomes among the methanol crude extracts tested. Pirbalouti (2013) showed that *Artemisia salina* had antiparasite and antipesticide effect; *Artemisia inoculate* had antiparasite and laxative effects. The anti-trypanosomal or cytotoxic activity of the plant might not be ascribed to a single entity of the extract. The phyto-chemical screening of the whole plant has also revealed the presence of alkaloids, flavonoids, triterpenes, tannins and volatile oil.

1.5. Antimicrobial and antioxidant activities

The antimicrobial activity of *A. herba-alba* has been evaluated in many studies of experimental nature. In studies examined the essential oils of *A. herba-alba* reported that it had a great potential on microbial activity against strains of *Staphylococcus aureus*, *Micrococcus luteus*, *Escherichia coli*, *Salmonella typhimurium*, *Bacillus cereus*, and *Enterococcus faecalis*. Furthermore, antimicrobial activity of *A. herba-alba* have been confirmed in some yeast strains of *Candida* (Mighri et al. 2010). In addition, highly growth inhibitory activity of the plant on many fungi has been demonstrated; the antifungal activities were tested using *Fusarium solani*, *Fusarium sp*, *Aspergillus oxysporum* and *Candida albicans* (Zouari et al. 2010). Plants often contain a wide variety of antioxidant molecules, such as phenolic acids, flavonoids and other natural antioxidants. In the context of *A. herba-alba*, it has been reported that the plant yields an aromatic essential oil which is rich in monoterpenes and sesquiterpene lactones widely distributed in plants and possess anti-inflammatory and anti-carcinogenic activities.

1.6. Toxicological properties

The toxic effects of *A. herba-alba* have been examined by determining the effect of acute and chronic administration of aqueous extract of the plant on the reproductive system (Almasad et al. 2007). In the later study, the toxic effects of *A. herba-alba* were measured in terms of number of pregnant rats, implantation sites, viable fetuses and respiration site. The results revealed no negative effect on fertility without the increase in ovarian weights and a decrease in viable fetus's number. Some studies concerning renal toxicity insist that there is no case of renal injury caused by the manipulation of this plant in experimental studies. Unlike, another recent study reported an exceptional case of acute renal failure (Mighri et al. 2010), the mechanism by which the plant constituents cause this impact remains yet unclear.

1.7. Constituents

Sesquiterpene lactones

Sesquiterpene lactones constitute a large and diverse group of biologically active plant chemicals which have been identified in several plant families. Plants containing sesquiterpene lactones have been used in some cultures to treat certain medical problems (Wu et al. 2006). The genus *Artemisia* contains biologically active type of secondary metabolites (Bora & Sharma, 2011). Interestingly, there are large differences in chemo types of sesquiterpene lactone constitution between countries and regions according to the properties of geographical location, soil and climate. Consequently, there are many groups of sesquiterpene lactones of *A. herba-alba* growing in Spain, Libya, Morocco, Algeria, Tunisia, Egypt, Palestine and Jordan (Mohamed et al. 2010).

Phenolic compounds and flavonoids

The flavonoids detected in *A. herba-alba* revealed a large structural variation ranging from common flavone and flavonol glycosides to more unusual highly methylated flavonoids such as Hispidulin and Cisilineol which possess an antiproliferative activity against multiple types of cancer cells (Bora & Sharma, 2011). The aerial parts of the *A. herba-alba* contain other flavonoids such as vicenin-2, schaftoside, isoschaftoside, 5',4'-dihydroxy-6,7, 3-trimethoxyflavone, quercetin-3-rutinoside, pultetin 3- rutinoside and pultetin 3 -glucoside .

Essential oils

The *A. herba-alba* essential oils, obtained by hydro-distillation from aerial parts, have been extensively examined (Ala-out et al. 2010; Bezza et al. 2010). Large diversity in terms of oil composition from plants grown in different countries, and occasionally in different localities of the same country, have been reported. However, the major components of the plant oil appear to be monoterpenoids mainly the oxygenated types such as 1,8-cineole, chrysanthenone, chrysanthenol, and 13-thujones and camphoras. More recently, a study has revealed that the essential oil of the Algerian *A. herba-alba* contained in majority: cis-chlysanthenyl acetate (25.1 2%); (2E, 3Z) 3,5-heptadienal-2-ethyliden-6-methyl(8.39%); myrtenyl acetate (7.3 9%); verbenone (7.1 9%) and chrysanthenone (4.980A) (Laid et al. 2008). While the major components of the Tunisian *A. herba-alba* essential oil extracted from aerial parts are the oxygenated monoterpenes, cineole, thuj ones, borneol and sabinyl acetate (Mohsen & Ali 2009; Mighri et al. 2010b; Zouari et al. 2010). In addition, in Spain, a study has revealed that monoterpene hydrocarbons and oxygenated monoterpene are the most abundant skeletons in *A. herba-alba* oil (Salida et al. 2004). The different compounds responsible of the pharmacological activity of *A. herba-alba* may act individually or in a synergistic manner.

III. Rosmarinus Officinalis

1.8. Morphological description and geographical distribution

Rosemary, *Rosmarinus officinalis* is an ever green perennial shrub grown in many parts of the world (Porte et al. 2000). The plant is an ever green perennial plant forming a stiff shrub, much branched and densely bushy, with a characteristic aromatic smell. The leaves are simple, tough, linear with revolted margins, greenish and crinkled on top and tomentose underneath, 2-4 mm wide. The flowers are grouped in little axillary and terminal clusters with bracts. Rosemary foliage has a seasonal dimorphism; it flowers abundantly in late spring. Its species are very widespread in many parts of the world (Porte et al. 2000). More specifically, it is common in the ecological ranges that include Libya and North Africa, the Mediterranean: in the northern Mediterranean, it extends from Portugal to Turkey; in the southern Mediterranean, it extends from eastern Morocco to Cyrenaica.

1.9. Traditional medicine

In Libya, rosemary leaves are used as an antispasmodic for the digestive tracts and as a vermifuge. Dried leaves ground up and mixed with olive oil are put on the recent circumcision wound as these products were used as antitrypanosomal effects (Awad et al., 2013 & 2014).

1.10. Essential oil composition

The essential oil of *Rosmarinus officinalis* encompasses several compounds at rather different concentrations. It is characterized by two or three major components at fairly high concentrations compared to other compounds present in traces. Generally, these major components determine the biological properties of the essential oil and can act in synergic manner or regulate one another. Studies of the composition of essential oil from different chemo-types of rosemary (α -pinene, 1,8 cineol, camphor, verbenone chemotypes) have mainly focused on the analytical characterization of phytochemical constituents (non-oxygenated monoterpene and sesquiterpene hydrocarbons, oxygenated monoterpenes and sesquiterpenes, phenolic derivatives, and non-isoprenoidic components including volatile alcohols, aldehydes, and ketones (Baratta et al. 1998; Bozin et al.

2007). Chemical composition of rosemary essential oil can vary between regions and it depends mostly on climate, soil composition, plant organ, age and stage of vegetative cycle.

1.11. Antioxidant activities

Among natural antioxidants, rosemary has been widely accepted as one of the species with the highest antioxidant activity (Wang et al., 2008). It is well known that the activity of rosemary extracts in medicine and food industry due to the presence of some important antioxidant oil and phenolic components, to prevent oxidative degradation of oil and lipid containing foods (Stefanovits-Banyai et al. 2003). Rosemary has long been recognized as having antioxidant molecules, such as rosmarinic acid, carnosol, rosmaridiphenol and these have been found in ethanol-soluble fraction.

1.12. Antidiabetic properties

There are a few scientific reports relating on the antidiabetic potential of various extracts from *R. officinalis* which demonstrated that the infusion of the plant had hypo-glycaemic effect whereas its volatile oils had hyper-glycaemic effects (Bakirel et al., 2008).

1.13. Cytotoxicity of rosemary essential oils

Oxygenated monoterpenes of essential oil seem to exhibit a variable degree of cytotoxicity. As typical lipophilic substances, they pass through the cell wall and cytoplasmic membrane and disrupt their structure. In bacteria, the membrane damage is related to the loss of ions and reduction in membrane potential, collapse of the proton pump and ATP depletion. This cytotoxic property is used to treat individuals affected by some human or animal pathogens or parasites Cheung & Tai (2007).

1.14. Antimicrobial activity

The antimicrobial activity of this plant has been examined against numerous bacterial strains and fungi, including *Candida albicans* and *dermatophytes*. The highest antibacterial activity of both essential oils was expressed on *E. coli*, *Salmonella typhi*, *S. enteritidis* and *Shigettasonei*(Ebrahimie et al., 2015). The cytotoxic effect of rosemary is of great importance in preservation of agricultural or marine products. The antimicrobial efficacy of plant essential oils depends on food composition.

Conflict of interests

The authors have not declared any conflicts of interest.

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