Chemical Constituents and Biological Activities of
Artemisia herba-alba

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Abstract: Artemisia, one of the larger genera in the family Asteraceae and the largest genus in the tribe
Anthemideae, comprises from 200 to more than 500 taxa at the specific or subspecific level. Many Artemisia
species have a high economic value in several fields, as food plants and as antihelminthic and antimalaria in
medicine. Artemisia herba-alba was known for its therapeutic and medicinal properties, it was used in both
traditional and modern medicine. Several papers have been published on the chemical composition of specimens
of A. herba-alba. The aim of this work is to review all available scientific literature published on A. herba-alba.
The focus will be on the chemical constitutions which have been identified from this species, in addition to all of
the reported biological activites of this species have been included as well as the pharmacology and toxicology.

Keywords- Artemisia herba-alba; sesquiterpenes; flavonoids; essential oil; biological activities.

1. Introduction

The genus Artemisia L. (family Asteraceae, tribe Anthemideae), comprises a variable number of species
(from 200 to over 400, depending on the authors) found throughout the northern half of the world. The genus
may be divided into sections Artemisia and Dracunculus [1]. The genus Artemisia is known to contain many
bioactive compounds; artemisinin exerts not only antimalarial activity but also profound cytotoxicity against
tumor cells [2] and arglabin is employed for treating certain types of cancer in the former USSR [3]. Over
the past decade Artemisia species have been used traditionally in varies populations, thus; A. keiskeana Miq
has been used as a Traditional Chinese drug for the treatment of gymnecopathy, amenerrea, bruise and
rheumatic disease [4], A. vestita Wall ex DC. has been utilized for the treatment of fungal infections such as
tinea, tympanitis, and thrush [5], A. abrotanum L. was found to possess spasmylytic activity on the

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carbacholine induced contraction of guinea-pig trachea [6]. Artemisia species are popular plants which are used for the treatment of diseases such as hepatitis, cancer, inflammation and infections by fungi, bacteria, and viruses [7]. Furthermore, several species of Artemisia are used in folk medicine, thus; A. vulgaris has been employed in the treatment of painful menstruation and in the induction of labor or miscarriage [8], A. mongolica Fisch has been used as a folk medicine for generations to cure inflammations and colds in northwest China [9], A. pontica L. is well known in Bulgarian folk medicine as a sedative and an appetizer [10].

Artemisia herba-alba Asso, known also as desert wormwood (known in Arabic as shih, Armoise blanche (Fr.)) [11], has been used in folk medicine by many cultures since ancient times, used in Moroccan folk medicine to treat arterial hypertension and/or diabetes [12-14]. Herbal tea from this species has been used as analgesic, antibacterial, antispasmodic, and hemostatic agents [15]. During an ethnopharmacological survey carried out among the Bedouins of the Negev desert, it was found that Artemisia herba-alba relieved stomach disorders [16]. This plant is also suggested to be important as a fodder for sheep and for livestock in the plateau regions of Algeria where it grows abundantly [17-19]. Ascaridae from hogs and ground worms were killed by the oil of the Libyan A. herba-alba in a short time [20, 21].

2. Botanical aspects

2.1 Morphology

A. herba-alba is a greenish-silver perennial herb grows 20-40 cm in height; it is a chamaeophyte (i.e. the buds giving rise to new growth each year are borne close to the ground). The stems are rigid and erect. The grey leaves of sterile shoots are petiolate, ovate to orbicular in outline whereas leaves of flowering stems are much smaller. The flowering heads are sessile, oblong and tapering at base. The plants flower from September to December. Plants are oblong and tapering at base. Plants are found on the steppes of the Middle East and North Africa where they are common and sometimes stand-forming (Figure 1) [22].

Figure 1. Photograph of Artemisia herba-alba.

2.2 Taxonomy

2.3 Distribution

The genus *A. herba-alba* is a medicinal and aromatic dwarf shrub that grows wild in arid areas of the Mediterranean basin, extending into northwestern Himalayas. This plant is abundant in the Iberian Peninsula and reaches highest population in the centre of Spain spreading over the eastern, southeastern and southern Spain. This taxon grows wild on nitrofilous and gypsum-rich substrata (Figure 2) [26, 27].

![Figure 2. Distribution map of Artemisia herba-alba](image)

3. Phytochemistry

Various secondary metabolites have been isolated from *A. herba-alba*, perhaps the most important being the sesquiterpene lactones that occur with great structural diversity within the genus *Artemisia*. Additional studies have focused on flavonoids and essential oils [28].

3.1 Sesquiterpene lactones

Sesquiterpene lactones are among the prominent natural products found in *Artemisia* species and are largely responsible for the importance of these plants in medicine and pharmacy. Several structural types of sesquiterpene lactones were found in the aerial parts of *A. herba-alba*. Eudesmanolides followed by germacranoles seem to be the most abundant types of lactones found in this species.

In course of investigation of *A. herba-alba* plants growing in Israel (Negev and Judean desert) five different chemotypes were identified on the basis of differences in their sesquiterpene lactone constitution (1-10) (Figure 3) [29-34]. In Spain, some phytochemical studies have investigated the sesquiterpene lactones from the *A. herba-alba*, (11-47) collected in different geographical location. (Figure 3) [35-41].

Many groups have studied the chemistry of *A. herba-alba* growing in Egypt. Most studies have been concerned with the sesquiterpene lactones. All the lactones isolated (48-57) differ from those found previously from *A. herba-alba* growing in Israel (Fig. 3) [42, 43]. Few literature papers studied the chemical constituent of Moroccan *A. herba-alba* species (58-64) [44, 45], and the Algerian one (65-66) [15], which proven that this genus is rich in sesquiterpenes (Figure 3).
Constituents and biological activities of *Artemisia herba-alba*

**R** = COMe, Herbolide A (1)  [29]
**R** = H, Deacetylherbolide A (2)  [29, 34]

Herbolide B (3)  [29, 34]
Herbolide C (4)  [29]
Herbolide D (5)  [30]

Herbolide E (6)  [31]
Herbolide F (7)  [31]
Herbolide G (8)  [32]
Herbolide H (9)  [32]

Herbolide I (10)  [32, 33]
Torrentin (11)  [35]
Dihydropseudosin (12)  [35]
11-Epiartesin (13)  [37]

Vachanic acid (14)  [37]
α,13-Dihydrocostunolide (15)  [37]
11β,13-Di-hydrodouglasin acetate (16)  [36]

Δ^4(15) (11αH), 11α,13-Dihydropseudosin (17)
Δ^4 (11αH), 11-Epiartesin (18)
α-Hydroxy-7α-eudesma-4(15),11(13)-dien-12-oic acid (19)  [38]

**Figure 3.** Sesquiterpene lactones from *A. herba-alba* growing in Egypt, Morocco, Spain, Algeria and Israel
1β,8α-Dihydroxyeudesm-4-en-6β,7α,11βH-12,6-olide (20) [36]

R = OH, Δ3,5αH, 11α,13-Dihydrosantamarin (21)
R = H, Δ4,5, 5αH,13-Dihydro-β-cycloestunolide (22) [37]

3-Epi-erivanin (23) [38]

1-Oxo-2α,3α,4α,5α-diepoxyeudesman-11βH-12,6α-olide (24) [39]

1β-Hydroxy colartin (25) [38]

R1 = H, R2 = Me, R3 = OH, 11-Epicolartin (26)
R1 = OH, R2 = Me, R3 = OH, 1β-Hydroxy-11-epicolartin (27)
R1 = OH, R2 = Me, R3 = Me, 1β-Hydroxy-4,11-diepicolartin (28) [37]

1β-OH, 1β-Hydroxy-3β-propionyloxy-6β,7α,11βH-eudesm-4-en-12,6-olide (29)
1α-OH, 1α-Hydroxy-3β-propionyloxy-6β,7α,11βH-eudesm-4-en-12,6-olide (30) [38]

R1 = β-OH, R2 = Ac (11αH), 11-Epitorrentin (31)
R1 = α-OH, R2 = Ac (11αH), 1,11-Diepitorrentin (32)
R1 = β-OH, R2 = H (11βH), Deacetyltorrentin (33)
R1 = βOH, R2 = H (11αH), 11-Epi-deacetyltorrentin (34) [41]

R = H, 1-Oxo-4α,5α-Epoxyeudesm-2-en-11βH-12,6α-olide (35)
R = OH, 1-Oxo-8α-Hydroxy-4α,5α-epoxyeudesm-2-en-11βH-12,6α-olide (36) [39]

Figure 3. Continued
Constituents and biological activities of *Artemisia herba-alba* 6

R = R' = H (11αH), 1-Oxoeudesma-2,4-dien-11αH-12,6α-olide  
R = R' = H (11βH), 1-Oxoeudesma-2,4-dien-11βH-12,6α-olide  
R = OH, R' = H (11αH), 1-Oxoeudesma-2,4-dien-11αH-12,6α-olide  
R = OH, R' = H (11βH), 1-Oxoeudesma-2,4-dien-11βH-12,6α-olide  
R = H, X = O (11αH), 1-Oxogermacra-4,10(14)-dien-6β,7α,11αH-12,6-olide  
R = OH, X = H, 11-Epishonachalin A  
R = OH, X = H, 1β-Hydroperoxy-8α-hydroxygermacra-4,10(14)-dien-6β,7α,11βH-12,6α-olide

Figure 3. Continued
R1 = H, R2 = OH, R3 = Ac, R4 = H, R5 = H, 5a-Hydroxy-11,13-dihydroreynosin acetate (53)
R1 = R2 = R3 = R4 = H, R5 = OH, 9b-Hydroxy-11,13-dihydroreynosin (54)

1β-Hydroxy-6βH,7αH,11αH-germacra-4(5)-10(15)-dien-6,12-olide (56) [42]

3β, 8α-Dihydroxy-6βH,7αH,11βH-germacran-4(14),9(10)-dien-6,12-olide (57) [42]

β-Hydroxy-6βH,7αH,11αH-germacra-4,10(14)-dien-6,12-olide (56) [42]

Herbalbin (58) [45]

(3R,4S,7R)-3,7-Dimethyl-4,7-epoxynon-8-enoic acid (59) [44]

1β,9β-Dihydroxyeudesm-3-en-5α,6β,11βH-12,6-olide (60) [44]

R = H, 1-Oxo-9β-Hydroxgermacra-4,10(14)-dien-6β,11βH-12,6-olide (61) [44]
R = Ac, 1-Oxo-9β-Acetoxygermacra-4,10(14)-dien-6β,11βH-12,6-olide (62) [44]

Figure 3. Continued
3.2 Flavonoids

The flavonoids detected in *A. herba-alba* show a large structural variation, ranging from common flavone and flavonol glycosides to more unusual highly methylated flavonoids. In studies of the leaves and stems of *A. herba-alba* collected from Sinai, a total of eight flavonoids O- and C-glycoside were isolated and identified [46, 47]. Examination of the aerial parts of *A. herba-alba* collected from Lebanese herbal stores led to the isolation of two flavonoids; hispidulin and cirsilineol [48] (Fig. 4). A new flavone, 5,4’-dihydroxy-6,7,3’-trimethoxyflavone, was isolated from the nonglycosidic extract of the aerial parts of *A. herba-alba* [49].

4. Phenolic compounds & waxes

Chlorogenic acid was observed in *A. herba-alba*, when a chemical survey of 49 Moroccan medicinal plant species was performed by ESR spectroscopy [50]. During a survey for antiulcerogenic principles of *A. herba-alba*, eight polyphenolics and related constituents were isolated. These included chlorogenic acid, 4,5-O-dicaffeoylquinic acid, isofraxidin 7-O-β-D-glucopyranoside, 4-O-β-D-glucopyranosylcaffeic acid, rutin, schaftoside, isoschaftoside, and vicenin-2 [51]. In a study of the components of *A. herba-alba* wax, obtained in 0.23% yield by extraction of the dry plant with ether, contained 32.1% saturated C16-32 acids (35.2% C28 and 26.5% C30), 23.2% saturated. C21-31 hydrocarbons (67.7% C29 and 24.2% C31), 27.1% esters (mainly of saturated C18, C19, and C20 acids and saturated C22 and C24 alcohols), and 16.96% saturated C16-26 alcohols. (C16 24.71%, C20 10.34%, C22 32.88%, and C24 22.96%) [52].
Figure 4. Flavonoids *Artemisia herba-alba.*
5. Essential oils

Over the last decades, the *Artemisia herba-alba* oil, called scheih oil [53], has been thoroughly investigated and the diversity in oil composition from plants grown in different countries and even those from different localities in the same country have led to the many oil-dependent chemotypes assigned to the plant [54]. Generally, the oil was largely reported to be composed of monoterpenoids, mainly oxygenated, such as 1,8-cineole, chrysantheneone, chrysanthenol (and its acetate), α/β-thujones, and camphor as the major components [55, 56].

High variability of volatile constituents was observed when different populations of *A. herba-alba* collected at various sites in Israel were compared [57]. Whereas samples of *A. herba-alba* collected at Elat contained chrysanthenyl acetate as major component (31%) followed by chrysanthenol (6.4%) and the acetophenone xanthocyclin, the essential oil of *A. herba-alba* from the Judean desert exhibited 1,8-cineole as the major compound (50%) followed by appreciable amounts of α- and β-thujone (27%) and other oxygenated monoterpenes such as terpinen-4-ol (3.3%), camphor (3%) and borneol (3%) [58, 59]. Essential oils of *A. herba-alba* collected at other localities in Israel contained some more unusual volatile terpenes including artemisia alcohol and lyratol [60]. Also, Two oil types were found for plants grown in Israel and Sinai, those of the cineol-thujane-bornane type and the pinane type; the oil of all studied populations contained 1,8-cineole in varying concentrations. More recently, it was reported that a further five chemotypes could be distinguished in plants growing in the Holy Land and Sinai due to the variation on the major components of the oil, suggesting the existence, in this region, of a greater number of chemovarieties than previously believed [61]. In addition, artemisia ketone was reported as the principle component of an Egyptian chemotype [62], while a French type [63] was found to predominate in 1,8-cineole, camphor and chrysantheneone.

In Jordan, regular monoterpenes were predominant (39.3%) and the principal components were α- and β-thujones (27.7%). The other major identified components were: sabinyl acetate (5.4%), germacrene D (4.6%), α-eudesmol (4.2%) and caryophyllene acetate (5.7%) [64].

In Morocco, the oil there was generally characterized by substantial levels of ketones such as α- and β-thujones and camphor [65, 66, 67], whereas davanone and/or chrysanthenyl acetate were the major oil components in other chemotypes [68]. In the market leader of *A. herba-alba* essential oil exports, 16 chemotypes were found [69], with 12 having monoterpenes as major components and for four sesquiterpene skeletons represent the major fraction of the oil, investigations reported no correlations between chemotypes and geographic distribution [70].

Studies from Spain showed that monoterpane hydrocarbons and oxygenated monoterpenes are the most abundant skeletons in *A. herba-alba* oil, but large amounts of sesquiterpenes were found for some populations. Camphor, 1,8-cineole, *p*-cymene and davanone were the major components found [71, 26]. Another study from Spain showed that the chemotaxonomic affinity between Spanish and Israeli populations of the same plant was not reflected in their oil compositions. The Spanish oil contained large amounts of sesquiterpenes but lacked significant quantities of thujane derivatives. However, a more recent investigation from Spain showed the sesquiterpene davanone to be the principal component of the oil, which was also dominated by the *p*-menthane and pinane skeletons [72, 73, 74,75].

In Tunisian oil oxygenated monoterpenes were found to be the major components of *A. herba-alba* oil extracted from aerial parts of plants originated from arid regions [76, 77]. In another study of the Tunisian *Artemisia herba-alba* oil, the main components were cineole, thujones, chrysantheneone, camphor, borneol, chrysanthenyl acetate, sabinyl acetate, davana ethers and davanone. Monoterpenes, sesquiterpenes are found in some samples as major components. The chemical compositions revealed that some samples have compositions similar to those of other *Artemisia herba-alba* essential oils analyzed in other countries [78].

In an Algerian oil, camphor, α/β-thujones, 1,8-cineole and chrysanthenyl derivatives were the major components [79, 80, 81]. In another studies, camphene (3%), borneol (3.6%), davana ether (8.8%), davanone (36.1%) were the major components [82-88]. The essential oil obtained from the aerial parts of *A. herba-alba* growing wild in M’sila-Algeria, contained camphor (19.4%), trans-pinocarveol (16.9%), chrysantheneone (15.8%) as major components. Monoterpenoids are the main components (86.1%) and the
irregular monoterpenes (3.1%) [89]. On the other hand, other components have previously been found in other A. herba-alba oils such as (Z)-jasmone, xanthoxylin were not detected in this oil [90, 91].

One study of A. herba-alba in Cyrenaica (Libya) had reported that the dried grass contained 0.29% of an essential oil containing 6.7% cineole [92].

6. Biological effect of A. herba-alba

6.1 Antioxidant activity

Many medicinal plants contain large amounts of antioxidant compounds, which could be isolated and then used as antioxidants for the prevention and treatment of free radical-related disorders. In a study by Djeridane [93], the purpose was the evaluation by a chemical method of the antioxidant capacity of phenolic compounds in some Algerian medicinal plants, including A. herba-alba. These medicinal plants showed stronger antioxidant activity and content in phenolics than the common nutritional plants. It has been also noted in this study that these Algerian plants are strong radical scavengers and can be considered as good sources of natural antioxidants for medicinal and commercial uses [93]. Raw and cooked ground beef patties were treated with an aqueous extract of A. herba-alba, rosemary, fennel and rue at levels of 5 mm of 10% (w/w vegetable matter to water) extract for every 100 g of meat. Patties were kept under refrigeration (4°) for a period of 16 days, and samples were drawn at 4-day intervals. Results showed that cooked meat was more susceptible to oxidative deterioration than raw meat. In addition, A. herba-alba had a somewhat less effective role than the other herbs [94]. In another study, 21 plant samples were collected from different Jordanian locations and used for antioxidant evaluation. The level of antioxidant activity, determined by DPPH and ABTS assays, showed that Artemisia herba-alba has a moderate antioxidant activity compared to the other plants [95].

Abid compare the long-term effects of Artemisia herba-alba decoction with a green or black tea decoction, prepared without sugar, on the antioxidant processes in rats. The conclusion of this study showed that Artemisia, as well as green tea decoctions, increased the total antioxidant status, whole blood glutathione peroxidase activity and zinc and copper status, and prevented weight gains and increased conjugated dienes, plasma glucose, lipids and iron status. The beneficial antioxidant effects were in descending order: Artemisia decoction ≥ green tea decoction > black tea decoction. So, Artemisia could constitute a good adjuvant to combat obesity, hyperglycemia, hyper-triglyceridemia, hyper-cholesterolemia and particularly oxidative stress [96].

The effects of seven medicinal plants including Artemisia herba-alba on protein degradation, lipid peroxidation, erythrocyte deformability and osmotic fragility of erythrocytes exposed in vitro to 10 mM H\textsubscript{2}O\textsubscript{2} for 60 min at 37°C have been examined. The result was that Artemisia herba-alba did not protect erythrocytes against lipid peroxidation [97].

6.2 Anti-venom activity

Aqueous extracts of 12 medicinal plants traditionally used in Jordan for the inhibition in humans of snake and scorpion venoms were evaluated for their possible anti-venom activity. Among the plants tested, 9 extracts were found to inhibit the hemolytic activities of both venoms. The most active plant extract was Artemisia herba-alba, which gave 100% inhibition [98].

6.3 Antifungal activity

The antifungal activity of Artemisia herba-alba was found to be associated with two major volatile compounds isolated from the fresh leaves of the plant. Carvone and piperitone were isolated and identified by GC/MS, GC/IR, and NMR spectroscopy. Antifungal activity was measured against Penicillium citrinum (ATCC 10499) and Mucora rouxii (ATCC 24905). The antifungal activity (IC\textsubscript{50}) of the purified compounds carvone and piperitone was estimated to be 5 µg/ml and 2 µg/ml against Penicillium citrinum, and 7 µg/ml and 1.5 µg/ml against Mucora rouxii, respectively [99]. In another study, the antifungal activity of the
essential oils of 25 Moroccan medicinal plants, including *A. herba-alba*, against *Penicillium digitatum*, *Phytophthora citrophthora*, *Geotrichum citri-aurentii*, and *Potrytis cinerea*. *A. herba-alba* essential oil showed only weak antifungal activity at 250 µg/ml concentration [100]. In addition, the effect of *A. herba-alba*, *Eucalyptus*, and *Rosmarinus* essential oils was evaluated on the mycelial growth and toxigenesis of *Penicillium aurantiogriseum* and *P. vindication*. A significant decrease in mycelial dry weight was obtained with the addition of 0.05-2.5% of each of the three essential oils in yeast extract sucrose broth. The inhibition of mycelium growth was tested on malt extract agar, Czapec yeast agar, yeast extract sucrose agar and broth at constant pH, and was highly effective for *A. herba-alba*, followed by *Eucalyptus*. A complete inhibition of toxin production was observed with 0.44% of each essential oil for *P. aurantiogriseum* and 0.22% for *P. viridicatum* [101]. The effect of *A. herba-alba* and *Oreganum* oils on spore germination, mycelial elongation and sporulation were studied in three fungi. All three stages of fungal asexual reproduction were affected but mycelium growth was the most sensitive, followed by spore germination and then sporulation of the three fungi studied. *Zygorrhynchus* sp. was found to be the most sensitive followed by *Aspergillus niger* and then *Penicillium italicum*. *A. herba-alba* was less active on the three phenomena studied than the *Oreganum* oil. [102]. In addition, *A. herba-alba* essential oil demonstrated a synergistic action on the inhibition of mycelium growth in *Zygorrhynchus* sp. and *Aspergillus niger* isolates, when associated with sodium chloride or fatty acid [103]. The essential oils extracted from 10 Algerian plants; including *A. herba-alba*, were analyzed for their potential activity against *Candida albicans*. A moderate efficiency was obtained with the essential oil from *A. herba alba* which showed an antifungal effect 5617-fold lower than that measured with amphotericin B. [104].

The inhibitory effects of *Artemisia* flower heads (*Artemisia herba-alba*), on the growth and aflatoxin production of a toxigenic strain of *Aspergillus flavus* was tested using different concentrations. The plant inhibited aflatoxin formation by 85-90% of that of control at a concentration of 10% [105].

The *in-vitro* antifungal activity of *A. herba-alba* essential oil has been evaluated on various microorganisms. The oil showed a very strong action vs. *Candida* and *Microsporum*. [106]

### 6.4 The nematicidal activity

The *in-vitro* nematicidal activity of methanolic extracts (20 µg/ml) from twenty Jordanian plant species against two species of root-knot nematodes was evaluated. The leaf extract of *Artemisia herba-alba* was the most effective causing 22, 51, and 54% mortality after 24, 48 and 72 h of exposure, respectively [107].

### 6.5 Antibacterial activity

The antibacterial activity of *Artemisia herba-alba* collected near Sde-Boker (Negev desert), Israel, has been investigated. Only the essential oil was found to be active against some Gram-positive bacteria (*Streptococcus hemolyticus* and *Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli*, *Shigella sonnei* and *Salmonella typhosa*). The essential oil was fractionated by column chromatography, and these fractions were tested for antibacterial activity. The principal component of the most active fraction was santolina alcohol [108]. Furthermore, the essential oils from four *Artemisia herba-alba* populations collected in Israel (Sde-Boker, Mizpe Ramon, Judean desert and Elat) were investigated for their antibacterial activity. All the oils had slight antibacterial activities in the concentration range of 1-2 mg/ml. The oils were active against gram negative bacteria (*Escherichia coli*, *Shigella sonnei*, *Salmonella typhosa*, *Serratia marcescens* and *Pseudomonas aerugenosa*) and against gram positive bacteria (*Bacillus subtilis*, *Streptococcus hemolyticus* and *Staphylococcus aureus*). The oil derived from the Sde Boker variety exhibited the highest antibacterial activity, especially against the *Streptococcus*, *Pseudomonas* and *Serratia* strains tested. This oil, as well as those from Mizpe Ramon and the Judean Desert, showed relative high activity against *S. sonnei* and *S. typhosa* whereas they were almost inactive against *E. coli*. The oil derived from plants collected near Elat possessed very low activities. The antibacterial effect may explain the extensive use of *A. herba-alba* in folk medicine [57,109]. Also, the *in-vitro* antibacterial activity of *A. herba-alba* essential oil has been evaluated on virous microorganisms, The oil showed a very strong action vs. *Staphylococcus*, The inhibiting
action of the oils was low vs. the enterobacteria [106]. The aqueous extract of A. herba-alba possessed relatively weak antibacterial activity and virtually little or no inhibitory activity against the yeast
Saccharomyces cerevisiae [110]. The antibacterial activity of A. herba-alba performed against Bacillus subtilis and Escherichia coli showed no significant activity against either species [111].

Mycoplasmas are one of the smallest free-living microorganisms. Unlike other bacteria they lack a rigid cell wall. Hence, they are not susceptible to penicillins and other antimicrobials that act on this structure. Artemisia herba-alba, was one among six Jordanian traditional medicinal plant methanolic extracts that were tested against 32 isolates of Mycoplasma species. The result of this study showed that the most effective plant extract in vitro against all Mycoplasma species was A. herba-alba with MIC values of 3.125-6.25 mg/ml. Therefore, this plant could be considered as a readily available alternative for drugs such as the fluoroquinolones, tetracyclines, macrolides and chloramphenicolsthat are currently used in the treatment of Mycoplasma infections [112].

6.6 Antispasmodic activity

The essential oils from four Artemisia herba-alba populations collected in Israel (Sde-Boker, Mizpe Ramon, Judean desert and Elat) were investigated for their antispasmodic activity. The A. herba alba oils were tested on isolated rabbit jejunum. The results indicate that the different oils showed similar relaxation patterns. The concentrations, which induced 50% relaxation were similar for the Sde Boker, Mizpe Ramon and Judean Desert oils (ca 3x10^{-5}%), while that of the Elat oil was ten times lower [57].

6.7 Anthelmintic activity

The anthelmintic activity of the powdered shoots of Artemisia herba-alba was investigated in experimental haemonchosis in six Nubian goats which had been infected with single doses of 800 to 1,000 infective Haemonchus larvae. The clinical signs of caprine haemonchosis included inappetence, dullness and soft faeces and were correlated with the pathological findings. None of these changes were observed in four of the six goats following the treatment with 2, 10 or 30 g of Artemisia shoots. This successful therapy was supported by the absence of eggs in the faeces or adult worms in the abomasum at necropsy and of significant lesions in the tissues of the goats and return of the concentrations of serum ammonia, sodium, potassium, total protein and creatinine and of the activity of aspartate aminotransferase (GOT) to normal. In two goats, treated with either 10 or 30 g of Artemisia shoots, egg production was not completely suppressed and a few adult Haemonchus worms were found in the abomasum [113, 109].

Al-Waili suggested that the aqueous extract of A. herba-alba might have a possible therapeutic value in intestinal infection with Enterobius vermicularis. Therefore the possible effect of A. herba-alba extract on E. vermicularis infection was examined in 10 patients. The results appeared to show that A. herba-alba extract eradicated intestinal infection with E. vermicularis within 3 days in all 10 patients treated [114].

6.8 In vitro Antileishmanial activity

The aqueous extract and essential oil of Artemisia herba-alba were tested for their antileishmanial activity against Leishmania major. The strongest leishmanicidal activity was observed with the essential oil at 2 µg/ml compare to the other two strains tested. The aqueous extract showed an antileishmanial activity at concentration of 4 µg/ml [115].

6.9 Neurological activities

In the recent decades the use of traditional medicine in Lebanon has increased. Aqueous, ethanol and ethyl acetate extracts of seven Lebanese plants that are used traditionally for neurological disorders as Alzheimer’s disease, epilepsy and affective disorders as depression were tested for inhibition of
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acetylcholinesterase and affinity to the GABA (A)-benzodiazepine site and to the serotonin transporter. Ethyl acetate extracts of *Artemisia herba-alba* exhibited weak activity in the acetylcholinesterase assay. An ethanolic extract of *Artemisia herba-alba* had good affinity to the GABA (A)-benzodiazepine receptor site [116].

Dinatin and skrofulein, two flavones were extracted from *Artemisia herba-alba*, inhibited the binding of [methyl-3H]diazepam to rat brain membranes in vitro with IC$_{50}$ of 1.3 and 23 µM, respectively. The GABA-ratios (the ratio of IC$_{50}$ values in the absence/presence of GABA in the binding assay) were 1.1 and 1.2 for dinatin and skrofulein, respectively. Both flavones induced a slight increase in [35S] TBPS binding. The data suggest that the flavones are antagonists or partial agonists of benzodiazepine receptors [117, 118].

6.10 Hypoglycemic activity

*Artemisia herba-alba* is a popular folk remedy, used in treatment of diabetes mellitus. For these reason many published papers studied its hypoglycemic activity [119, 120]; thus Twaij found that the aqueous extract of the aerial parts of *A. herba-alba* caused a significant fall in plasma glucose levels in both normoglycemic and the alloxanized rabbits [121]. Al-Waili reported that the water soluble extract of this species played a role in reducing elevated blood pressure and blood glucose levels, and it also had antiarrythmic and anxiolytic actions [122, 123]. The same results are given in later study by Ibrahim [124]. Al-Yahya [125] reported that the ethanolic and chloroform extract of the whole plant had no effect on blood glucose levels. Al-Khazraji [126] studied the *Artemisia herba-alba* aerial parts and demonstrated that the aqueous extract of the roots does not contain hypoglycaemic agents, but the aqueous extract of the leaves was relatively more effective than the aqueous extract of the bark. He also found that the methanolic extract of the plant did not significantly change blood glucose levels of fasted rats. Al-Shamaony [127] gave a clear view that *A. herba-alba* extract prevented a significant elevation in the glycosylated haemoglobin in both diabetic rats and rabbits, fed daily for 2-4 weeks with *A. herba-alba* extract. Marrif [110] reported that the aqueous extract of *A. herba-alba* produced an initial hyperglycaemia which was followed by hypoglycaemia in normoglycaemic and alloxan-treated rabbits and mice. The extract also had no effect on the activity of alkaline phosphatase or concentrations of creatinine and urea in plasma. Also, Essway [128] concluded that the volatile oil of *A. herba-alba* (sage) have an antidiabetic effect after injection to rats. The study of the aqueous extract of *A. herba-alba* by Tastekin [129] came in agreement with Twaij [116] and Marrif [110] studies. Also, Bennani-Kabchi [130] reported that *Artemisia herba-alba* is a hypoglycemic, antihyperglycemic plant in diabetic sand rat, with hypolipemic action in case of severe obesity. *A. herba-alba* is one of the traditional plants used in Turkey, and the aqueous extract of *A. herba-alba* had been studied lately by Iriadam [131], who studied the effect of *A. herba-alba* and *Teucrium polium* effect on blood glucose levels. The results concluded that administration *A. herba-alba* might be useful in preventing hyperglycaemia by having insulin-like action and can significantly reduce the blood glucose in normoglycemic and hyperglycaemic rabbits but do not shows any action on creatinine and cholesterol in both normal and STZ-induced diabetic rabbits in acute diabetic experiment.

The aqueous extracts of *Artemisia herba-alba* has been tested on male albino rats. The results demonstrated that administration of *A. herba-alba* in a dose of 100 mg/kg of body weight for 60 days induced a very significant decrease in glucose level with a significant (p <0.01) increase in total serum cholesterol level, triglycerides, phospholipids, serum aspartate aminotransferase (AST) and serum alanine aminotranserase (ALT) were found [132].

6.11 Cytotoxicity and gene induction

Essential oil (EO) extracted from *Artemisia herba-alba* was tested for its genotoxic effects using the yeast *Saccharomyces cerevisiae*. Clear cytotoxic effects were observed in the diploid yeast strain D7, with the cells being more sensitive to EO in exponential than in stationary growth phase. Clearly induced cytoplasmic peptide mutations took place indicating damage to mitochondrial DNA. However, no nuclear genetic events such as point mutations or mitotic intragenic or intergenic recombination were induced. The
capacity of EO to induce nuclear DNA damage-responsive genes was tested using suitable Lac-Z fusion strains for RNR3 and RAD51, which are genes involved in DNA metabolism and DNA repair, respectively. At equitoxic doses, the EO demonstrated significant gene induction, approximately the same as that caused by hydrogen peroxide, but much lower than that caused by methyl methanesulfonate (MMS). Essential oils affect mitochondrial structure and function and can stimulate the transcriptional expression of DNA damage-responsive genes. The induction of mitochondrial damage by EO appears to be closely linked to overall cellular cytotoxicity and appears to mask the occurrence of nuclear genetic events. EO-induced cytotoxicity involves oxidative stress, as is evident from the protection observed in the presence of ROS inhibitors such as glutathione, catalase or the iron-chelating agent deferoxamine [133]. In contentions study, investigated for their possible antigenotoxic effects in an eukaryotic cell system, the yeast Saccharomyces cerevisiae. The EO alone showed some cytotoxicity and cytoplasmic petite mutations, i.e. mitochondrial damage, but they were unable to induce nuclear genetic events. In combination with exposures to nuclear mutagens such as 254-nm UVC radiation, 8-methoxypsoralen (8-MOP) plus UVA radiation and methylmethane sulfonate (MMS), treatments with these EO produced a striking increase in the amount of cytoplasmic petite mutations but caused a significant reduction in revertants and mitotic gene convertants induced among survivors of the diploid tester strain D7. In a corresponding rho0 strain, the level of nuclear genetic events induced by the nuclear mutagens UVC and 8-MOP plus UVA resulted in the same reduced level as the combined treatments with the EO. This clearly suggests a close relationship between the enhancement of cytoplasmic petites (mitochondrial damage) in the presence of the EO and the reduction of nuclear genetic events induced by UVC or 8-MOP plus UVA. After MMS plus EO treatment, induction of these latter events was comparable at least per surviving fraction in wild type and rho0 cells, and apparently less dependent on cytoplasmic petite induction. Combined treatments with MMS and EO clearly triggered switching towards late apoptosis/necrosis indicating an involvement of this phenomenon in EO-induced cell killing and concomitant decreases in nuclear genetic events. After UVC and 8-MOP plus UVA plus EO treatments, little apoptosis and necrosis were observed. The antigenotoxic effects of the EO appeared to be predominantly linked to the induction of mitochondrial dysfunction. [134].

6.12 Reproductive toxic effects

Artemisia herba-alba toxic effect was investigated on the reproductive system after administration to female Sprague-Dawley rats weighting 250-300 g for two time periods 4 and 12 weeks. The effect of A. herba-alba exposure on fertility was assessed in terms of the number of pregnant rats, implantation sites, viable fetuses and resorption sites. Exposure to A. herba-alba for 4 weeks did not have much effect on fertility. Significant decrease in the relative ovarian weights and embryo weights in rats exposed to A. herba-alba were observed. Exposure to A. herba-alba for a 12 weeks resulted in a reduction in the percentage of pregnancies and in the number of implantation sites when compared with controls in both treatment periods. Rats receiving 12 weeks treatment showed an increase in ovarian weights and a decrease in the number of viable fetuses. These results indicate that long-term exposure of female rats to A. herba-alba causes adverse effects on the reproductive system and fertility. The results of the current study suggest that ingestion of Artemisia herba-alba by adult female rats causes adverse effects on fertility and reproduction [135].

Treated rats testicular cell population showed a decrease in number of spermatocytes and spermatids (p <0.01) when compared to controls. Serum hormonal assay indicated a decrease in testosterone and follicular stimulating hormone (FSH) levels in treated rats. A decrease in the number female rats impregnated by males receiving treatment was observed and demonstrated by a decrease in the implantation sites and number of viable fetuses (p < 0.01) [132].

6.13 Pesticidal activity

The potential of crude extracts from Artemisia herba-alba were evaluated for their ability to control Tetranychus cinnabarinus mites under controlled conditions. The assay revealed that the extract from A. herba-alba was not toxic to animal cells up to concentration of 100 µg/mL. The mortality and repellency
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Artemisia herba-alba essential oil was tested against three sucking insect pests under laboratory and greenhouse conditions. These pests included *Bemisia tabaci* (Gennadius), *Aphis gossypii* (Glover) and *Thrips tabaci* (Lindman). The results showed that the LC50 of *A. herba-alba* was 0.042% for eggs and 0.074% for immature stages of *B. tabaci*. Also, the oil showed a high toxicity on *A. gossypii* with LC50 0.023 and 0.085%. *Artemisia herba-alba* was more toxic on *T. tabaci* and *A. gossypii* than *B. tabaci* in the laboratory test while *T. tabaci* was sensitive (LC50 0.011 and 0.038%). The oil was efficient for controlling tested insects on cucumber plants at greenhouses. This treatment caused 85.41, 83.57% reduction in the population of *B. tabaci*, 90.44, 88.00% for *A. gossypii* and 87.45, 84.45% for *T. tabaci* [137, 138].

A study was designed to evaluate the effect of essential oils extracted from *Rosmarinus officinalis* and *Artemisia herba-alba* on *Acanthoscelides obtectus* (Coleoptera: Bruchidae) under laboratory conditions. The doses used were 1 to 5 µL/30 g seed for the essential oil of each plant. The results show that the two tested essential oils were very toxic to adults of *A. obtectus*, and they also cause a significant reduction in fertility by bruchids. The LD50, calculated after 48 hours of exposure, showed that the essential oil extracted from *Rosmarinus officinalis* was the more toxic to adults with an LD50 = 0.59µL/30g seed, while the LD50 = 1.69µL/30g seeds for *Artemisia herba-alba* [139]. Larvicidal activity of *A. herba alba* against *Culex pipiens* mosquito and cotton leafworm *Spodoptera littoralis* (Biosd.) larvae, insecticidal activity against houseflies *Musca domestica* L. and rodenticidal activity against white mice *Mus musculus*, [111].

6.14 As Antibiotic resistant inhibitor

There are indications that some herbal materials can act as inhibitors of antibiotic resistance. A study was carried out to screen the effect of the herbal material in combination with antibiotics to identify systems that might be used advantageously to improve the efficiency of the antibiotics used. Preliminary results showed that saturated solutions of the plant extracts gave different levels of inhibition depending on the strain of microorganism. *Artemisia herba-alba*, for example, showed some inhibitory effects on the resistant strain and on standard strain of *S. aureus* [140].

6.15 Allelopathic effect

Plant-plant interference in semiarid Mediterranean environments may involve competition for resources, facilitation, or allelopathic phenomena in which toxic organic compounds produced by one plant are released into the environment. The potential allelopathic role of *Artemisia herba-alba* has been evaluated in order to explain the community pattern of the gypsum semiarid environments of central Spain. This pattern shows a sharp ecotone between a gypsumophile shrubby community dominated by *Helianthemum squamatum*, which grows on slopes with gypsum surface crusts, and a nitrohalophilous community on the gypsum alluvial soils of piedmont dominated by *Artemisia herba-alba*. In order to explain the pattern, resource limitation was discarded because there were no significant differences in several soil parameters. Results confirm the inhibitory effect of aqueous extracts on the final germination percentage of scarified seeds of *Helianthemum squamatum* and also on the shape of the germination curves, which indicate delay of germination was strongly inhibited in soils obtained below the canopy of mature plants and retarded in other treatments [141].

6.16 Inhibition of the binding of 3H-benzo[a]pyrene

The aqueous and ethanolic plant extracts obtained from 10 Iraqi cultivated plant species were studied for their ability to inhibit aryl hydrocarbon hydroxylase (AHH) activity and [3H]benzo[a]pyrene ([3H]BP) binding to rat liver microsomal protein. None of the aqueous extracts tested showed any inhibitory effect. The ethanolic extracts from 8 species exhibited strong inhibitory effect on both AHH and [3H]BP binding to the microsomal protein. Ethanolic extracts from *Adiantum capillus-veneris* and *Salsola rosmarinus*
showed no effect. Nevertheless, ethanolic extracts from Anchusa strigosa, Myrtus communis, and Artemisia herba-alba were more effective than other plant extracts [142].

6.17 Cytoprotective properties of A. herba-alba

In a study by Gharzouli [143], investigated cytoprotective properties of Q. ilex, P. granatum and A. herba-alba aqueous extracts against ethanol-induced damage of the stomach. The gastroprotective effect of tannic acid and the aqueous extract of Quercus ilex L. root bark, Punica granatum L. fruit peel and Artemisia herba-alba Asso leaves were investigated in the rat against ethanol-induced damage. Tannic acid, Q. ilex and P. granatum extracts gave 100% precipitation of ovine haemoglobin in vitro, whereas A. herba-alba extract was devoid of any protein-binding property. Oral administration of these plant extracts or tannic acid induced a significant decrease in gastric lesions (47.7%– 76%). The observed protection was more pronounced when the test solution was given at the same time with ethanol, except for Q. ilex extract. The acid content of the stomach was significantly increased by P. granatum (368%) and A. herba-alba (251%) extracts prepared in ethanol. It is suggested that monomeric and polymeric polyphenols can strengthen the gastric mucosal barrier.


Guenaoui aimed to study and investigate the response of A. herba-alba to water deficit stress. Plants were submitted for 36 days to 70 and 40 % CC and the reversibility of water deficit effect was assessed by analyzing the behaviour of water-stressed plants, once transferred to 100% CC treatment for 40 days. Several parameters known as indicators of plant status were monitored after drought treatment and subsequent re-watering. It was specially, about biomass production, plant water content, chlorophyll, sugars and praline contents and osmotic potential. Water drought led to a significant decrease of biomass accumulation, water content and chlorophyll content under both 70% and 40% CC, however, the intensity of water stress showed a positive correlation with sugars and praline accumulation. Well watered plants showed the higher biomass production but the lowest organic components unlike treated plants which showed the contrary evolution of these parameters. Drought stress, again, had a significant impact on the osmotic potential of plants, thereby it showed a significant decrease (P< 0.05) when irrigation was reduced to 70% CC or 40% CC. the stop of stress and the re-watering allowed the progressive return to the initial values and helped in the recovery of plants. Altogether, these data indicated that A. herba-alba has high aptitude permitting adaptation to unkind environmental conditions of the natural habitat [144].

8. Thermodynamic properties and moisture sorption isotherms of A. herba-alba

Sorption isotherms of A. herba-alba were determined at three temperatures (30, 40 and 50 °C) and in the range of water activity varying from 0.0572 to 0.898. The hysteresis effect was distinctly observed in the range of temperature tested. Five sorption models were used to fit the experimental data. The GAB equation was the best model describing the equilibrium moisture data for desorption. The modified Halsey equation was the most suitable model for describing adsorption isotherms. Thermodynamic properties such as differential enthalpy and entropy were determined from moisture sorption data, using the Clausius-Clapeyron equation. The experimental data showed that enthalpy-entropy compensation theory was applicable for the moisture sorption behaviour of Artemisia herba-alba [145].

9. Genetic polymorphism study of A. herba-alba

The morphological and chemical polymorphism observed for A. herba-alba may be due to a genetic variability [146]. To investigate this variability, Mohsen and Ali [1] studied the genetic polymorphism of
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this plant on DNA level using inter simple sequence repeats (ISSR). The result of this study show that a total of 60 polymorphic loci were scored using our primers revealed no direct relation between morphological traits, geographic distance and genetic distance. Correlogram analysis showed a patchy distribution of the genetic variability of *A. herba-alba* accessions revealing the contribution of local ecological and geographic conditions on variability.

10. Microbial and heavy metals contamination

Alwakeel was conducted to evaluate the microbial contaminants and presence of toxic heavy metals on some herbal medicines. Twenty-seven samples (3 kg each) of well-known herbs and 5 kinds of henna available in herb markets around Riyadh, Saudi Arabia were collected for microbial and toxic metal contamination. *Artemisia herba-alba* was among the tested plants, which show the highest in calcium [147].

11. Inhibition corrosion of steel

Benabdellah tested *Artemisia* oil which is extracted from *Artemisia herba-alba* collected in Ain es-sefra-Algeria, as corrosion inhibitor of steel in 2 M H$_3$PO$_4$ using weight loss measurements, electrochem. polarization and EIS methods. The naturally oil reduces the corrosion rate. The inhibition efficiency was found to increase with oil content to attain 79% at 6 g/l. Ar acts as a cathodic inhibitor. The effect of temperature on the corrosion behavior of steel indicates that inhibition efficiency of the natural substance decreases with the rise of temp. The adsorption isotherm of natural product on the steel was determined [148]. Also, the Essential oil from *Artemisia herba-alba* tested as corrosion inhibitor of steel in 0.5 M H$_2$SO$_4$ using weight loss measurements and electrochem. polarization methods. Results gathered show that this natural oil reduced the corrosion rate by the cathodic action. Its inhibition efficiency attains the max. (74%) at 1 g/L. The inhibition efficiency of Arm oil increases with the rise of temp. The adsorption isotherm of natural product on the steel has been detd. *A. herba-alba* essential oil was obtained by hydrodistillation and its chemical oil compounds were investigated by capillary GC and GC/MS. The major components were chrysanthene (30.6%) and camphor (24.4%) [149].

12. Biological effects to *Artemisia herba-alba*

12.1 G6PDH AND 6PGDH activities

Phenolic compounds were found to be phytotoxic constituents of many plant species extracts. Phenolic compounds caused seeds dormancy, inhibit seed germination and suppress photosynthesis in *Artemisia herba-alba*. Phenolic compounds are primarily synthesized through the pentose phosphate, and shikimate pathway. Glucose-6-phosphate dehydrogenase (G6PDH) and 6-phosphogluconate dehydrogenase (6PGDH) are the key enzymes of pentose phosphate pathway, used in the biosynthesis of phenolic compound. Al-Quadan and Al-Charchafchi studied the role played by the Phenolic compound esculetin in regulating pentose phosphate pathway activity in *Artemisia herba-alba* during seed germination. This is accomplished by studding G6PDH and 6PGDH activities in the presence and absence of esculetin. The result of these study showed that germination of *Artemisia herba-alba* seeds in the presence of esculetin showed lower G6PDH or 6PGDH activities compared to that germinated in esculetin absence; however, the same enzymes showed higher activities upon germination in the dark compared to that under light. Both enzymes were continuously increased from day one to day five during germination [150]. Al-Quadan, Ibrahim and Al-Charchafchi measured also the effect of Chlorogenic and caffeic acids on G6PDH and 6PGDH activities of *A. herba-alba* seeds during early stages of seed germination under conditions of light and dark. G6PDH and 6PGDH activities were inactivated in the presence of both phenolic acids and were stimulated upon germination in the dark. This study provide evidence or the variable needs of pentose phosphate pathway
activity, depending on concentrations of phenolic acids present and/or light conditions; moreover, a clear response of such germination condition was earlier expression of a second isoenzyme for G6PDH in the presence of 0.4 mM Chlorogenic or caffeic acids with apparently variable inhibitory pattern [151, 152].

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