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Review Article

Pharmacological Promises of Genus *Artemisia* (*Asteraceae*): a Review

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Abstract: A huge amount of scientific literature is available about plant extracts and their compounds having great pharmacological importance. Although, plant-based medicines have been used since antiquity, but knowledge about their effectiveness on human health is still unclear. *Artemisia* genus belongs to the plant family *Asteraceae*. This genus comprises of about 500 species, which are well known for their medicinal properties. The aim of this review was to provide an insight about recent published scientific literature concerning pharmacological aspects of genus *Artemisia*. The compilation of literature has been done by using references from important databases such as Science Direct, Medicinal and Aromatic Plants Abstracts, PubMed, Chemical Abstracts, Kings American Dispensatory, SciFinder, Research gate, Google Scholar and Phytochemical and Ethnobotanical Databases. In this review, special emphases have been given to the reported chemical compounds and biological activities from different *Artemisia* species. This review emphasis on the plant species from genus *Artemisia* possessing significant phytochemicals holding a broad range of biological actions like antimicrobial, antimalarial, anti-cancerous, antioxidant and anthelmintic activity. Certain crucial drugs have been unveiled from different species of *Artemisia*. One important constituent focused by researchers is artemisinin, which retains potential anti-malarial assets and is attained from *Artemisia annua*. Other groups of phytochemicals like flavonoids, steroids, glycosides, terpenoids, caffeoylquinic acids, acetylenes, coumarins and sterols are also found in this crucial genus. This genus also holds great possibilities for comprehensive scrutiny for other biological activities. The effects of constituents from various species of this genus on other deadly diseases may give better consequences.

Keywords: *Asteraceae,* genus *Artemisia,* phytochemicals, biological activities, bioactive compounds

1. INTRODUCTION

Asteraceae is one of the largest families of angiosperms, which contain 1,600 to 1,700 genera and nearly 24,000 species which are distributed in mostly all parts of the world, but not found in Antarctica [1, 2]. *Artemisia* belongs to the family *Asteraceae* which is pharmacologically one of the crucial polymorphic genera. Plants of this genus are mostly found in the temperate sectors of northern hemisphere, but limited numbers of species are also found in the southern hemisphere of the world [2-3]. Around five hundred species of herbs and shrubs fall in this genus [4, 5]. This is basically a cosmopolitan [6] and is considered as the diverse and largest genus of the *Asteraceae* family [2, 4, 7]. Different other conducts although have accredited to the genus from 350 to 550 species [3, 5, 8, 9, 10, 11]. Studies by Oberprieler et al. [2] further stretched out the contemporary modifications of subtribe Anthemideae corroborating 522 species to the genus. Since

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ancient times plants sources are utilized for food and medicinal purposes and it has been estimated that around 70-95% population of the globe trusts on these plant based remedies for primary care [12].

It has been found that plants have the ability to generate a lot of secondary metabolites which occurs naturally, and may be important in pharmacologically. These essential metabolites may include essential oils, saponins, flavonoids, cyanogenic glycosides, phenols, tannins, phenolic glycosides, unsaturated lactones, and glucosinolates [13, 14, 15] and are predominantly utilized in contradiction of multiple diseases like cancer, malaria, hepatitis, inflammation, and fungal, bacterial, and viral infections. *Artemisia* is expanding medicinal genus among the variety of world cultures [16, 17, 18]. Ethnobotany, economic botany, medicinal importance and phytotherapy of this genus have been reviewed [19] and an extensive work on *Artemisia* unfolded different traditional and medicinal uses of its species [17].

In a lot of investigations, plants and their products have been screened for health purposes, because voluminous number of people has been indulged openly or ramblingly in the traditional usage of different products from plant origin. Among the numerous herbs used in modern medicine, many species of genus *Artemisia* are also included. So in this review, the primary objective is to deliver a brief understanding on different species of the genus *Artemisia* with extraordinary attention on their phytochemistry and pharmacological potentials.

2. PHYTOCHEMICALS AND ANTIOXIDANT ACTIVITY OF *Artemisia* SPECIES

A plant encompasses a lot of extracts and phytochemicals and their utilization could be a milestone in developing therapeutic strategies for the treatment of many diseases. This milestone could be easily achieved if their antimicrobial and antioxidant worth is well understood [20]. *In vitro* studies have shown that, polyphenols with antioxidant potential are plant based compounds which are pharmacologically active against neurological ailments [21]. These complexes may also play their part as anti-cancerous, antimutagenic and cardio-protective agents because they have free radical hunting capacity [22]. Studies by Ferreira and Stade [23] revealed that polyphenols are chemo preventive representatives because they pull down the level of cholesterol and have preventive cell damage property. Due to these astounding findings, researchers are looking for the replacement of synthetic antioxidants used in foods/medicinal purposes with new naturally occurring harmless antioxidants [21].

The phytochemical and antioxidant activity of different *Artemisia* species have been checked and confirmed by numerous researchers suggesting that the species from genus *Artemisia* are rich in different phytochemical constituents with better antioxidant activity [24–31]. One of the important plants paved with highest attention pharmacologically is *Artemisia annua,* which has been extensively studied and hundreds of secondary metabolites have been discovered and acknowledged so far [32, 33]. Phytochemical analysis of this plant authenticates the presence of sesquiterpenoid along with sesquiterpene lactones and between these constituents artemisinin is highly focused. This compound has endoperoxide sesquiterpene lactone that act as a bioactive drug constituent [34]. In a study, Iqbal et al. [29] confirmed that the ethanolic extract of *A. annua* leaves possess highest amount of phenolics and flavonoids.

Besides *A. annua,* another important plant is *Artemisia amygdalina* having prodigious therapeutic and economic prominence. Its chloroform, ethyl acetate, ethanolic, methanolic, aqueous and crude extracts encloses flavonoid and alkaloids while tri-terpenoids exists only in the ethanolic extract. Tannins are present only in the ethyl acetate extract while saponins are present in ethanolic and aqueous extracts which is absent in methanolic, chloroformic and ethyl acetate extract respectively [28]. Moreover the petroleum ether extracts of *Artimesia amygdalina* contain artemisinin, while other compounds like terpenes,

alkaloids, phenolics, tannins, cardiac glycosides, and steroids in tissue cultured and wild *Artimesia amygdalina* were also observed [24].

Also, with their antimicrobial activity, the methanolic extracts from *Artemisia scoparia* and *Artemisia spicigera* have a vigorous free radical rummaging potential [35]. *Artemisia nilagirica* (Clarke) also contain essential compounds in its extracts like sesquiterpene lactones, exiguaflavone (A and B), benzo furan and macckianin [36]. This plant is anti-leishmanial, antimalarial anthelmintic, antiseptic, astringent, aromatic, anti-inflammatory, appetizer, diuretic, antiasthma, and also used for the treatment of leprosy and skin diseases [37]. Additionally, its oil also has an antioxidant activity [38]. Extracts of *Artemisia nilagirica* also encloses certain other compounds i.e., steroids, terpenoids, flavonoids, saponins, tannins, proteins and essential oil. Due to the existence of these compounds this plant holds a remarkable antibacterial activity [31]. In one study it has been corroborated that the hexane, ethyl acetate, methanol and water extracts from leaves and flower of this plant contain different phytochemicals. Leaves contain saponins, alkaloids, tannins, flavonoid, coumarins, phenols with steroids and flower contain alkaloids, coumarins, saponins, terpenoids, tannins, flavonoids, and phenols which confirms its high therapeutic potential [26].

Another important medicinal plant *Artemisia parviflora* is employed for injuries, cuts and for skin infections [39]. High blood pressure, diabetes, and anthelmintic infections are also treated with this plant [40]. These advantages of *Artemisia parviflora* might be due to the amalgamation of phytochemicals present in it [41]. This could be easily confirmed by a study where various extracts of aerial parts of *Artemisia parviflora* showed the presence of flavonoids, triterpenoids, sterols, tannins, alkaloids, and coumarins that makes it a best nominee for *in vitro* antioxidant activity and phytochemicals extraction [42]. Also, Ahameethunisa and Hopper [43] reported that the methanolic extracts of *A. parviflora* possess greater amount of phenolic compounds as compared to other extracts.

Oils from *Artemisia absinthium* **(**also called Wormwood**)** can be used as a cardiac stimulating agent that have the tendency to mend circulation of blood and also employed as a stomach remedy [44]. The whole plant i**s** also used against diseases like tuberculosis, diabetes, and antihypertensive [45**]**. Studies substantiated that the leaves of this plant contain certain type of compounds which are antimalarial [46], antimicrobial activity [47], antidiabetic activity [48] and antifertility [49]. On the other hand, some traditional uses of *Artemisia absinthium* have also been reported by many researchers [30-50]. Its extracts have shielding influence on hepatic impairment and used as a remedy for gastric pain [50]. Furthermore, the antioxidant activity and occurrence of phenolic compounds and flavonoids in *Artemisia absinthium* have also been reported [30]. Flavonoids are essential because they impede the sensitivity of pain and shows anti-inflammatory properties [51]. These inhibit the enzymes responsible for the synthesis of prostaglandins, that's why they are anti-inflammatory. Other studies for the revelation of actions of the pain killing activity, hepatoprotective and anti-inflammatory potential of *Artemisia annua* and *Artemisia absinthium* were also performed [27]. In one study, the important compound santonin was detected in different *Artemisia* species and its quantitation was done with the help of HPLC-UV. The identification and quantification of santonin was done in the leaves of *A. gmelinni*, *A terra-albae*, *A. scoparia*, *A. sublesingiana*, *A. foetida*, *A. schrenkiana*, *A. frigida*, *A. absinthium* from Kazakhstan and also in the extracts of leaves of *A. cina* [52].

The methanolic extract of *Artemisia vulgaris*, contain phenolics, flavonoids and sesquiterpenoid type compounds [53] and possess antimicrobial, antitumour, antispasmodic, antiseptic, antimalarial, hepatoprotective and antirheumatic qualities [54].

Aerial parts of *Artemisia vulgaris* contain polysaccharides which are employed to treat numerous diseases and carbohydrates extracted from this plant exhibit several beneficial properties. However the main polysaccharide in

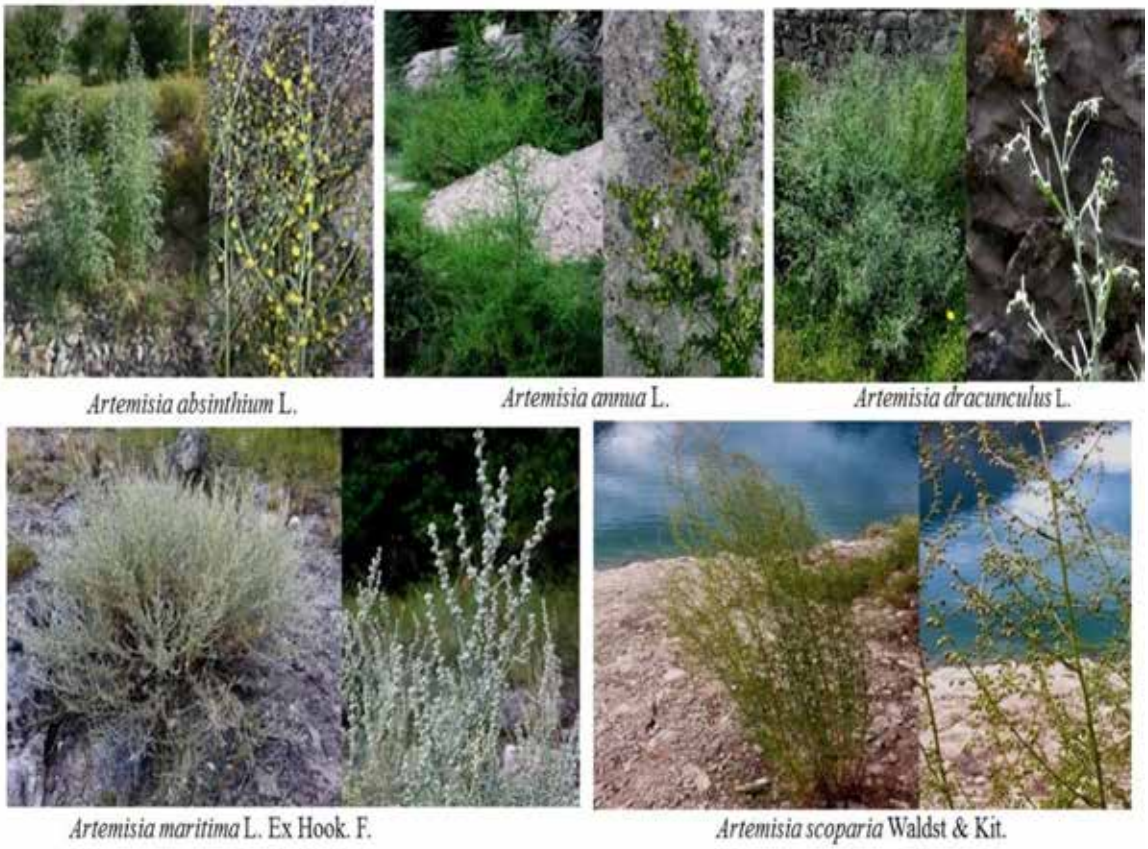

Fig. 1. Plant and synflorescences of *Artemisia* species (Photographs by Adil Hussain).

the infusion is inulin-type fructan [55]. Another revelation showed that the oils from *Artemisia feddei* contain camphor, borneol, cineole, alpha terpineol, chamazulene, alpha thujone, alpha phellandrene, alpha terpinyl acetate, beta caryophyllene, and teroinen-4-ol with antibacterial potential [56]. Similarly, oil from different plant parts (stem, leaf and flower) of *Artemisia chamaemelifolia* Vill. contains compounds like Menthyl acetate, (Z)-nerolidol, 1,8-cineole, yomogi alcohol, and artimesyl acetate while the aerial parts of *Artemisia turcomanica* have compounds like spathulenol, camphor, santolina alcohol and trans beta terpineol [57] and oil of *Artemisia spicigera* have many chemical ingredients like camphor, 1,8-cineole, camphene, p-cymene with alpha and beta thujone showing antibacterial activity [58].

In another investigation, the essential oil of *Artemisia aucheri* was assessed in-vitro and identified compounds includes Linalool, Camphor, Borneol, p-Cymene, Davanone, α-Thujone, β-Thujone, 1,8-Cineole and α-Pinene having pharmacological importance [59]. An Iranian flora *Artemisia khorassanica* have been assessed and antimalaric compounds like Chrysanthenone, palmitic acid and cis-thujone were confirmed [60]. Studies on *Artemisia indica* Willd revealed that this plant is helpful to lessen chronic fever, hepatobiliary and dyspepsia like illnesses [61]. The stem and leaves are anthelmintic, antiseptic, antispasmodic, expectorant and stomachic [62]. Methanol, ethanol and hydro-methanol extracts from the aerial parts of this plant are rich in flavonoids, sterols carbohydrates, tri-terpenoids, reducing sugars, glycosides and phenolics. The ethanolic extracts do not contain Saponins and tannins, while methanol and hydro-methanol extracts contained Saponins and tannins. Also, with these compounds, methanolic extracts of *A. indica* contain amino acids and alkaloids [25].

In one investigation, phenolic compounds have been detected in *Artemisia judaica* L. where the crude ethanol extract of this plant was tested

on the black bean aphid *Aphis fabae*. The insecticidal activity of the tested crude extract was due to the phenolic compounds present in it, which makes this plant known for the bio-insecticidal activity [63]. Different representative species of the genus *Artemisia* reported globally are illustrated in figure 1.

3. ANTIMALARIAL ACTIVITY OF *Artemisia SPECIES*

Malaria is a severe and highly contagious infection faced by human being [127] and a universal health problem leading to death about 1 million per annum [128]. Malaria in terms of sickness and death is the world's most dangerous parasitic disease [129] and *Plasmodium sp*. protozoa are responsible for malaria, where the *Plasmodium falciparum* is prominent in causing infection. The transmission can be initiated through transfusion or inoculation of infected blood from person to person. It could also be transferred through the placenta of an infected mother to her unborn child [130]. Now a day, five species of *Plasmodium* primarily, *Plasmodium falciparum, Plasmodium ovale, Plasmodium malariae, Plasmodium knowlesi* and *Plasmodium vivax* are active in causing human malaria. The life cycle of malaria begins when blood is searched as meal by a female *Anopheline* mosquito (*Plasmodium* infected) and inserts sporozoites into the dermal cells [131, 132].

The parasite is resistant to conventional antimalarial drug that's why; there is a dire need to develop multiple approaches that can control distribution of this disease [34, 129]. Recently multi-drug resistant strains of the *Plasmodium* have developed and there are also evidences of the

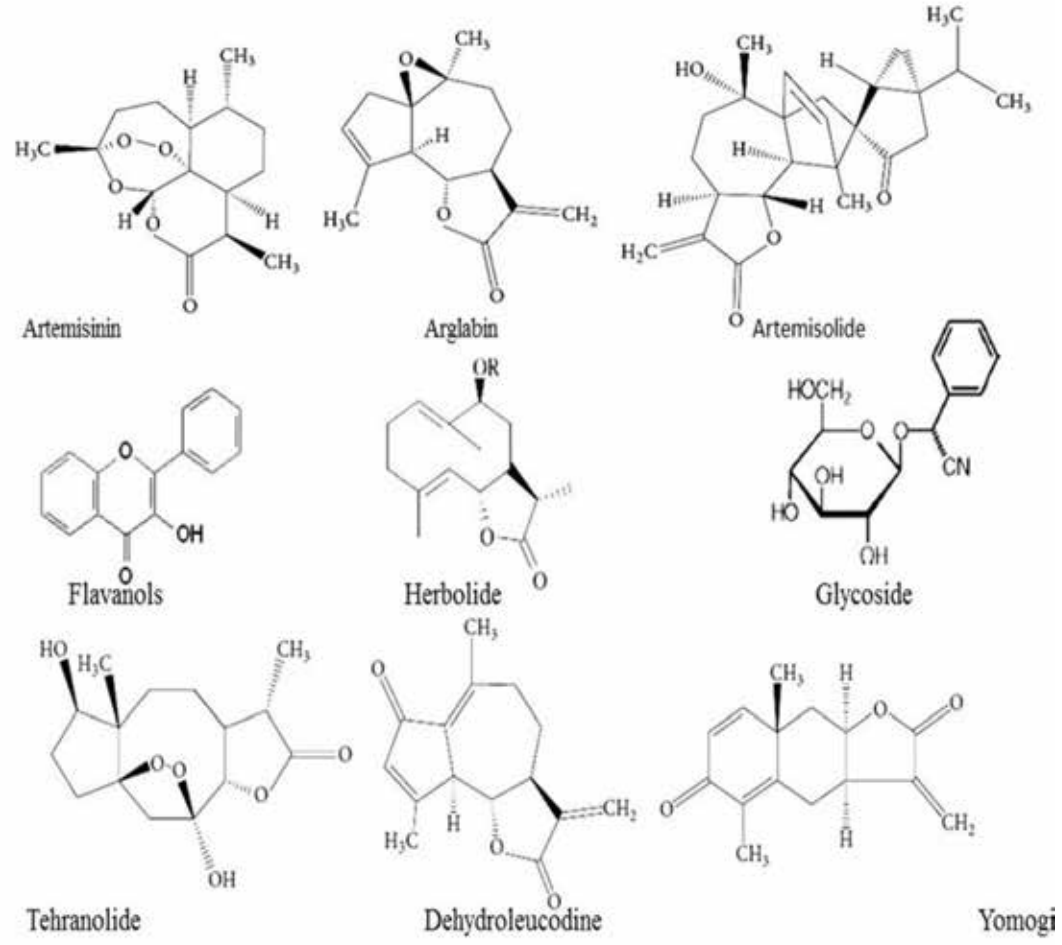

Fig. 2. Structure of some bioactive compounds derived from different *Artemisia* species (Source: Wikipedia commons).

occurrence of parasites resistant to artemisinin [133]. Several species of *Artemisia* are employed in China as antimalarial since prehistoric times especially *Artemisia annua, Artemisia apiacea* Hance and *Artemisia lancea* Vaniot [16, 134]. In 1970s, Chinese scientists found the effective antimalarial medicine, i.e. artemisinin from *Artemisia annua* L. which is a Chinese traditional medicinal plant [71]. Artemisinin is also obtained from different species of *Artemisia* and other microbial sources through genetic engineering techniques. Malaria and other diseases are treated with Artemisinin, which is actually a current drug of choice against *plasmodium falciparum*.

Artemisinin is essentially a sesquiterpenoid, and it is obtained from the glandular trichomes of *Artemisia annua* [135]. It contains endoperoxide bridge with in the 1, 2, 3-trioxane system (as shown in figure 2) that holds a significant rank due to its antimalarial properties. *Artemisia annua*, is wide spread in China and it is utilized since 2000 years to treat malaria [134]. Besides that, the presence of artemisinin has also been documented in *Artemisia lancea* and *Artemisia apiacea* [134], *Artemisia cina* [136] *Artemisia vulgaris*, *Artemisia japonica* [137] and in the upper portions of *Artemisia sieberi* [138]. Moreover, its presence has also been confirmed in *Artemisia absinthium* [139], *Artemisia dubia* and *Artemisia indica* [140].

Currently, the supreme operational means to get rid of the spreading rate of malaria is Artemisinin combination therapy (ACT) [141] and ACT is recommended by the World Health Organization (WHO) as a principal treatment for malaria initiated by *Plasmodium falciparum* [142]. Artemisinin also showed its detrimental effects against some other parasites together with *Schistosoma* [143], *Leishmania* [144] and *Toxoplasma* [145. ACT is comparatively harmless medication because it has no clear antagonistic reactions or sterling side effects [146].

Studies confirmed that the hydro alcoholic and aqueous extracts of *Artemisia annua* L. are very operative on malaria and it gives antimalarial activity by potentiating artemisinin activity on *Plasmodium* [75]. Another study corroborated that the crude methanolic and ethanolic extracts of *Artemisia nilagirica (Clarke)* have reasonably high potency against *plasmodium falciparum* [147]. An *In vitro* examination of crude extracts of *Artemisia abrotanum* L. showed that two compounds (isofraxadin and a novel sequiterpene 1(S*)-hydroxy-a-bisabloloxide A acetate) are effective against *plasmodium falciparum* [148].

In a rodent antimalarial model, *Artemisia vulgaris* leaf extract is orally active, nontoxic against *Plasmodium yoelii* and as well as antiparasitic and antidisease weed. This plant has the tendency to be a low cost antimalarial source [149]. In other study, the light petroleum and ethanol extracts of *Artemisia maritima, Artemisia nilegarica and Artemisia japonica,* inhibit schizont maturation and are found to be atimalarial [150]. Another investigation revealed fifteen extracts of 3 *Artemisia* species from Iran namely*; Artemisia ciniformis, Artemisia biennis and Artemisia turanica* have better antimalarial activity. Dichloromethane extracts of *Artemisia ciniformis* have highest activity followed by *Artemisia biennis* and *Artemisia turanica* [81]. The dichloroethane extract of *Artemisia armeniaca* Lam. and *Artemisia aucheri* Boiss. also have better antimalarial activity [79].

In the quest of novel antimalarial compounds from plants, chloroform extracts fractions of *Artemisia maciverae* against *plasmodium berghei* have been assessed where triterpenes and alkaloids were found with antimalarial activity [151]. Investigations showed that the diverse solvent extracts and volatile oil of *Artemisia indica* have Artemisinin and polymethoxy flavanoid having antiprotozoal potential against different protozoal parasites, showing the antiparasitic worth of *Artemisia indica*. This plant extracts also have a potential malaria prophylactic effect, due to the inhibition of two plasmodial fatty acid biosynthesis enzymes [152].

An *In vitro* anti leishmanicidal analysis of ethanolic extracts of *Artemisia ciniformis, Artemisia santolina* and *Artemisia kulbadica* showed some compounds which have better anti leishmanicidal activity and found best for leishmaniasis management [153]. In another study, the anti-malarial effect have been found *In vivo* in

Iranian flora *Artemisia khorassanica* [60] and in *Artemisia turanica* Krasch crude extracts against *Plasmodium berghei* [116]. A dose dependent antiplasmodial activity of the methanolic extract from upper part of *Artemisia abyssinica* against chloroquine sensitive *Plasmodium berghei* has promising antiplasmodial activity [69]. Moreover, other *Artemisia* species like *Artemisia scoparia* Waldst. & Kit. And *Artemisia spicigera* C. Koch also possess antimalarial and free radical scavenging action and the dichloromethane extracts of these species have moderate level of antimalarial action [35]. These studies collectively endorse the pharmacological importance of *Artemisia* plants because of their high potency to combat with malaria.

4. ANTIMICROBIAL ACTIVITY OF *Artemisia* SPECIES

Since past decades, a lot of studies have been performed to reveal the anticancer, anti-inflammatory and antimicrobial properties of different constituents of plants [154–159]. The exploration of novel antimicrobial compounds with high effectiveness for deadly diseases is today's continuous and dire need [160]. Researchers are trying to develop effective drugs against microbial diseases by dragging their attention towards traditional medicine [161]. There are a lot of scientific revelations on the antimicrobial activity of plants [162] and numerous antimicrobial components have been identified from plant origin which are aromatic or might be some saturated carbon-based compounds. These aromatic compounds are attained by means of ethanolic or methanolic extraction [163]. Saponins and sterols are important compounds which can be extracted easily when methanol and ethanol are used as extracting solvents [164]. Other compounds like polyphenols [165] alkaloids [166] and terpenoids [167] can also be extracted using methanol and ethanol as extracting solvent. On the other hand, dichloromethane is also used for terpenoids extraction [162].

Fore mostly, the crude alcohol extraction method is employed in initial plant screening for antimicrobial activities and secondly, several other organic extraction methods are implemented [121]. Numerous investigations validate the methanolic and ethanolic extracts of *Artemisia* species as better antimicrobial candidates [64, 66, 76, 97, 110, 120, 121, 168, 169, 170]. In a study antimicrobial efficacy of methanolic extracts of upper section of *Artemisia diffusa*, *Artemisia oliveriana, Artemisia scoparia and Artemisia turanica* against *S. aureus, B. subtilis, E. coli, C. albicans* and *P. aeruginosa* has been documented [169]. Important compounds like flavones could be obtained from *Artemisia giraldii* that have extraordinary antibiotic action contrary to several microorganisms including *P. aeruginosa, S. aureus, S. lutea, E. coli, Proteus sp, T. viride* and *A. flavus* [91].

Essential oils of *Artemisia aucheri* contain compounds such as decane, p-cymene borneol, 1,8-cineole, linalool, lavandulol, triene, bornyl acetate, p-mentha-8-ol, chrysanthenyl acetate and caryophyllene oxide. These all essential compounds are recovered from the upper portions of *Artemisia aucheri* and the oils from seeds of this plant have better antimicrobial activity against *E.Coli, S. aureus* and *Listeria monocytogenes* [171].

Similarly, in the essential oil of *Artemisia spicigera* compounds like, camphor-a-theojone, B-theojone, 1,8-cineole and p-cymene are active against various types of bacteria, i.e., *Bacillus cereus, Serratia marcescens, E. Coli, Enterobacter aerogenes, Citrobacter amalanoficus, Bacillus megaterium, St. saprophyticus* and *Bacillus megatarium* [58]. Oils obtained from the aerial portion of *Artemisia incana* L. also contain a lot of compounds where camphor and borneol are abundant, showing inhibitory efficacy against twenty six bacteria, fifteen fungi and three yeast species [172]. Oils from *Artemisia feddei* also contain important compounds, which are highly active against obligate anaerobic bacteria [56]. *Artemisia chamaemelifolia, Artemisia turcomanica* and *Artemisia sipicigera* also possess antibacterial activity [58]. Invitro assessment of essential oil of *Artemisia aucheri* Boiss for antimicrobial effect authenticates better results against *B. cereus, P. vulgaris, P. aeruginosa, S. cereviciae, C. utilis, P. digitatum and A. niger* [59].

Table 1. Biological activities of substances, parts and fractions derived from *Artemisia* species.

Plant Species	Bioactive part or fraction	Bioactive substance	Reference
Artemisia abrotanum L.	Ethanolic extract	Antifungal Antibacterial	[64]
Artemisia absinthium L.	Aqueous MeOH extract	Antitumor	[65]
	Essential oil, methanolic and ethanolic extract	Antioxidant	[66-30]
	Hot alcoholic extract	Antimalarial	[67]
	Ethanolic extract	Cytoprotective	[30]
	Essential Oil	Antifungal	[68]
	Aqueous extract	Anthelmintic	[214]
Artemisia abyssinica	Methanolic extract	Antiplasmodial,	[69]
	Water and alcoholic extract	Antioxidant	[70]
Artemisia annua L.	Petroleum ether and ethyl acetate extract	Antimalarial	[71-72]
		Anti-algal	[73]
	Methanol, water extract	Antibacterial	[74]
	Aqueous and hydro alcoholic extract	Antimalarial	[75]
	Essential oil	Antibacterial	[76]
	Ethanolic extract	Antiulcerogenic	[77]
	Methanol and water extracts	Anticancer	[74]
Artemisia arborescens	Essential oils and methanolic extract	Antioxidant	[66]
Artemisia argyi	Methanolic extract	Antitumor	[78]
Artemisia armeniaca Lam	Dichloromethane extract	Antimalarial	[79]
Artemisia aucheri Boiss	Essential oil	Antimicrobal	[59]
	Dichloromethane extract	Antimalarial	[79]
Artemisia barrelieri	Eudesmanolides	Anti-inflammatory	[80]
Artemisia biennis	Ethyl acetate extract	Antimalarial	[81]
Artemisia capillaris	Methanolic extract	Antitumor	[82]
	Polyacetylene extract	Antiviral	[83]
	Crude extract	Antihepatitis	[84]
	Methanolic extract	Anticancer	[82-85]
	Methanolic extract	Antiobesity	[82-86]
	Methanolic extract	Anti-inflammatory	[82]
Artemisia cina	Essential Oil	Antibacterial Antioxidant DNA protecting	[87]
Artemisia ciniformis	Dichloromethane extract	Antimalarial	[81]
Artemisia douglasiano	Methanolic extract	Hepatoprotective	[88]
	Ethanolic extract	Antiulcerogenic	[89]
Artemisia feddei	Essential Oil	Antibacterial	[56]
Artemisia fukudo	Ethanol, n-hexane, dichloromethane, ethylacetate, and butanol	Cytotoxic	[90]
Artemisia giroldu Pamp.	Flavones	Antimicrobial	[91]
Artemisia iudoviciana	Methanolic extract	Antimicrobial	[92]

Contd.....

Table 1 (Contd.....)

Artemisia indica	Chloroform, ethyl acetate and n-hexane extract	Antimicrobial	[93]
	Methanol extract	Anti-inflammatory	[94]
	Ethyl acetate extract	Antitumor	[97]
Artemisia judaico	Flavone, cirsimaritin	Antispasmodic	[95]
	Ethanol extract	Insecticidal	[63]
Artemisia montana	Ethanolic extract	Cytoprotective	[30]
	Ethanolic extract	Antioxidant	
Artemisia myriantha	Arglabin	Antitumor	[96]
Artemisia Nilagirica	Ethanolic extract	Antibacterial	[31]
	Petroleum ether, n-hexane, dEther, Ethanol and water	Phytochemical analysis	[98]
	Essential oil	Antioxidant	[38]
Artemisia pacifica		Antimicrobial	[99]
Artemisia princeps	Smoke and water soluble extract	Anticancerous	[100]
Artemisia parviflora	Ethanolic extract	Antioxidant	[42]
	Methanolic extract	Anthelmintic	[213]
Artemisia rehan	Ethanolic extract	Antimalarial	[101]
Artemisia scoparia	Methanolic extract	Cytotoxic	[102]
	Dichloromethane extract	Antioxidant	[103]
	Methanol extract	Insecticidal	
	Essential oil and methanolic extract	Antioxidant Antibacterial Antimalarial	[66]
Artemisia sieversiana	Flavonoids	Antitumor	[65]
	Methanolic extract	Anthelmintic	[213]
Artemisia stolonifera	Ethanolic extract	Cytostatic Antiobesity Anticancer Anti-inflammatory	[104]
Artemisia tridentata Nutt.	Ethanolic extract	Plant growth regulator	[105]
Artemisia xanthochroa	Flavonoids	Antitumor	[65]
Artemisia herba-alba Asso.	Ethyl acetate, Butanol, Water and Chloroform extract	Anti-inflammatory Antioxidant Activity	[106
	Essential oils	Antibacterial	[107]
	Aqueous extract	Hypoglycemic	[108]
	Essential oil	Antiradical	[107]
	Essential oil and crude extract	Hypoglycaemic	[109]
	Methanol extract	Anti-Listerial	[110]
Artemisia Japonica	Methanol extract	Anticancer Antiobesity Anti-inflammatory	[82]
Artemisia Montana	Methanol extract	Anticancer Antiobesity Anti-inflammatory	[82]
Artemisia judaica	Water and alcoholic extract	Anti-Diabetic	[111]

Contd.....

Table 1 (Contd.....)

Artemisia Sylvatica	Methanol extract	Anticancer Antiobesity Anti-inflammatory	[82]
Artemisia Keiskeana	Methanol extract	Anticancer Antiobesity Anti-inflammatory	[82]
Artemisia Selengensis	Methanol extract	Anticancer Antiobesity Anti-inflammatory	[82]
Artemisia khorassanica	Ethanol extract	Anti-plasmodial	[60]
Artemisia kulbadica	Methanol extract	Anticancer	[112]
Artemisia sieberi	Crude extracts	Antimalarial	[113]
	Essential oils	Antimalarial	[114]
	Ethanol extract	Antidiabetic	[115]
Artemisia turanica	Ethyl acetate extract	Anticancer	[112]
	Crude extract	Antimalarial	[81]
	Ethanol extract	Antimalarial	[116]
Artemisia santolina	Ethanol extract	Anticancer Activity	[112]
Artemisia diffusa	Essential oil	Anticancer Activity	[112]
Artemisia campestris L.	Ethanol, hexane and water extract	Antiradical	[107]
	Aqueous extract	Antioxidant, Antitumor	[117]
	Essential oils, Ethyl acetate extract	Antidiabetic	[118]
	Methanolic extract	Antibacterial	[119-107]
	Essential oils and methanolic extract	Antibacterial	[120-121]
	Essential oil	Antioxidant	[120, 66, 121]
	Dichloromethane extract, aqueous extract	Antimutagenic	[122]
	Water and alcoholic extract	Anti-venomous	[123-124]
Artemisia afra	Ethanolic extract	Antioxidant	[70]
	Essential Oil	Antimalarial	[101]
Artemisia dracunculus L.	Essential Oil	Antioxidant	[68]
Artemisia santonicum	Essential oil and methanolic extract	Antifungal, Antibacterial	[68]
	Essential Oil	Antibacterial	[66]
Artemisia spicigera	Essential Oil	Antifungal, Antibacterial	[68]
	Dichloromethane extracts	Antimalarial Insecticidal	[103]
	Methanolic extract	Antioxidant	[103]
Artemisia thuscula	Ethanolic extract	Diuretic	[125]
Artemisia pallens	Ethanolic extract	Antibacterial Antifungal	[64]
Artimisia vulgaris L.	Essential oil	Antibacterial Antioxidant DNA protecting	[87]
	Methanolic extract	Anti-inflammatory	[126]

Against certain type of microorganisms, the methanolic extracts of *Artemisia campestris* L. are considered to be vigorous [120]. This might be due to the presence of bioactive metabolites of countless chemical types, like phenolic compounds. Shoko et al. [170] confirmed that phenolic compounds are very dynamic substances against microorganisms particularly bacteria. These compounds are quite active in contradiction of few Gram-positive species while the same extracts are weak against some Gram-negative species. *Artemisia campestris* is not merely an antimicrobial plant but also contains effective phenolic antioxidants [121]. The antimicrobial compounds modes of action in bacteria comprises membrane damage, membrane potential, changes in pH inside the cell, and the synthesis of ATP [173, 174].

Another study revealed the effective anti-viral properties of *Artemisia Parviflora* [41]. The antibacterial effect of crucial oil and crude extracts of *Artemisia herba-alba* Asoo. against *Listeria monocytogenes* have properties, that can hinder the progression of psychrophils resistant organisms [110]. One more study showed that the aqueous and solvent extracts of *Artemisia indica* were highly active against Gram-positive organism where *S. aureus*, was maximally inhibited [168]. These inhibitions might be due to the presence of essential compounds like phenols, steroids, triterpenoids, valavinoids, carotenoids, tetratriterpenoids azadirachtin and ketones [175]. Even though, extracts of few *Artemisia* species like *Artemisia aspera* and *Artemisia parviflora,* were not effective or having negligible inhibition on human and phytopathogenic bacteria [168].

Ethanolic extracts of other species of genus *Artemisia* like *Artemisia abrotanum* and *Artemisia pallens* are active against *Pseudomonas cepacia* and *Bacillus stearothermophilus.* These plants extracts not only possess antibacterial activity but also have maximum antifungal activity against *Trichosporon beigelii* and *Saccharomyces cerevisiae.* This suggests that the ethanolic extracts of these two novel plants have both antibacterial and antifungal potential [64]. *Artemisia nilagirica* is another important plant containing numerous compounds including saponins, tannins, steroids, flavonoids, terpenoids, proteins and essential oil with better antibacterial action [97].

Studies of Erel et al. [66] substantiated that the methanolic extracts and essential oils of *Artemisia santonicum* and *Artemisia scoparia* holds fine antimicrobial activity where *Staphylococcus aureus* was the supreme sensitive bacteria to oils. Also these two plants are active against *Candida albicans* respectively. Some bacterial species, viz., *Salmonella enteritidis*, *Escherichia coli* O157, *Salmonella typhi*, *Listeria monocytogenes* and *Yersinia enterocolitica* were tested against the essential oil and compounds of *Artemisia annua* showing their high sensitivity [76]. In another study, Javid et al. [93] showed the chloroform, butanol and ethyl acetate extracts of *Artemisia indica* with better inhibitory activities towards *Salmonella typhi.* On the other hand, chloroform and n-Hexane extracts of this plant fully hinder the progression of fungal species like *Aspergillus flavus* and *Fusariun solani*.

Another study indicated that the methanolic extracts of *Artemisia ludoviciana* are more active against *Vibrio cholera* because these extracts encompasses compounds which are able to disturb the cell membranes of *Vibrio cholerae* cells with pH reduction, cell membrane hyperpolarization, and cellular ATP reduction [92]. Besides the antibacterial and antifungal activities, compounds from the extracts of *Artemisia annua* have anti-algal activity against *Microcystis aeruginosa*. This might be due to the presence of artemisinin which escalates the level of reactive oxygen species (ROS) in algae cells [73].

5. ANTICANCEROUS ACTIVITY OF *Artemisia* SPECIES

Medicinal plants possess a lot of natural products with better properties for cancer treatment [176]. Plants have numerous essential products like lignin and flavonoids of polyphenols. These products are evaluated *in vitro* and *in vivo* to find potential biological activities like antitumor activity [177]. Beforehand, a lot of studies have

been conducted to unfold the in vitro cytotoxic action of various plant extracts for their anticancer action on different types of human cancer cell lines [178, 179].

Like previously reported in other plants, several studies confirmed *Artemisia* species as better cytotoxic and anti-cancerous candidates [30, 90, 102, 126, 180, 197]. The poisonousness of *Artemisia* species on cancer cells has also shown *in vitro* [181, 182] and *in vivo* [183] respectively. These activities might be due to the presence of one or more essential compounds present in the plant. Among those compounds, Artemisinin, is very active ingredient of many *Artemisia* species mainly *Artemisia annua*, having better cellular toxicity against human lymphoid leukaemia cells [180]

Also the artemisinin and its allied compounds have the capacity to thwart cellular growth of human colorectal and breast cancer [180, 184]. Other compounds like terpenoids, cesquiterpen lactones and flavonoids are correspondingly important antitumor constituents acquired from *Artemisia* species [185]. Another offshoot of artemisinin, called Artesunate, possess both *in vitro* and *in vivo* anticancer properties [186].

A lot of beneficial compounds have also been well-known in *Artemisia absinthium* and *Artemisia vulgaris*, which have low molecular weight. These compounds are flavonoids, sesquiterpene, lactones, lignans and monoterpenes [187, 188, 189]. These are considered to be the main vigorous anticancerous compounds of these plants [190, 191, 192]. Another study corroborate the infusions from aerial parts of *Artemisia vulgaris* and *Artemisia absinthium* contain polysaccharides which are used in traditional plant made medicine [55]. Studies showed that the crucial consequence of the vigorous constituents of *Artemisia* species is apoptosis; it is a programed cell death which is initiated via the cell cycle arrest [85, 90]. Instigation of caspases, mitochondrial membrane depolarization potential or the down governing expression of Bcl-2 gene might also induce apoptosis of cells [100]. Kim et al. [90] validates the utilization of *Artemisia fukudo* as a defensive measure against cancer. The most active compound artemisinin induces apoptosis and it does not induce necrosis against human lymphoid leukaemia (Molt-4) cells [180].

Hitosugi et al. [193] reported, in the myelogenous leukaemia cell line of human (HL-60), *Artemisia capillaries* smoke and aqueous extracts are responsible for cellular decease, but these extracts are not effective in breast cancer (MCF-7) and other sort of tumour cells. On the other hand, macro molecular constituents of *Artemisia capillaris* are liable to encourage apoptosis in hepatoma cell lines in human [85]. The water soluble extracts of *Artemisia argyi* are not very much active against human tumour cell lines and also in breast cancer cell lines, but profoundly active in murine tumour cells [194]. In a study, the induction of apoptosis caused by the smoke and water extracts of *Artemisia princeps* in human breast cancer MCF-7 cells diminishes cells through the mitochondrial alleyway that seems to be a milestone for breast cancer treatment [100].

Artemisia argyi and *Artemisia Asiatic* also contain essential compound called flavones, which have the potency to impede certain types of cancer by promoting apoptosis including human lung cancer, prostate cancer, myeloid leukaemia, gastric cancer and melanoma [78, 195]. Nevertheless, other researchers found flavones to be unproductive in contradiction of human breast cancer cells [196]. Similarly, n-hexane extracts of *Artemisia turanica* Krash. possess better cytotoxic, antiproliferative and anticancer effects against two leukemic cancer cell lines predominantly HL-60 and K562 [197]. In another study dichloromethane, methanol, ethyl acetate, and n-hexane extracts from upper parts of different *Artemisia* species (*Artemisia ciniformis, Artemisia diffusa* Karasch, and *Artemisia vulgaris*) have potent antiproliferative properties which could be a promising chemotherapeutic agent in cancer treatment [198].

Studies confirmed that the ethanolic extracts of *Artemisia montana* and *Artemisia absinthium* are rich in essential compounds like, flavonoids and phenolic acids. These compounds have better antioxidant activity and also have cytoprotective influence towards oxidative damage in fibroblast-

like cells. This validates *Artemisia montana* and *Artemisia absinthium* both as better nominees for the treatment of skin disorders [30].

Extracts of *Artemisia scoparia* in human muscle cancer cells have devastating effect against 88-93% cancer cells that endorse anticancer activity of this plant extract [102]**.** Moreover, the apex parts of two novel species of *Artemisia* i.e., *Artemisia vulgaris* and *Artemisia absinthium* have anthelmintic, antipyretic, cytostatic, stomachic, antibacterial, and antitumor actions [68, 199, 200] while the *In vitro* assessment of methanol extracts of other species like *Artemisia Japonica*, *Artemisia stolonifera*, *Artemisia montana*, *Artemisia selengensis*, *Artemisia capillaris*, *Artemisia sylvatica*, *Artemisia scoparia* and *Artemisia keiskeana* possess better anti-inflammatory, anticancer, and antiobesity activity [82]. Studies of Emami et al. [112] corroborated *Artemisia sieberi, Artemisia kulbadica, Artemisia santolina, Artemisia turanica,* and *Artemisia diffusa* with cytotoxic activity in contradiction of human Caucasian hepatocyte and larynx carcinoma (HepG-2 and Hep-2) cell lines.

6. ANTHELMINTIC ACTIVITY OF *Artemisia* SPECIES

Helminthic problems are exceedingly widespread, predominantly in the3rd world countries [201] and documented as the cause of much chronic ailments. Numerous studies have found *Artemisia* species with potent anthelmintic activity [62, 202, 203, 204, 205]. *Artemisia cina* is one of the best candidates with anthelmintic activity which contains santonin, a sesquiterpenic lactone that might be the reason of this activity [206, 207]. Other species like *Artemisia santonica* L, *Artemisia maritima*, *Artemisia herba-alba*, *Artemisia absinthium*, *Artemisia vulgaris*, *Artemisia afra* and *Artemisia ludoviciana* are also most prominent species with the same activity [208].

In one study, Extracts from *Artemisia vestita* and *Artemisia maritima* are found active against *Haemonchus contortus* in infected sheep's and indicated significant activity against larvae and adult worms [209]. Moreover, in ruminants, the water, aqueous, sodium bicarbonate, dichloromethane, and ethanol extracts obtained from leaves of *Artemisia annua* have better anthelmintic action [202]. Perennial plant *Artemisia indicia* also possess this activity. In a study chloroform, methanol and aqueous extracts of this plant confirmed anthelminthic property against adult earthworm *Pheretima posthuma* [62]. *Artemisia absinthium* extracts are also a promising way to treat GI nematodes of sheep [210]. An important member of Artemisia is *Artemisia herba alba,* that can be employed for controlling heterakid infection because it induces anthelminthic consequence by dropping worm burden and egg shedding in the diseased birds [203] and also the methanolic extracts from leaves of *Artemisia herba-alba* possess nematicidal activity [211]. The anthelmintic effects on *Haemonchus contortus* from methanol and crude aqueous and of *Artemisia brevifolia* have been proved and it is confirmed that the whole plant holds strong anthelmintic activity against nematodes [212]. On the other hand, the essential oil of *Artemisia pallens* have tendency of strong anthelmintic action against *Taenia solium, Pheritima posthuma* and *Ascaris lumbricoides* [204]. Chloroform extracts of stem and root of *Artrmisia siversiana*, also hold potency to eradicate *H. nana* from infected mice [205].

The anthelmintic activity of extracts from *Artemisia parvflora* and *Artemisia sieversiana was* evaluated *in vitro* and *in vivo* on *Haemonchus contortus*, which is a parasitic nematode of small ruminants. Methanolic extract of these plants tested against three different developmental stages using different assays were found to be better anthelmintic candidates [213].

An *in vitro* study was conducted to find an alternative to anthelmintic praziquantel by checking the activity of the crude aqueous extract of *Artemisia absinthium* against *H. nana.* The extract from *Artemisia absinthium* was found to increase ultrastructural alterations, worm paralysis and ultimately death in a dose-dependent manner. Also a significant decrease in the EPG and worm burden has been noticed in mice treated with *A.*

absinthium [214]. Such studies clearly indicate *Artemisia* species with their ability to control helminthic disease to a broad spectrum.

7. CONCLUSIONS

Artemisia is a noteworthy genus with a large variety of biological activities. Plants of this genus possess an extensive range of pharmacological activities which could be used in numerous medical applications. Various active compounds achieved from these plants need to be characterized and well documented; also, the exploration of other novel species with disclosure of new chemical constituents is necessary. Their clinical effectiveness must be tested to obtain better results against lethal diseases. Finally, the toxic effect of these plants should also be clarified and the genetically modified varieties of *Artemisia* need to be cultivated.

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