

Artemisia Species from Iran as Valuable Resources for Medicinal Uses

Mohammad Reza Naghavi, Farzad Alaeimoghadam, Hossein Ghafoori

Abstract—*Artemisia* species, which are medically beneficial, are widespread in temperate regions of both Northern and Southern hemispheres among which Iran is located. About 35 species of *Artemisia* are indigenous in Iran among them some are widespread in all or most provinces, yet some are restricted to some specific regions. In this review paper, initially, GC-Mass results of some experiments done in different provinces of Iran are mentioned among them some compounds are common among species, some others are mostly restricted to other species; after that, medical advantages based on some researches on species of this genus are reviewed; different qualities such as anti-leishmania, anti-bacteria, antiviral as well as anti-proliferative could be mentioned.

Keywords—*Artemisia*, GC-Mass analysis, medical advantage.

I. INTRODUCTION

CARING for health is one of the most important concerns of human being, and man has always been seeking for different approaches to tackle this concern. Finding methods to cure diseases has a history as long as human arrival. At the beginning, certain medical plants were used, then after advent of new chemistry science, synthetic drugs, which were the results of that science, quenched the thirst for health. Nowadays, after revealing that chemistry science was not able to synthesize certain medicines such as Artemisinin and Taxol, and the high price of certain drug production under chemical methods, attentions have been focused on the natural way of getting desired drugs. But, natural systems such as plants and fungi are not efficient in medical material production and this is because of secondary identity of these materials which are not basic and important substance for organisms as primary ones.

To overcome the low efficiency of drug production in organisms, there are two ways: first, increasing acres under culture and second, improving organism's potential in desired material production. The first method's difficulties can be listed as: more field, more water, more money for drug extraction because of low efficiency of organisms' drug content and so on that makes it either impossible or too expensive to do so. The second way is divided into two methods that consist of agronomic and genetic manipulation. Agronomic approach, which concerns using better and advanced techniques and equipment, is limited to organism's

natural potential after which there will be no improvement in yield. But genetic manipulation of organisms is a promising way of overcoming the natural barriers of production to satisfy human's requirement.

Among many of medically important organisms, plants are outstanding and among plants *Artemisia* is one of the beneficial genus. The name is believed that has been taken from one of Greek's goddesses called Artemis (goddess of forests, childbirth and hunt) [1]. *Artemisia* is from *Asteraceae* (*Compositae*) family; plants of this genus are tolerate herbs and bushes and are profoundly known for chemical content in their essential oil. *Artemisia* plants grow in temperate areas of both northern and southern hemisphere and usually are found in arid and semiarid regions. There are over 500 species in this genus and are mostly widespread in Asia, Europe and North America [2].

Artemisia species inhabit in all provinces of Iran, some of species are restricted to particular regions. Species such as *A. scoparia* Waldst and *A. sieberi* Bessers are widespread in all provinces; on the other hand some species are confined to some specific provinces such as *A. kulbadica* Boiss which is restricted to Golestan province and *A. melanolepis* Boiss which is limited to Semnan province. In the Table I the distribution of *Artemisia* in different provinces of Iran is represented [3].

II. GC-MASS ANALYSIS OF TERPENE PATHWAYS

Terpenes are the most frequent secondary material found in plants, and study of their pathways is useful in view of understanding different potential of plants in producing this group of compounds; they are produced through two pathways. Those two pathways consist of Mevalonate (MVA) and Methyl erythritol 4-phosphate (MEP). In the first pathway, from some acetyl coA molecules after some stages a range of compounds such as sesquiterpene and sterol are resulted; on the other side, glyceraldehyde 3-phosphate accompanied with a pyruvate via some enzymatic stages, in MEP pathway, are converted to materials such as monoterpenes. On the following, species of *Artemisia* are evaluated based on their most frequent terpene content.

A. absinthium:

According to GC-MS results obtained from different locations of Iran, most frequent constituents of the essential oil were monoterpenes either hydrocarbon or oxygenated, the existence of some of which are shared in plants from diverse locations whereas some others are unique to specific locations. For instance in one experiment the most frequent constituent

M. R. Naghavi and F. Alaeimoghadam are from Agronomy and Plant Breeding Department, Agricultural & Natural Resources College, University of Tehran, Karaj, 31587-11167, Iran (phone: 98-263-2246074; fax: 98-263-2246074; e-mail: mnaghavi@ut.ac.ir, fa111365@yahoo.com).

Hossein Ghafoori is from Department of Biology, University of Guilan, Rasht, Iran (e-mail: h.ghafoori@guilan.ac.ir).

was alpha-phellandrene (=25.5% of the total essential oil), while in another one the highest level of frequency was for beta-pinene (=23.80 of the total essential oil) [4], [5]. Moreover, p-cymene percentile of total essential oil in one location was 10.35% while in another one was 16.50% [6], [7].

TABLE I
ARTEMISIA SPECIES AND THEIR DISTRIBUTION IN DIFFERENT PROVINCES OF IRAN [3]

Species	Distribution in provinces
<i>A. absinthium</i> L.	Mazandaran, Gilan, Ardebil, East Azarbaijan, Kurdistan
<i>A. annua</i> L.	Golestan, Mazandaran, Gilan, Kurdistan, Tehran
<i>A. armeniaca</i> Lam	Ardebil, East Azarbaijan
<i>A. aucheri</i> Boiss	Almost in all provinces
<i>A. biennis</i> Willd	Mazandaran, Hamedan, Baluchestan, Khorasan, Tehran
<i>A. ciniformis</i> Krasch	Khorasan
<i>A. deserti</i> Krasch	Hamedan, Baluchestan, Khorasan, Tehran
<i>A. diffusa</i> Krasch. ex Poljak	Golestan, Khorasan, Semnan
<i>A. dracunculus</i> L.	Cultivated in most parts
<i>A. fragrans</i> Willd	Golestan, Gilan, Ardebil, East Azarbaijan, West Azarbaijan, Tehran
<i>A. gypsacea</i> Krasch	Golestan, Khorasan
<i>A. kermanensis</i> Podl	Kerman
<i>A. khorasanica</i> Podl.	Khorasan, Semnan
<i>A. kopetdaghensis</i> Krasch	Golestan, Khorasan
<i>A. kulbadica</i> Boiss.	Golestan
<i>A. oliveriana</i> J. Gay ex. DC.	Golestan, Esfahan, Semnan, Tehran
<i>A. persica</i> Boiss.	Kermanshah, Lurestan, Esfahan, Bakhtiari, Kuhgiluyeh va Boyer Ahmad
<i>A. santolina</i> Schrenk	Kerman, Baluchestan, Khorasan
<i>A. scoparia</i> Waldst	In all provinces
<i>A. sieberi</i> Bessers	In all provinces
<i>A. spicigera</i> C. Koch	Mazandaran, Gilan, East Azarbaijan, West Azarbaijan, Tehran
<i>A. splendens</i> Willd	Mazandaran, East Azarbaijan, West Azarbaijan
<i>A. tschernieviana</i> Besser	Mazandaran
<i>A. vulgaris</i> L.	Golestan, Gilan, East Azarbaijan, West Azarbaijan, Kurdistan,

A. annua L. (Quinghao):

About most *A. annua* species evaluated in Iran, 1,8-cineole and camphor, which are two oxygenated monoterpene, were the most frequent constituents. In addition, all species evaluated were from the North of Iran. For instance, in one inspection two most frequent constituents were 1,8-cineole= 9.39% and camphor= 48.00%(49) and in another one more than half of the content was composed of these two constituents (1,8-cineole= 13.90% and camphor= 43.51%) [4], [8], [9]. *A. annua* L. is a promising and potent source of antimalarial herbal drug. Its activity has been ascribed to the content of artemisinin; it has been analyzed by different chromatographic techniques. In previous studies, we have developed a TLC/UV, a simply available, rapid, and cost-efficient method, for the simultaneous determination of artemisinin. The crude extracts from plant samples were used together with a standard in our HPLC/UV and TLC/UV techniques. Artemisinin was converted into a UV-absorbing compound at 254 nm. The new technique has enabled us to

screen high artemisinin producing plants from a large number of samples [10].

A. armenica Lan:

About this species two most frequent constituents are two monoterpenes that include of alpha-pinene= 41.90% and 1,8-cineole= 20.60% [11].

A. aucheri Boiss:

The most frequent constituents were from monoterpene oxygenated group, the kind of material is different in diverse locations, though. Although there were different kinds of monoterpene oxygenated in different species, some of those constituents are more common in species than others, they consist of linalool (12.70% in one species and 27.10% in another) and geranyl acetate (17.20% in one species and 12.20% in another) [12], [15].

A. biennis Willd:

All of the most frequent constituents were monoterpenes either hydrocarbon or oxygenated; they consist of: alpha-pinene= 10.20%, camphor= 24.60% and Artemisia ketone= 12.40% [16].

A. ciniformis:

General categories were: monoterpene hydrocarbon= 35.5%, monoterpene oxygenated= 23.1% and sesquiterpene= 33.9%. The most frequent constituents were: myrcene= 14.40%, p-cymene= 9.60%, camphor= 10.60% and davanone= 29.60% [17].

A. deserti Krasch:

Like other species of *Artemisia*, the most essential oil content of this species is composed of monoterpene among which two constituents were common in different experiments, they consist of: 1,8-cineole and camphor. For instance in one experiment the most frequent constituents were: 1,8- cineole= 10.40%, camphor= 18.00% and trans-thujone= 16.40 (all of them are monoterpenes) in addition, in another experiment the most frequent materials were: 1,8-cineole= 16.70% and camphor= 45.50% [18], [19].

A. diffusa Krasch:

The high percent of the essential oil content was monoterpenes (=60.70%). In this species two monoterpenes composed the most portion of the essential oil, they consist of 1,8-cineole= 25.70% and camphor 35.00% [20].

A. dracunculus L.:

In this species the most portion of the essential oil was composed of one material which is not a terpene that is methyl chavicol (84.83% of the total essential oil); yet, the percent of monoterpene (more than 10%) is more than the percent of sesquiterpene (less than 1%) [21].

A. fragrans Willd:

Various monoterpenes were found in the aerial part of this species among which 1,8-cineole (in one experiment 52.10% and in another one 23.70%) was shared; in the root of this

species two monoterpenes were the most frequent ones, they were camphene= 16.90% and camphor= 67.00% [22], [23].

A. gypsacea:

According to one evaluation, the most frequent constituents were 1,8-cineole= 36.50% and beta- thujone= 28.40% [24].

A. herba-alba:

In one experiment in the middle of Iran (Kashan city), the most frequent constituents were 1,8-cineole= 18.30% and camphor= 42.50%; in another evaluation done in the northwest of Iran (West Azerbaijan province) the most frequent constituents were camphor= 34.94% and beta-thujone= 35.66% [25], [26].

A. kermanensis:

In one evaluation on this species in the south of Iran (Kerman province), the most frequent constituents were: 1,8-cineole= 26.93% and camphor= 16.97% [27].

A. khorasanica:

In some evaluations, all of which were done in the northeast of Iran, different constituents were found in this species; however among them were some shared components. Those components consist of: 1,8-cineole (17.75% in one experiment and 33.90% in another one), camphor (13.90% in one experiment and 12.60% in another one), alpha-thujone (43.40% in one and 11.90% in another one), beta-thujone (16.20% in one and 20.10% in another one) and davanone (12.20% in one and 36.40% in another one) [17], [28], [22], [29].

A. kopetdaghensis:

According to the evaluation carried out on this species in the northeast of Iran, the general results were as follow: monoterpene hydrocabone= 46.35%, oxygenated monoterpene= 46.5% and sesquiterpene= 5.5% of the whole of the essential oil. Among different components, myrcene= 30.40%, linalool= 21.90% and camphor= 16.80% were the most frequent ones [17].

A. kulbadica:

Among 27 components were found in this species, sabinene= 25.10% and gamma-cadinene= 16.00% were the most frequent ones [30].

A. oliveriana:

According to the evaluation done in Isfahan province of Iran, the general percentiles of the essential oil were as follow: monoterpene hydrocarbon= 1.4%, oxygenated monoterpene= 95.8% and sesquiterpene= 0.0%. The most frequent components were camphor= 11.50% and alpha-thujone= 65.40% [18].

A. persica:

According to findings of this species in Iran, in addition to diverse components in different experiments on this species, the components in different parts of the plant were miscellaneous. For instance in one evaluation the most

frequent constituent was cis-davanone (60.56%) whereas in another experiment z-ocimene (39.60%) was the most frequent one. Moreover, in root of this species beta-cedren-9-one (76.70%) was found to be the most frequent component while in the flower of that plant cis-sabinene hydrate (41.20%) was the most frequent component [31],[32].

A. scoparia:

Results of the essential oil content were different in various evaluations in the north and the northeast of Iran. In one evaluation in the north of Iran, capillene (48.50%) was found to be the most frequent component; while in another evaluation in the north of Iran 1,8- cineole= 27.80%, camphor= 37.90% and borneol= 21.10% were found to be the most frequent constituents. Moreover, in the evaluation in the northeast of Iran spathulenol= 4.45% and caryophyllene oxide= 7.56% were outstanding in terms of frequency [4], [6], [33].

A. sieberi:

There were more reports on this species than the others, and those reports were from different locations of Iran (the north, northeast, west and center of Iran). Although constituents measured in different locations were not the same, there were some shared components among various locations, they consist of: camphor, 1,8-cineole and somehow alpha and beta thujone [12], [14], [22], [34], [35].

A. spicigera:

Evaluations were done in the northwest and the north of Iran; and there were some sound shared constituents, they consist of 1,8-cineole (13.89%) and camphor (20.99% and 40.00% in two experiments) [4], [36], [37].

A. splendens:

According to two independent experiments on this species there were different results in terms of the identity of the most frequent constituents. In one of them the most abundant components were alpha-pinene (11.30%), 1,8-cineole (14.50%), germacrene D (14.30%) and bicycle-germacrene (11.30%); while in another one the most abundant components were: caryophyllene oxide (3.77%), valencene (3.46%), alpha-terpinyl acetate (3.35%) and 1,8-cineole (4.68%) [11], [36].

A. tschernieviana Besser:

In one evaluation on this species the most abundant constituents were as follow beta-pinene= 17.80% and p-cymene= 21.30% (Notice that in contrast to most other species listed here, in this species the most frequent components are monoterpene hydrocarbons; whereas in the most other species the most prominent compounds are from oxygenated monoterpene group) [38].

A. vulgaris:

Again like the previous species, about this species monoterpene hydrocarbones are more frequent than oxygenated monoterpenes. In one experiment the most frequent compound was alpha-pinene (23.56%), and in

another evaluation the total monoterpene hydrocarbon was 49.90% and the total oxygenated monoterpene was 42.04% of the whole essential oil [39], [40].

III. MEDICAL IMPORTANCE OF ARTEMISIA

In this section the medical importance of *Artemisia* evaluated in Iran will be reviewed. Some of the medical characteristics are shared among species, yet some qualities in certain species are stronger as it is compared with others. Species will be discussed separately.

A. herba-alba:

Anti-leishmanial activity against *Leishmania tropica* and *L. major* in their promastigotes phase was reported [41].

A. absinthium:

Anti-leishmanial and anti-plasmodial activity as well as cytotoxic activity, which are affected by altitude of culture, were explored. Anti-leishmanial activity was reported to be underlain by natural components such as monoterpene and sesquiterpene, and the anti-leishmanial activity of the ethanol extract had a dose-dependent effect [41]. Anti-plasmodial activity was observed against multidrug-resistant and sensitive strain of *Plasmodium falciparum*; the extract of this species reduced parasitemia in BALB/C mice infected with *Plasmodium bergeri* by 94.28% [42]. Methanol extract of flower, leaf, stem and root showed considerable cytotoxic activity that may have great potential exploring new anticancer drugs; moreover, the cytotoxic effect at high altitude was 20% to 30% more as compared with lower altitude [43], [44]. We have investigated in previous studies the effect of extraction temperature and solvent type on the biochemical compounds and antioxidant capacity of *Artemisia absinthium*. HPLC results showed that extraction solvents had significant effects on anabsinthin amount. This was supported by the result that showed highest anabsinthin extraction was obtained by 75% methanol (16.58 µg/g DW), but lowest by 25% methanol (9.45 µg/g DW) [45].

A. annua L.:

Anti-leishmanial, antifungal, antibacterial, anti-plasmodial and antiviral activities were reported for this species. Likewise *A. absinthium*, anti-leishmanial activity was reported to be related to the essential oil content and also had a dose-dependent effect [41]. In one evaluation, antifungal activity of the essential oil was reported to be more than that for antibacterial activity; however, in another experiment antibacterial activity was reported against some strains such as *Escherichia*, *Subtilis* and *Bacillus*; it was recommended that the essential oil can be useful as medicinal and preservative compositions [9]. Significant anti-plasmodial activity against *Plasmodium falciparum* was reported [42]. It was reported that the extracts obtained from *A. annua* L. was maybe an appropriate candidate for further development of anti HSV1 (Herpes Simplex Virus type 1 (HSV1)) infection [46].

A. aucheri:

This plant is conventionally being used as astringent, disinfectant, antimicrobial and anti-parasitic; moreover according to new experiments, this plant has antimicrobial, antioxidant, cytotoxic and anti-proliferative as well as allergenic activity. The antimicrobial activity of this plant was observed against *Escherichia coli*, *Staphylococcus aureus* and *Listeria monocytogenes*, but in another experiment it was stated that the essential oil is more effective against gram-positive than against gram-negative bacteria. It was stated that the antimicrobial activity is related to the composition of essential oil; it was doubtfully informed that the presence of linalool or geraniol in the essential oil increased the antimicrobial activity of the oil [12], [13], [15]. Methanol extract of this species showed cytotoxic effect on brine shrimp, and antioxidant effect was detected as a lipid peroxidation and free radical inhibitor [15], [47]. One study showed the anti-proliferative effect of *A. aucheri* petroleum ether extract on malignant cell lines, and can be as a promising chemotherapeutic agent in cancer treatment [48]. According to one experiment on Guinea pigs the allergenic effect of this plant was confirmed [49].

A. ciniformis:

Anti-leishmanial, antioxidant and anti-proliferative activities of this species have been confirmed. It was believed that anti-leishmanial activity was related to content composition such as monoterpene and sesquiterpene; ethanol extract had favorable anti-leishmanial activity and killed *L. major* promastigotes in a dose-dependent manner [41]. Extracts of *A. ciniformis* protected H9c2 cardiac muscle cells against cytotoxicity induced by hydrogen peroxide through the inhibition of reactive oxygen species [50]. One study showed the anti-proliferative effects of *A. ciniformis* on malignant cell lines, but different extracts exerted various growth inhibitory effects, for instance dichloromethane and methanol extracts of *A. ciniformis* showed the highest growth inhibitory effect [51].

A. deserti:

Extract of flowering taps of this species showed minimal hepatotoxicity, but showed allergenic effect. The flowering taps extract of *A. deserti* caused several histopathological alternations; these observations indicate minimal hepatotoxicity potential of *A. deserti* in rats. It also seemed that liver tissue disorders are resolved with time [52]. Results from one study showed that the numbers of eosinophils, neutrophils and amount of IgE were increased in the treated animals with extracts compared to control groups. The results were shown to have allergenicity of 10% due to the presence of allergenicity proteins [53].

A. dracunculus:

The essential oil showed good antioxidant and somewhat antibacterial activity, and might be replaced by synthetic antioxidant and preservatives in food industry. The essential oil exhibited different degrees of inhibitory effects on the growth of tested bacterial strains; the gram-negative bacteria

especially *Serratia marcescens* and *Shigella dysenteriae* were the most sensitive ones [21].

A. fragrans:

Anti-leishmanial, antibacterial and antiviral activities of this species were confirmed; however, it didn't show any cytotoxicity. Like other species the anti-leishmanial activity of this species is related to some compounds such as monoterpene and sesquiterpene, and that is dose-dependent [41]. The antibacterial activity of the essential oil was tested on some certain gram-negative and gram-positive bacteria; the mentioned activity was observed in both bacterial groups [23]. The highest antiviral activity was found at 12.5 µg/ ml, which was 60% [46]. This species did not show any cytotoxic activity against cancer cell line; on the contrary, increased the number of cancer cells [44].

A. incana:

Two activities including cytotoxicity and antiviral were observed. Leaf methanol extract of *A. incana* was stated that could be used as cytotoxic agent [44]. The highest anti-HSV1 activity was observed at 12.5 µg/ ml, which was 50.69% [46].

A. khorasanica:

Anti-leishmanial and anti-inflammatory effects have been confirmed, but powerful anti-malarial activity has not been confirmed. Again like other species, the anti-leishmanial activity of this species is dose-dependent, and is a result of some components such as monoterpene and sesquiterpene [41]. In one study, although the study confirmed less anti-malarial effects of *A. khorasanica* against murine malaria *in vivo*, there were some evidences on reducing pathophysiology by this medication [28].

A. kulbadica:

Anti-leishmanial and antibacterial activities of this species have been shown. In one study, the ethanol extracts taken from *A. kulbadica* had one of the strongest anti-leishmanial effects among some other species of *Artemisia* [41]. The antibacterial activity was determined against six bacterial and one fungal strain, and the oil was active against all the tested strains [30].

A. Persia:

Reduction on blood pressure and heart rate were observed. Oral consumption of *A. Persia* extracts after 20 min. reduced systolic blood pressure in normotensive and hypertensive rats; also the aqueous extract of *A. Persia* reduced the blood pressure of hypertensive rats more effectively than enalapril [54].

A. santolina:

Anti-leishmanial and anti-proliferative activities of this species have been observed. Ethanol extract of this species had significant effect on *in vitro* leishmanicidal activity and may be suitable candidate in the treatment of leishmaniasis [41]. Another study showed anti-proliferative effect of *A. santolina* extract on malignant cell lines. This species could be

also considered as promising chemotherapeutic agent in cancer treatment [51].

A. sieberi:

Anti-leishmanial and antimicrobial activities as well as the inhibitory effect against *Pityriasis versicolor* have been showed. Ethanol extract of this species showed significant effect on *in vitro* leishmanicidal activity, and could be thought as a potential drug treating leishmaniasis. In another study the result indicated that aqueous extract of *A. sieberi* had anti-leishmanial effect more than pure artemisinin; the decrease in leishmania affected by the extract showed a dose-dependent style [41]. The result of a study on this plant demonstrated that *A. sieberi* 5% lotion was more effective than clotrimazole 1% lotion in the treatment of *Pityriasis versicolor* [55].

A. spicigera:

This plant showed insecticidal, antibacterial and antioxidant but not cytotoxic activity. According to one experiment, the insecticidal activity of the oil was notable [36]. In one study, studied oil had good antibacterial activity [37]. One study reported weak antioxidant activity of this species; in another study it was stated that there was a positive relationship between antioxidant activity of the oil and total phenol and flavonoid content [36]. In two of studies no cytotoxic activity of this species was reported, so based on these findings it was recommended that due to significant insecticidal property and no toxicity, this species is suitable to be utilized as natural insecticide [36].

A. splendens:

Likewise *A. spicigera*, notable insecticidal activity and no cytotoxic effect were observed, yet the relationship between antioxidant activity and total phenol and flavonoid content was shown [36].

A. turanica:

Anti-leishmanial activity and anti-symptomatic effect on mice infected by malaria were reported. The ethanol extract showed significant effect on *in vitro* leishmanicidal activity [41].

A. vulgaris:

Experiments on this species showed cytotoxic and somehow antiviral activities. Methanol extracts of flower, leaf, stem and root of *A. vulgaris* exhibited considerable cytotoxic activity. The flower extract was found to have the highest cytotoxic effect on breast cancer cell line [44]. Methanolic extract of *A. vulgaris* showed a protection rate (= ratio of viable cells to the dead cells) of 63.94% against HSV1 [46].

A. biennis:

In one evaluation, it was found that the ethanol extract of *A. biennis* showed powerful *in vitro* anti-leishmanicidal activity and may be suitable candidate in the treatment of leishmaniasis [41].

A. kopardaghensis:

In one study, like *A. biennis*, *A. kopardaghensis* showed anti-leishmanial activity. Several extracts were tested among which IC₅₀ (inhibitory concentration) was the most for hexane extract and was the least for ethanol extract [41].

A. kermanensis:

One experiment showed that the antimicrobial features of the essential oil was in full adaptation with the percent of oxygenated terpenoids, and the essential oil of aerial parts of this plant had antimicrobial activity on microorganism in urban water, so it was recommended to utilize the essential oil of this plant purifying water from microorganism [27].

A. tschernieviana:

Antimicrobial activity was determined against certain bacteria and fungus; the result showed that the essential oil was active against all tested strains [38].

A. diffusa:

The result of one study showed the anti-proliferative effect of *A. diffusa* extract on malignant cell lines, so this species could be also considered as a promising chemotherapeutic agent in cancer treatment [51].

A. compesteris:

This species showed antiviral activity against HSV1. The highest protection rate of *A. compesteris* methanolic extract was observed at concentration of 6.25 µg/ ml which was 73.32% [46].

A. chamaemelifolia:

In one study, *A. chamaemelifolia* showed the lowest activity against HSV1 among some other species from *Artemisia*. The highest protection rate of *A. chamaemelifolia* was observed at 12.5 µg/ ml concentration which was 46.53% [46].

A. persica:

This species showed anti-HSV1 activity. The high protection rate of methanolic extract of this species was observed at 12.5 µg/ ml which was 81.37% [46].

IV. CONCLUSION

Artemisia plants evaluated in this paper have different tendency producing different compounds. Although the frequency of compounds are not the same in all species, certain compounds occur more than others (such as 1,8-cineole and camphor).

When medical importance of *Artemisia* is considered, some features such as antibacterial, antiviral, anti-leishmanial and the others could be listed. The strength of these features in species is different and makes them to be suitable for a little various purposes.

As mentioned, Iran is a country inhabiting different species of *Artemisia*, and especially when the medical importance of these plants as well as different frequencies of compounds are considered, the necessity of doing research becomes inevitable. Researches should be conducted to decipher the

relationship between the effect of climate and the production level of different compounds in this genus as well as decoding the key components underlying the medical traits, so from one side the medical importance of different materials, separately and in company with other materials, could be understood and from the other side the information taken from the effect of climate on the pathways (terpene) can feed fields of science (with the view of the relationship between the frequency of a specific terpene and the surrounding climate).

ACKNOWLEDGMENT

This work was supported by the Iranian National Science Foundation (INSF) under Grant number 90002271.

REFERENCES

- [1] M. Willcox, "Artemisia species: from traditional medicines to modern anti-malarials and back Again," *J. Alter. Compl. Med.*, vol. 15, pp. 101–109, 2009.
- [2] M.J. Abad, L. Miguel Bedoya, L. Apaza and P. Bermejo, "The *Artemisia* L. Genus: A review of bioactive essential oils", *Molecules* vol. 17, pp. 2542-2566, 2012.
- [3] M.R. Naghavi, A. Dovlatyari, H. Moazzenj, H. Shahzadeh Fazeli, Diversity of the genus *Artemisia* in Iran" Accepted for publication, 2014.
- [4] A. Jalili, M. Rabie, F. Sefidkon, "Chemical composition of the essential oil of four *Artemisia* species from north of Iran", *Pajouhesh Sazandegi J.*, vol. 16, pp. 54-63, 2010.
- [5] A. Rezaeinodehi and S. Khangholi, "Chemical composition of the essential oil of *Artemisia absinthium* growing wild in Iran", *Pakistan J. Biol. Sci.*, Vol. 11, pp. 946- 949, 2008.
- [6] K. Morteza- Semnani, and M. Akbarzadeh, "Essential oils composition of Iranian *Artemisia absinthium* L. and *Artemisia scoparia* Waldst. et Kit," *J. Essent. Oil Res.*, Vol 17, pp. 321- 2005.
- [7] A. Nezhadali, and M. Parsa, "Study of the volatile compounds in *Artemisia absinthium* from Iran using HS/SPME/GC/MS," *Advan. Appl. Sci. Res.*, Vol. 1, pp. 174-179.
- [8] M.R. Vardian- Rizi, "Variation in the essential oil composition of *Artemisia annua* L. of different growth stages cultivated in Iran", *African J. Plant Sci.* Vol. 2, pp. 016-018, 2008.
- [9] A. Massiha, M.M. Khoshkolgh- Pahlaviani, K. Issazadeh, S. Bidarigh and S. Zarrabi, "Antibacterial activity of essential oils and plant extracts of *Artemisia* (*Artemisia annua* L.) in vitro", *Zahedan J. Res. Med. Sci.*, Vol. 15, pp. 14 -18, 2013.
- [10] H. Ghafouri, R. Sariri, M. R. Naghavi, E. Aryakia, A. Dolatyari, S. A. Shahzadeh Fazeli, H. Ramazani, Z. Farahmand. "Analysis of artemisinin isolated from *Artemisia annua* L. by TLC and HPLC", *J. of Liquid Chrom. & Related Tech.*, Vol. 36, pp. 1198–1206, 2013.
- [11] M. Kazemi, M.R. Zand, K. Roshanaei, M. Mehrzad and A. Rustaiyan, "Composition of the volatile oils of *Artemisia armenica* Lan. and *Artemisia splendens* Willd. from Iran", *J. Essen. Oil Res.*, Vol. 22, pp. 126-128, 2002.
- [12] M. Mahboubi, and F. Ghazian Bidgoli, "Biological activity of essential oil from aerial parts of *Artemisia aucheri* Boiss. from Iran", *Kerla Polonica*, Vol. 55, 94-97, 2009.
- [13] G. Asghari, M. Jalali, E. Sadoughi, "Antimicrobial activity and chemical composition of essential oil from the seeds of *Artemisia aucheri* Boiss; Jundishapur", *J. Nat. Pharm. Prod.*, Vol. 7, pp. 11-15, 2012.
- [14] F. Sefidkon, A. Jalili, and T. Mirhaji, "Essential oil composition of three *Artemisia* spp. from Iran", *Flav. Frag. J.* Vol. 17, pp. 150-152, 2002.
- [15] R. Dehghani Bidgoli, A. H. Ebrahimabadi, G. A. Heshmati and M. Pessarakli, "Antioxidant and Antimicrobial activity evaluation and essential oil analysis of *Artemisia aucheri* Boiss. from Iran", *Curr. Res. Chem.*, Vol. 5, pp. 1-10, 2013.
- [16] Nematollahi, A. Rustaiyan, K. Larijani, M. Nadimi and S. Masoudi, "Essential oil composition of *Artemisia biennis* Willd. and *Pulicaria undulata* (L.) C.A. meyer., two compositae herbs growing wild in Iran", *J. Essen. Oil Res.*, Vol. 18, pp. 339-341, 2006.
- [17] A. Firouzini, H. Vahedi, F. Sabbaghi, and M. Bigdeli, "Composition of the essential oil of *Artemisia ciniformis* , *A. kopetdaghensis* , and *A. khorasanica* in Iran", *J. Chem. Natur. Comp.*, Vol. 44, pp. 80-93, 2008.

- [18] A. Rustaiyan, H. Komeilizadeh, S. Masoudi, A. Monfared, M. Yari, M. Kardar and A. Shahgholi, "Composition of the volatile oil of *Artemisia deserti* Krasch. and *Artemisia oliveriana* J. Gayex DC. From Iran", *J. Sci. I. R. Iran*, Vol. 11, pp. 213-215, 2000.
- [19] M. Kazemi, S. Shafizadeh and K. Larijani, "Comparison of essential oils composition of stem, leaf and flower from *Artemisia deserti* Krasch", *J. Appl. Chem. Res.*, Vol. 18, pp. 29-34, 2011.
- [20] K. Khazraei Alizadeh and A. Rustaiyan, "Composition of the volatile oil of *Artemisia diffusa* Krasch. ex Poljak. growing wild in Iran", *J. Essent. Oil Res.* Vol. 13, pp. 185-186, 2001.
- [21] R. Sharafati Chalashtori, N. Rokni, V. Razavilar and M. Rafieian Kopaei, "The evaluation of the antibacterial and antioxidant activity of Tarragon (*Artemisia dracunculus* L.) essential oil and its chemical composition", *Jundishapur J. Microbiol.*, Vol. 6, pp. 1-5, 2013
- [22] N. Yousefzadeh, J. Zeinivand and M.H. Meshkatsadat, "Quantitative and qualitative study of bioactive compounds of essential oils of the medicinal plant *Artemisia sieberi* grown in Lorestan (Iran) by use of GC-MS technique", *Organic Chem. Curr. Res.*, Vol. 1, pp. 109, 2012.
- [23] A. Shafaghath, Y. Noormohammadi and M. Zaifzadeh, "Composition and antibacterial activity of essential oils of *Artemisia fragrans* Willd. leaves and roots from Iran", *Nat. Prod. Commun.* Vol. 4 pp. 279-282, 2009.
- [24] A. Rustaiyan, S. Balalaei, F. Mohammadi, S. Masoudi and M. Yari "Comparison of the volatile oils of *Artemisia santolina* Schrenk and *Artemisia gypsacea* Krasch., M. Pop. et Lincz. ex Poljak. from Iran", *J. Essent. Oil Res.*, Vol. 12, pp. 330-332, 2000.
- [25] A. Bamoniri, "Constituents of the essential oil of *Artemisia herba alba* in Kashan area", *Iranian J. Pharm. Res.*, Vol. 203, pp. 83, 2004.
- [26] M. Aghaei and I. Sharifian, "Chemical composition of essential oil of *Artemisia herba-alba* from West Azerbaijan, Iran", *J. Env. Agri. Food Chem.*, Vol. 10, pp. 2413- 2416, 2011.
- [27] A. Ganjali and M. Pourramezani Harati, "Antimicrobial effect of essential oil of *Artemisia kermanensis* on water by HPC method", In: International Conference on Agriculture, Chemical and Environmental Sciences Oct. 6-7, 2012 Dubai (UAE)
- [28] H. Nahravanian, B. Esmaeili, M. Kazemi, H. Nazem and M. Amini, "In vivo antimalarial effects of Iranian flora *Artemisia khorassanica* against *Plasmodium berghei* and pharmacology of its natural components", *Iranian J. Parasitol.*, Vol. 5, pp. 6 -19, 2010.
- [29] M.M. Barazandeh, "Essential oil composition of *Artemisia khorassanica* Podl. from Iran", *J. Essent. Oil Res.*, Vol. 15, pp. 259-260, 2001.
- [30] Z. Aghajani, M. Kazemi, M. Dakhili and A. Rustaiyan, "Composition and antimicrobial activity of the essential oil of *Artemisia kulbadica* from Iran", *Nat. Prod. Comm.*, Vol. 4, pp. 1231-1236, 2009.
- [31] O. Sadeghpour, G. Asghari and M.R. Shams Ardekani, "Composition of Essential Oil of *Artemisia persica* Boiss. from Iran" *Iranian J. Pharm. Res.*, Vol. 203, pp. 65-67, 2004.
- [32] B.F. Mirjalili, M. H. H. Meybody, M. M. Ardakani, A. Rustaiyan, N. Ameri, S. Masoudi and a. Bamoniri, "Chemical composition of the essential oil from aerial parts, leaves, flowers and roots of *Artemisia persica* Boiss. from Iran", *J. Essent. Oil Res.*, Vol. 18, pp.544-547, 2006.
- [33] N.M. Danesh, A. Gazanchian, M. Rahimizadeh and M. Hassanzadeh Khayyat, "Essential oil compositions of *Artemisia scoparia* Waldst. et. Kit Native to North East of Iran", *Advan. Env. Biol.*, Vol. 4, pp. 254-257, 2010
- [34] R. Dehghani Bidgoli, M. Pessarakli and G. A. Heshmati, "Comparison of essential oils in aerial parts of *Artemisia Sieberi* from Kashan Province of Iran", *J. Agricul. Sci. Tech.*, Vol. 2, pp. 392-396, 2012.
- [35] H. Azamivand, M. Chahouki and A. Zare, "Compositional characteristics of the essential oil from the aerial parts of *Artemisia sieberi* Besser" *Inter. J. Plant Res.*, Vol. 24, pp. 13- 17, 2011
- [36] F. Heshmati Afshar, A. Delazar, H. Nazemiyeh. and S. Esnaashari "Chemical composition, antioxidant, insecticidal and general toxicity activities of essential oils isolated from the aerial parts of *Artemisia spicigera* and *Artemisia splendens*" *Res. Pharm. Sci.*, Vol. 7, pp. 2012.
- [37] A. Chehregani, M. Atri, S. Yousefi, Z. Albooyeh and F. Mohsenzadeh, "Essential oil variation in the populations of *Artemisia spicigera* from northwest of Iran: chemical composition and antibacterial activity", *Biol. Lab. Plant Cell Biol.* Vol. 51, pp. 246-252, 2013.
- [38] M. Kazemi, M. Dakhili, A. Rustaiyan, K. Larijani, M.A. Ahmadi and V. Mozaffarian, "Chemical composition and antimicrobial activity of *Artemisia tschernieviana* Besser from Iran", *Phcog. Res.*, Vol. 1, pp. 120-124, 2009.
- [39] G. Tajadod, A. Mazooji, F. Salimpour, N. Samadi and P. Taheri, "The essential oil composition of *Artemisia vulgaris* L. in Iran", *Annals Bio. Res.*, Vol. 3, pp. 385-389, 2012.
- [40] M. Alizadeh, M. Aghaei, M. Saadatian and I. Sharifian, "Chemical Composition of essential oil of *Artemisia vulgaris* from West Azerbaijan, Iran", *J. Environ. Agricul. Food Chem.* Vol. 11, pp.1579-4377, 2012.
- [41] S.A. Emami, S. Zamanai Taghizadeh Rabe, A. Ahi and M. Mahmoudi, "Inhibitory activity of eleven *Artemisia* species from Iran against *Leishmania Major Parasites*", *Iranian J. Basic Med. Sci.*, Vol. 15, pp. 807- 811, 2011.
- [42] A. Ramazani, S. Sardari, S. Zakeri and B. Vaziri, "In vitro antiparasitoid and phytochemical study of five *Artemisia* species from Iran and in vivo activity of two species", *J. Parasit. Res.*, Vol. 107, pp. 593- 599, 2010.
- [43] B. Gordanian, M. Behbahani, J. Carapetian and M. Fazilati, "Cytotoxic effect of *Artemisia absinthium* L. grown at two different altitudes on human breast cancer cell line MCF7", *J. Res. Med. Sci.*, Vol. 36, pp. 124-131, 2012.
- [44] B. Gordanian, M. Behbahani , J. Carapetian and M. Fazilati, "In vitro evaluation of cytotoxic activity of flower, leaf, stem and root extracts of five *Artemisia* species", *Res. Pharm. Sci.*, Vol. 9, pp. 91-96, 2014.
- [45] H. Ghafoori, R. Sariri, M. R. Naghavi, "Study of effect of extraction conditions on the biochemical composition and antioxidant activity of artemisia absinthium by HPLC and TLC", *J. Liquid Chrom. & Related Tech.*, Vol. 37, pp. 1558-1567, 2014.
- [46] M. Khajeh Karamoddini, S.A. Emami, M.S. Ghannad, E. Alizadeh Sani and A. H. Sahebkar, "Antiviral activities of aerial subsets of *Artemisia* species against Herpes Simplex virus type 1 (HSV1) in vitro", *Asian Biomed. J.* Vol. 5, pp. 63-68, 2011.
- [47] A. Rezaei, S. ShekarForoush, S. Changizi Ashtiyani, H. Aqababa, A. Zarei, M. Azizi, and H. Yarmahmodi, " The effects of *Artemisia aucheri* extract on hepatotoxicity induced by thioacetamide in male rats", *Avicenna J. Phyt.* Vol. 3, pp 293-301, 2013
- [48] M. Ghazi- Khansari, M. Mojarrah, F. Ahmadi and L. Hosseinzadeh, " The anti-proliferative effects of petroleum ether extract of *Artemisia aucheri* on human cancerous cell lines", *J. Rep. Pharm. Sci.*, Vol. 2, pp. 150-155, 2013.
- [49] M. Babaahmadi, L. Amjad and S. Roozbehani, "The effect of allergenicity of *Artemisia aucheri* flowering taps in guinea pigs", *Intern. J. Agric. Crop Sci.*, Vol. 5, pp. 2079-2083, 2013.
- [50] M. Mojarrah, M. Jamshidi, F. Ahmadi, E. Alizadeh and L. Hosseinzadeh, "Extracts of *Artemisia ciniformis* protect cytotoxicity induced by Hydrogen Peroxide in H9c2 Cardiac Muscle Cells through the inhibition of Reactive Oxygen Species", *Advan. Pharm. Sci.*, pp. 1-5, 2013.
- [51] S. Z. Taghizadeh Raba, M. Mahmoudi, A. Ahi and S. A. Emami, "Antiproliferative effects of extracts from Iranian *Artemisia* species on cancer cell lines", *Pharm. Biol.* Vol. 49, pp. 962-969, 2011.
- [52] F. Yazdani, A. Noori and L. Amjad, "Effect of *Artemisia deserti* flowering taps extract on liver in male rats", *Intern. J. Agri. Crop Sci.*, Vol. 5, pp. 1432-1436, 2011.
- [53] M. Naemi, L. Amjad and S. Roozbehan, "A Study on the allergenicity of *Artemisia Deserti* flowering taps in Guinea pigs", *Inter. J. Agron. Plant Prod.*, Vol. 4, pp. 3296-3300, 2013
- [54] F. Esmaeili, G. Sepehri, G. R. Moshtaghi- Kashanian., M. Khaksari, N. Salari and e. Sepehri, "The effect of acute administration of *Artemisia Persia* extracts on arterial blood pressure and heart rate in rats", *American J. Appl. Sci.*, Vol. 6, pp. 843-847, 2009.
- [55] F. Rad, F. Aala, N. Reshadmanesh and R. Yaghmaie, "Randomized comparative clinical trial of *Artemisia sieberi* 5% lotion and clotrimazol 1% lotion for the treatment of pityriasis versicolor", *Indian J. Dermatol.* Vol. 53, pp. 115-118., 2008.