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A status review on the pharmacological implications of *Artemisia absinthium*: A critically endangered plant

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ABSTRACT

Medicinal plants are the nature's gift for the humanity to treat various diseases and to spend a prosperous healthy life. There are almost 500 species of *Artemisia*. Among them, *Artemisia absinthium* (*A. absinthium*) which is commonly known as wormwood is a well-known herb. It is mentioned in almost all the herbal medicinal books of the Western world. The aim of this review article is to gather information about *A. absinthium* which is currently scattered in form of various publications. Through this review article tried to attract the attention of people for therapeutic potential of *A. absinthium*. The present review comprises upto date information of active ingredients, up and down in absinthe, controversy, essential oil, traditional uses, *in vitro* production of secondary metabolites for pharmaceutical, pharmacology such as antitumor, neurotoxic, neuroprotective, hepatoprotective, antimalarial, anthelminitc, antipyretic, antidepressant, antiulcer, antioxidant, antibacterial, antiprotozoal and challenges of *A. absinthium*. Some progress has been made, but still consistent efforts are required to explore the individual compounds isolated from *A. absinthium* to validate and understand its traditional uses and clinical practices. This review article provides preliminary information and gives a direction for the basic and clinical research on *A. absinthium* (wormwood).

1. Introduction

1.1. Geographic distribution

Artemisia absinthium L. (*A. absinthium*) has been used as herbal drug throughout Asia, Middle East, North Africa and Europe. This species is native to temperate region of Eurasia, Northern Africa and widely naturalized in the United States and Canada. It is grown as ornamental plant and acts as ingredients in spirits and other alcoholic drinks[1].

1.2. Morphogenic description of A. absinthium L.

A. absinthium L. belonging to family Asteraceae commonly known as wormwood is an erect, medium sized plant (30–60 cm), with greenish silvery ovate to obovate leaves. The stem is whitish and about 24–48 cm high and hairy[2]. Roots are taproot with a diameter of 5 cm and branching extends in all directions upto 72 cm. *A. absinthium* flowering season is usually between July to October. Fruit is one seeded and indehiscent (achene) and about 1.5 cm long. The ripened fruits are not crowned by pappus[3].

1.3. Taxonomic hierarchy of A. absinthium L.

A. absinthium is known as wormwood, is highly medicinal plant and almost mentioned in all the books of herbal medicine. Wormwood belongs to family Asteraceae which is the largest family of angiosperms. *A. absinthium* belongs to Kingdom Plantae, Division Magnoliophyta, Class Magnoliopsida, Order Asterales, Family Asteraceae and Genus *Artemisia*.

1.4. Vernacular names

Wormwood is known by different vernacular names. Afsantin

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(Urdu); green ginger, absinthe, absinthium, wormwood (English); Apsinthion (Greek); *A. absinthium* (Latin); Afsanteen, Damseeh (Arabic); Ku ai, Yang ai (Chinese); Vermouth, Genepi (French), Wermut, Absinth (German); Anjenjo (Mexican); Majri, Karmala, Majtari, Mastiyarah (Hindi); Afsanteen (Unani) and Absinthium (Hemopathy)[4].

2. Active ingredients of *A. absinthium*

Phytochemically, *A. absinthium* contains absinthin, artabsin, essential oil, anabsinthin, anabsin, matricin, organic acids, lactones and resins[5]. Wormwood also possesses flavonoids such as rutin, quercetin and other flavonoid glycosides including quercitin-3-O-d-glucoside, isoquercitrin, quercitin-3-O-rhamnoglucoside, isorhamnetin-3-glucoside, isorhamnetin-3-O-rhamnoglucoside and phenolic acids (syringic, chlorogenic, coumaric, vanillic acids and salicylic acid) which are possibly involved in the mechanism of free radical scavenging assay[6]. These pharmacophores exhibit effective free radical scavenging, anti-inflammatory activity and antioxidant potential[7]. Chemically key constituents in *A. absinthium* are trans-sabinyl acetate, myrcene, and trans-thujones. The dry leaves as well as stems of this plant have 0.25%–1.32% essential oil, absinthin, matricin, artemisinin and artabsin. Thujone is considered as most important component. Thujone is less soluble in water as compared to ethanol, only 8% of thujone is recovered in water as compared to extraction in 90% ethanol.

3. The rise and fall of absinthe

Use of alcoholic decoctions of wormwood as well as other plants as remedies were in the practiced from 18th century, however, it was not up to the start of the 19th century that the alcoholic extracts of wormwood and distillates were not considered just as patent medicines, but moreover as aperitifs and the start of large degree production of absinthe.

Utilization of absinthe as medicine was still more than its utilization as recreational beverage for the duration of the French occupation of Algeria. Moreover, it was specified to the troops as precautionary measures for helminthiasis and fevers. In addition, it was considered to kill germs and ward off dysentery when mixed with the water[8]. The yearly per capita consumption of absinthe increased 15 times in France from 1875 to 1913. French utilization of pure alcohol was 15 500 hL in 1876 while it reaches 10 times more than that amount in 1908 and it was up to 239 492 hL in 1913, presenting 60l per inhabitant. Consequential effects to this mass consumption and chronic utilization of absinthe was declared to turn out into a syndrome described as absinthism, which was specified by hyper-excitability, addiction, hallucination and epileptic fits[8,9].

The main constituent of absinthe, wormwood was rapidly pronounced to be culprit. This was primarily based on animal experimentation conducted with pure extract of wormwood. Wormwood extracts if utilized in its pure form showed conspicuously different symptoms as compared to alcohol. The most believable hypothesis nowadays is that absinthism was only misidentified alcoholism, as ethanol alone can clarify all of suspected absinthe's effects[10].

4. Controversy

A banned spirit drink commonly known as absinthe is made from *A. absinthium*. At the beginning of the 20th century, the spirit was banned in most of the countries including United States as it supposed to be hallucinogenic. An important chemical which is present in the essential oil of wormwood was thujone. It was responsible for the hallucinogenic action. But in early 2000s the bans on this spirit was repealed. Switzerland was the first country who repealed its ban in 2005, making it legal once again. In 2007, two brands of this spirit were considered legal and sold in the United States.

5. *A. absinthium* essential oil

Essential oils of aromatic plants are frequently used in traditional medicine as antimicrobial agents. These are mixtures of natural volatile compounds mostly isolated by steam distillation. Several essential oils proved to possess significant antimicrobial activity against bacteria, yeasts, dermatophytes plus aspergillus strains. These essential oils have high therapeutic potential, generally in diseases like cutaneous, mucosal and respiratory tract infections. The major constituents of many of these oils are phenolic compounds including terpenoids, phenylpropanoids, thymol, eugenol, and carvacrol[11]. *A. absinthium* oil is mainly composed of beta-thujonecis-sabinyl acetate (chamazulene, nuciferol butanoate, nuciferol propionate, caryophyllene oxide, beta-ocimene, (Z)-anethole and limonene. Strong inhibitory effects has been observed on the growth of bacteria and fungi. The oil also revealed antioxidant activities[12,13]. *A. absinthium* oil is characterized by having high amounts of trans-sabiny-l-acetate (26.4%), myrcene (10.8%) and trans-thujone (10.1%). Monoterpene esters and sesquiterpenes are also present in *A. absinthium* oil. The oil yield from the aerial parts of *A. absinthium* mostly ranges from 0.3% to 0.5%.

6. Pharmacology–Medicinal uses

In the middle Ages, this plant is regarded as a broad remedy for all diseases owing to its curative medical powers. The aerial part of *A. absinthium* possesses strong anti-snake venom activity[14]. Antimalarial and anticancer activities are the most well-known biological effects accounted for different species of the genus *Artemisia*[15,16]. This species found its medicinal potential because of its tremendous insecticidal, vermifuge, diuretic, antispasmodic, and trematocidal properties. It proves its effectiveness in curing diarrhoea, cough and common cold[17,18]. The medical use of absinthism is also proved by the freshly published monograph of the

European Medicines Agency[19]. The European Medicines Agency has proposed that medicinal properties of this plant are mainly due to presence of its constituent thujone. Daily intake of 3.0 mg/person is proved to be acceptable for a maximum duration of 2 weeks. Presently, it is somewhat unclear that how much thujone is present in medically used wormwood formulations. Wide variations are expected because of the natural thujone variation in wormwood. Approximately 0%–71% thujone is found in the essential oil of wormwood.

6.1. Antitumor activity

Cancer is still one of the most devastating diseases throughout the world including Pakistan. Among various types of tumors, breast cancer is the most common demoralizing disease in the entire world with high incidence and mortality rates. The risk prevalence and differences in the comparative risk were explained by various factors, mainly dietary factors[20]. However, at the present scenario, the efficacy of existing drugs is limited, and antitumor agents that usually have multiple targets in the apoptotic cascade, so synergistic measures are immediately requisited. Numerous phytochemicals have been used in the clinical practices of cancer chemotherapy. These phytochemicals obtained from plants particularly from herbs, such as alkaloid, etoposide, paclitaxel and camptothecin[21]. Definite compounds from certain foods have been reported to reduce the breast cancer proliferation through cell cycle arrest and apoptosis. The toxicity effects of *Artemisia* species on cancerous cells have been shown *in vivo*[22] as well as *in vitro*[23]. Various antitumor substances such as flavonoids, cesquiterpen lactones and terpenoids were extracted from *Artemisia* species. A derivative of artemisinin, artesunate, showed both *in vivo* and *in vitro* antitumor effects[24]. Extract from *Artemisia* species has anti-angiogenic effects to starve tumor cells. The methanolic extract of *A. absinthium* on MCF-7 and MDA-MB-231 cell proliferation was checked. These cells were treated with different concentrations of *A. absinthium* for almost 3 days. The extract of *A. absinthium* at 20 g/mL caused 50% inhibition in MDA-MB-231 cells and 50% inhibition in cell proliferation of MCF-7 cells at 25 g/mL as compared to the control[25].

6.2. Neurotoxic and neuroprotective activity

Regarding the renowned neurotoxic uses of wormwood, the headline of article showed that wormwood has neuroprotective consequence on reperfusion-provoked cerebral damage[26]. The outcomes of animal based experimentations showed promising potential and expectantly lead to a resurgence of investigation on wormwood designed to validate the ethnological along with traditional uses of plant. Promising consequences on Crohn's disease relating to the beneficial therapeutic utilization of wormwood were also attained in earlier studies[27].

Stroke is the second important leading reason of casualty all over the world and believed as the most universal cause of disability in adults[28]. It is anticipated that stroke is accountable for about 102 000 per annual casualty cases in India, which signifies about 2% of the total mortality in the country. Whereas in USA, the occurrence of stroke is expected approximately 750 000 annually with deaths of 150 000 per year. The main patho-biological mechanism of ischemia and reperfusion harm includes oxidative stress, apoptosis inflammation and excite-toxicity[29]. These changes are linked with mitochondrial dysfunction resulted into the quick drop off in ATP concentration, follow-on decrease in free radical production and per-oxidation of lipid. Oxidative stress is a major responsible factor in cerebral ischemia and reperfusion damage[30].

Ethnopharmacological literature provides evidences about the utilization of *A. absinthium* in Pakistan and Europe as an antispasmodic, antiseptic, cardiac stimulant, febrifuge, for inflammation of the liver, to improve memory and most importantly for the restoration of falloff mental function. *A. absinthium* improves the cognitive ability as evidence by its muscarinic and nicotinic receptor activity in homogenates of cerebral cortical membranes of humans. Extracts of *A. absinthium* exhibit free radical scavenging activity both *in vivo* and *in vitro*. Furthermore, ethanol extract of the plant increased neurite outgrowth which was induced by PC12D cells and the nerve growth factor. Conventional Chinese medicine practitioners utilize the plant to deal with neuro-degenerative disorders, cancers and acute bacillary dysentery[31].

6.3. Hepatoprotective activity

Hepatic ailments are one of the major serious health issues throughout world nowadays, but regardless of remarkable advances in the modern medicine, their prevention options and treatments still remain inadequate. However, pathogenesis of liver disorders in response to the inflammation and oxidative stress has been well ascertained[32]. Therefore, blockage or retardation of the chain reactions of inflammatory process and oxidation considered as efficient therapeutic approach for prevention as well as treatment of hepatic injuries. In recent times, the most frequent and well recognized *in vivo* model used for the investigation of novel hepato-protective agents is rodent model of hepatic disorders induced via CCl_4 which is a hepatotoxin that triggers hepato-cellular damage mediated by free radicals[33]. *A. absinthium* extracts reveal strong *in vitro* antiradical activity as well as antioxidant potential and moreover anti-parasitic potential in animal based models[34].

One of a chemical hepatotoxin; carbon tetrachloride is identified in animal model to provoke the features analogous to acute hepatitis in the human being. While on the other side, immunological hepatic issues model reveals clinical situation of the hepatitis more appropriately. As it is renowned, immune mechanisms have a very significant role in initiation and also in progression of number of hepatic diseases, such as drug and alcohol based hepatitis and severe viral induced hepatitis[35].

6.4. Antimalarial activity

The incidence of malaria in different regions of the globe was due to appearance of strains resistant to antimalarial drugs together with lack of vaccine. Therefore, it is necessary to go on with investigations for naturally and new synthetic occurring antimalarial. Among various species of *Artemisia*, the most potential antimalarial activity was reported from *Artemisia annua*. Wormwood also showed antimalarial activity. *Plasmodium falciparum* is causal agent of malaria in humans was inhibited from the sesquiterpene lactone fraction as well as from the aqueous extract of *A. absinthium*. The aqueous extract of *A. absinthium* at the dilution of 1:35 showed maximum inhibition percentage (89.9%). The LD_{50} value was 31.4 μg/mL of sesquiterpene lactone fraction[36].

6.5. Anthelmintic activity

There are several factors that need to be highlighted as alternative strategies to control parasite because the broad spectrum anthelmintic drugs are quite costly. Investigations from different regions of the world have proved that various plant species may efficiently reduce the extent of parasite infestation and are considered to be promising alternative strategies as compared to conventional anthlmintics[37]. Thujone which has been reported from *A. absinthium* showed anthelmintic activity. In Turkish folk medicine, *A. absinthium* has been used as anthelminitic, tonic, diuretic, treatment of stomach aches, antiseptic and antipyretic. In comparison to albendazole, anthelmintic efficacy of crude ethanolic extracts and crude aqueous extract of aerial parts of wormwood against the gastrointestinal nematodes revealed that crude ethanolic extract and crude aqueous extract have significant anthelmintic effects on live *Haemonchus contortus* worms. *A. absinthium* is considered to be an effective natural alternative remedy for parasite control both in humans as well as in animals[38].

6.6. Antipyretic activity

An investigation showed that fever induced in rabbits through yeast injection, by using an esophageal probe, the application of diverse fraction of wormwood was reduced to a certain extent[39]. Different reports suggested that water soluble, hexane and chloroform extract of wormwood exhibited antipyretic activity. The plant extract of wormwood upto 1.6 g/kg has documented no side effects[39].

6.7. Antidepressant activity

In the clinical practice, depression is considered to be the 2nd most chronic condition and up to the year 2020, it will become the 2nd leading cause of disability and premature birth worldwide. More or less two-thirds of the depressed and nervous victims counter to the existing treatments but it is disappointing regarding the magnitude of improvement. Although, nowadays there are various efficient antidepressant available[40]. Traditional medicinal plants have been assessed for psychotherapeutic potential against depression in various animal models. The investigations showed the antidepressant activity in tail suspension test and forced swimming test by using *A. absinthium* at flowering stage and it considerably reduced the immobility period both in tail suspension test as well as in forced swimming test[41].

6.8. Antiulcer activity

The investigations showed that various solvent extracts such as carbon tetrachloride, chloroform, methanol, ethanol and hexane of *A. absinthium* had shown antiulcer effects in rats. The acetyl-salicylic acid was responsible for inducing ulcer in rats. The study showed reduction in ulcer index, increase in level of mucin, reduction in peptic activity and decrease in gastric juice volume[42].

6.9. Antiprotozoal activity

Numerous medicinal plants are used to treat various gastrointestinal disorders such as dysentery and diarrhea which are particularly common in rural areas throughout the world. Different factors which are influencing the development of these infections include population explosion, infections of reservoirs, poor sanitary conditions and insufficient vectors control. Two protozoa *Giardia lamblia* and *Entamoeba histolytica* are responsible for these symptoms[43].

The antiparasitic drugs which have been evaluated against the pathogenic protozoa often have severe side effects. The more recent focus has been paid on extract derivatives from plants which are used in traditional medicines. The potential of plants as a source against protozoa attracted a considerable attention in the development of new drugs such as quinine, artemisinin and emetine, which are isolated from various plant species[43]. Due to the presence of artemisin, ethanol and aqueous extract of *A. absinthium* showed growth inhibitory effects against *Naegleria fowleri*. *A. absinthium* also contained oxygenated monoterpene camphor, which showed anti-leishmanial activity against axenic amastigote and promastigote forms of *Leishmania donovani* and *Leishmania aethiopica*[44]. Wormwood also exhibited antiprotozoal activity against *Leishmania donovani*, *Leishmania infantum*, *Plasmodium falciparum* and *Trypanosoma cruzi*[45].

6.10. Antioxidant activity

Reactive oxygen species eagerly assault and persuade oxidative damage to various biomolecules such as DNA, proteins, lipids and lipoprotein. This damage is considered to be vital factor in different chronic diseases of human such as diabetes mellitus, cerebrovascular diseases, rheumatism, cancer and cardiovascular diseases[46]. The existing therapeutic approaches often have severe side effects such as strong host immune response and cytotoxicity to normal cells. Therefore, there is a requirement of usefulness of antioxidant to protect against chronic diseases. Antioxidants are considered as chemical substances that lessen and prevent oxidation. Antioxidants have the ability to protect from the damaging effects of radicals

in tissue. They are supposed to counteract against heart disease, tumor, arteriosclerosis, cerebrovascular diseases and various other diseases[47].

Phenolic compounds may have direct contribution in the antioxidant activity. A strong relationship exists between antioxidant activities and phenolic compounds which have been produced in various plants *in vitro*. The presence of phenolic compounds in various medicinal plants has been known to possess antioxidant potential[48].

Wormwood contains various flavonoids such as rutin and quercetin, phenolic compounds (vanillic acid, chlorogenic salicylic acid, coumaric and syringic) are possibly involved in the mechanism of free radical scavenging activity. These pharmacophores have been known to possess anti-inflammatory activity, potent antioxidant and free radical scavenging activity. It is considered that *A. absinthium* improve the cognitive aptitude, as it is known to possess muscarinic receptor and nicotinic activity of human cerebral cortical membranes. The 2,2-diphenyl-1-picrylhydrazyl-free radical scavenging activity in *A. absinthium* was found to be independent on biomass accumulation in callus culture but it is dependent on secondary metabolites production. Maximum accumulation of total flavonoids (0.48 mg quercetin equivalent/g dry weight), total phenolics (1.48 mg gallic acid equivalent/g dry weight) and the highest antioxidant activity (63.3%) was observed from 35-day-old callus culture[49].

6.11. Antibacterial activity

A. absinthium is extensively grown in Turkey, Europe and Asia. It produces a green-bluish essential oil. The most important ingredients of this essential oil are; b-myrcene, b-pinene, *endo*-bornyl acetate and a-fenchene. Many *Artemisia* species have a distinguishable scent and taste, based on sesquiterpenes and monoterpenes that are mainly responsible for their utilization in folk medicine. The methanolic extract and acetone extracts of *A. absinthium* reveals no antibacterial potential. *A. absinthium* extracts (50 mL) against different specific bacterial strain possess same effects[50]. Accordance to an investigation, ethanol extracts of *A. absinthium* branches inhibit *Staphylococcus aureus* with inhibition zones 10–15 mm in diameter, however, not shown antibacterial potential against *Candida albicans, Escherichia coli, Streptococcus faecalis* and *Bacillus subtilis*[50].

7. Traditional uses

It is a renowned traditional herb, stated in almost all books of herbal medicine in the Western world[51]. A most popular drink absinthe is prepared from this plant, and is consumed to raise creativity and excitement. This plant has strong anthelmintic properties that is why it has been given the name "wormwood" by the ancient Egyptians. The word absinthe is derived from Greek word apsinthion, meaning "undrinkable". Traditionally, this word is used in French for the plant species plus for the alcoholic beverage. The famous Greek mathematician and philosopher, Pythagorasof Samos (569–475 B.C.), experimented that wine-soaked wormwood leaves used to lessen labor pains. Hippocrates (460–377 B.C.) utilized wormwood extracts for the treatment of rheumatism as well as to alleviate menstrual pain. Traditionally, the plant has been used as diuretic, anti-helmintic, antiseptic, depurative, choleretic, balsamic, emmenagogue, digestive and in treating sclerosis and leukaemia[52]. Several *Artemisia* species are also used as spices and in folk remedies as antiseptics. Powdered leaves of *A. absinthium, Artemisia frigid, Artemisia ludoviciana* and *Artemisia biennis* have been externally applied in salves and washed by North American native people for curing sores and wounds as well as taken to treat chest infections.

8. *In vitro* production of secondary metabolites for pharmaceutical

Plant secondary metabolites are recognized as unique sources for pharmaceuticals, flavors, food additives and other industrial materials eitheras a raw material or as a part of final product. Among various classes of secondary metabolites, polyphenols comprise the major group of innate antioxidants[53]. Flavonoids and phenolics possess biological properties like anti-carcinogen, anti-aging, antioxidant and protection from brain dysfunctions, *viz.* Huntington's diseases, Parkinson's, Alzheimer's immune/autoimmune and cardiovascular diseases[54].

Secondary metabolites from plants have important biological and pharmacological activities, such as anti-oxidative and anti-carcinogenic. The biological activities of phenolic compounds and flavonoids are associated to their antioxidant potential.

The role of flavonoids in the anticancer and antimalarial as well as antioxidant activities has been reviewed by using the extract of *Artemisia*[55]. Callus culture and cell suspension cultures are the effective ways for the production of secondary metabolites which have various therapeutic potential. To study the production and growth kinetics, cell suspension cultures are proposed to be simple system to implement and evaluate the most favorable scheme for the production of medicinal compounds in good quantities[56]. Light regimes play a significant role in all the fundamental process of plant and fundamental building blocks like primary and secondary metabolism, growth and development[56]. By optimizing *in vitro* conditions like light regime, production of secondary metabolites can be proficiently stimulated. Various stimulatory effects of light regime have been observed for the accumulation of secondary metabolites such as artemisinin, anthocyanins, derivatives and flavonoids[57]. Light is very crucial as the inhibitory and stimulatory effects for the production of secondary metabolites.

Total flavonoids and phenolics contents in callus culture of wormwood were not preferably dependent on growth and biomass accumulation. Initial boost in the total flavonoid contents and total phenolic contents was observed on the 21st day. However, peak values, 0.48 mg quercetin equivalent/g dry weight (4.1–fold increase) of total flavonoids content and 1.48 mg gallic acid equivalent/g dry weight (4.9–fold increase) of total phenolic content,

were observed on Day 35[58]. Various medicinal plants have been exploited via callus culture for the investigation of total phenolic content[59]. Various researchers reported that during the log phase of callus culture, the highest flavonoids content was observed in various medicinal species including *A. absinthium*[60].

Under continuous dark and light, total phenolic content was found to adopt various growth phases from the cell suspension cultures of *A. absinthium*. Under continuous light, peak values for total phenolic content and total phenolics production were observed as 5.32 mg/g dry weight on 24 day and 42.96 mg/L on 27 day. Other scientists also reported the increased production of total phenolic content in callus culture of *A. absinthium*[61].

9. Challenges in conservation, sustainable use and way to forward

A. absinthium is considered as highly medicinal plant as it is mentioned in all the books of herbal medicine in Western world. Due to high demand, most of natural population of *A. absinthium* is under severe pressure at the present scenario. Due to excessive exploiting of this species, it is declining day by day. Due to the various known uses of this herb, there is a high demand at local and international level pharmaceutical industry. During the last decade, this species has attained a considerable attention because it is critically endangered and will become extinct in upcoming years if exploited at the same rate. So there is a need of sustainable use of this highly medicinal species.

A multidimensional approach is required to maintain and includes selection of better quality genotype and *ex-situ* as well *in-situ* conservation followed by multiplication both by conventional as well as biotechnological methods that could provide solution to the existing problem. The *in vitro* plantlets regeneration is an effective method for plant conservation from the wild plant such as *Solanum villosum*[62] to highly economic plant species like *Citrus reticulata*[63]. The importance of any medicinal plant depends on its active ingredients which is present in that species. It would be desirable to carry out cultivation of elite clones. The superior clones can be approved by the use of various molecular markers techniques and chemo-profiling. The conventional methods of propagation as well as plant tissue culture techniques can be used to multiply and raise the commercial plantation for conservation. Tissue culture can be employed as substitute to conservative methods *in vitro* propagation with the purpose of increasing the developmental rate of preferred genotypes and commercial micropropagation[64]. The conservation of highly medicinal plants species which include in the threatened category should be given prior focus[65-67]. This technique is helpful in the production of millions of healthy, vigorous and disease free plants in less time, space, labor and with less cost. Besides, *in vitro* propagation, cell suspension culture is useful for the large scale production of secondary metabolites.

Post-harvest handling is another factor upon which the quality of plants is dependent. The collectors of herbal material pay less attention to quality of material during harvesting, handling and storage. It has been found that herbal drugs samples which are stored harbor mycotoxin producing fungi. Cultivation practices also need to be addressed. Due to genetic and environmental differences wild harvested plants vary in consistency and quality. Regional environmental conditions also influence the efficacy of medicinal plants. Some of the factors such as temperature, photoperiod, soil characteristics and rain fall have severe effects on the production of active constituents. Therefore, consistent efforts should be taken for the sustainable management of medicinal plants such as *A. absinthium* at community level.

10. Conclusion

The present review article focuses on the phytochemistry, absinthe, controversy, essential oils, toxicological information, traditional uses, pharmacological studies, challenges and sustainable use of *A. absinthium*. In the recent years main focus is on the phytochemical studies which have attained a considerable attention to get familiar with many unknown and known ingredients of clinical importance that can be screened for their therapeutic potential to treat severe health disorders without any side effects. Therapeutic potential of *A. absinthium* has been exposed which is crucial for standardization and further consideration as medicine at safer level. However, there is a need to evaluate the therapeutic potential on modern scientific lines through clinical trials, phytochemicals and pharmacological studies. Experimental studies have demonstrated its anticancer/antitumor, neurotoxic and neuroprotective, hepatoprotective, antimalarial, anthelmintic, antipyretic, antidepressant, antiulcer, antibacterial, antiprotozoal and antioxidant activities. Looking at the broad spectrum of *A. absinthium* for various purposes, it is useful to cultivate this plant at large scale. *A. absinthium* is indexed in critically endangered category, so consistent efforts should be made to protect this plant species to become extinct. A multidimensional approach is required to maintain and includes selection of better quality genotype and *ex-situ* as well *in-situ* conservation followed by multiplication both by conventional as well as biotechnological methods that could provide solution to the existing problem.

Conflict of interest statement

We declare that we have no conflict of interest.

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