Chapter 3
Artemisia indica Willd.: Ethnobotany, Phytochemistry, Pharmacological Attributes, and Safety Profile

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Abstract The present book chapter is about the phytochemistry, pharmacological properties, and ethonobotanical, safety, and toxicological aspects of the species, *Artemisia indica*. This genus *Artemisia* belonging to Asteraceae family comprises of more than 400 species, among which *A. indica* (also called mugwort) is a perennial medicinal herb found majorly in cold temperate zones of Asia including Pakistan, China, India, Thailand, Korea, Japan, etc. It is extensively utilized by the traditional people in many countries for treating Malaria, chronic fever, dyspepsia, ringworms,

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hepatic diseases, and diarrhea-like health problems. Artemisinin is one of the prime phytochemical components accountable for the potential antimalarial activity, found in this species. Besides this, the plant comprises chiefly sesquiterpenes and davanone in its volatile oil. Modern pharmacological studies have revealed that its crude extracts exhibit a wide range of pharmacological activities such as anti-inflammatory, anthelmintic, anticancer, antidiabetic, antimicrobial, antidepressant, and many more as a result of the existence of several bioactive components in it. Few toxicological evaluation have documented on this species but in depth experiments, safety, and toxicological evaluation are needed to explore medicinal properties of this species more.

Keywords *Artemisia indica* · Asteraceae · Traditional uses · Phytochemical components · Artemisinin · Pharmacological properties

3.1 Introduction

Humans have depended on plant kingdom for their daily need which is as old as the humans' existence in the world. The plant kingdom includes all the important medicinal flora, and these are used for ages to treat various diseases. Almost 87% human diseases or problems are cured with naturally occurring compounds, derived from medicinal herbs, and their allied medicines (Hussain 2020). One of such important medicinal plant is the genus *Artemisia,* commonly known as "worm wood." This genus is a member of Asteraceae family comprising more than 400 species (Adewumi et al. 2020). One of the mostly known species of this genus is *Artemisia indica*, commonly called "mugwort" or Indian wormwood. This common perennial herb generally spreads in forest edges, grasslands, abandoned lands, roadside, fallow fields, etc. very quickly. This species is found in India, China, Nepal, Pakistan, Thailand, Japan, Korea, and many more cold-temperate regions of Asia; and in most of the regions, this plant is commonly called as "Titepati" (Jassal et al. 2019; Shimono et al. 2013). It is suitable for medium loamy and light sandy soils with well drainage system. This plant can be sometimes annual or woody subshrub that spreads through rhizomatous root-stock. The stem ranges from

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80–150 cm tall, with many branches. Leaves are either stalkless or short – stalked and ovate, elliptic, or oblong-ovate shaped. Flowers are erect, ovoid or oblong-ovoid, bisexual, and borne in conical. Fruit is achene type and brown obovoid or oblong shaped. These plants are hardier and aromatic. It is generally propagated by seeds, also by stolon (Ken Fern 2022; Flowers of India 2021). This species had been widely utilized traditionally in many countries to treat many diseases and health problems like dyspepsia, hepatic diseases, chronic fever, diarrhea, ringworms, wounds, Malaria, and many more (Adewumi et al. 2020; Nigam et al. 2019; Bhattarai 2020). This plant primarily comprises of sterols, terpenoids, acetylenes, coumarins, flavonoids etc.; among these oxygenated sesquiterpenes and davanone are the main compounds found in its volatile oil (Adewumi et al. 2020; Haider et al. 2014). Because of its various biologically active components, it shows numerous pharmacological activities like antimalaria (main activity because of its component artemisinin), anticancer, anthelmintic, antiseptic, inflammatory, antioxidant, and many more; and these activities can be shown at specific safe doses of its extracts. So, the purpose of this study is to discover the traditional and folk medicinal uses, phytoconstituents, pharmacological activity, clinical studies, and safety and toxicity related to this study of *A. indica* in more details.

3.2 Traditional Uses

One of the most necessary health sources is traditional medicinal system in the entire world (especially the developing countries), derived from beneficial medical plants or herbs. *A. indica* is one of those beneficial perennial herbs, found in the different regions of Western Himalayas with the familiar name "Titepati." Local people of this region used this herb for ages to heal dyspepsia, hepatic diseases, and also for chronic fevers (Adewumi et al. 2020). This plant had majorly utilized by the local peoples of China, Nepal, Pakistan, India, Thailand (especially for Malaria), and several other countries or areas of southeast Asia in medicines to treat various ailments (Nahid et al. 2017). In Nepal, the juice of this plant had been utilized in treatments of abdominal pain, diarrhea, ringworms, wounds, cuts, leech infestation, and dysentery. Different parts of this plant had been eaten here such as cooked young leaves were consumed with Barley, also with rice to add some color and flavors. Here, the dried leaf and flowers were used as insecticides and the juice of the leaf were used to heal the skin ailments (Rashid et al. 2013; Nigam et al. 2019). Local peoples of Eastern Nepal, this species along with some other plant species had been found in a survey to treat many infections or infestations such as for helminths, fever, diphtheria, malaria, scabies, gonorrhea, etc. (Bhattarai 2020). In Okinawa, a famous island of Japan in whole world for the presence of long-lived individuals in abundance, it was utilized as an important food plant with some other plants (Niwano et al. 2009). In Xishuangbanna of China, Dai people uses various plants as mosquito repellent but *A. indica* was found to be the most effective mosquito repellent, especially in the cases of Dengue (Gou et al. 2020). In South Uganda, this plant was used as pesticide or for pest control by the local peoples (Mwine et al. 2011). In northeast areas of Pakistan, leaves of this species had been used medicinally by their indigenous peoples, especially for ear problems (Afzal et al. 2009). In Assam, also it had been found to be used by the local people of Tejpur as antimalarial drug to treat malaria and associated symptoms such as fever, headache, sweating, joint pains, weakness, vomiting, and shivering (Namsa et al. 2011). Fried tender shoots of this plant were also reported to eat as a vegetable food by the indigenous people of Garo in Norkek-Biosphere Reserve of Meghalaya state of India, through a survey (Singh et al. 2012). In another state of India, Darjeeling, it was used to cure asthma, amoebic dysentery, helminthic infections, several skin, and stomach problems (Tiwary et al. 2015). Young leaves had also been consumed as vegetable by the indigenous people of different areas (like Arunachal Pradesh) of India (Joram et al. 2021). The flowering shoots and leaves had been documented to show several pharmacological efficacies such as anthelmintic, antispasmodic, anti-septic, cytotoxic, antimicrobial, and anticancer (Rashid et al. 2013). Usage of *A. indica* traditionally in different places is given below in Table 3.1.

3.3 Chemical Constituents (Fig. 3.1)

A. indica represents a rich source of numerous biologically active components, responsible for various pharmacological activities. Quantitative and qualitative composition of these compounds differ hugely that might be linked with species variation; climatic, geographic, genetic, and environmental conditions; vegetation phase; anatomical part and age of plant; soil; method and season of harvesting; etc. (Nigam et al. 2019). This plant chiefly comprises of sterols, terpenoids, acetylenes, coumarins, flavonoids, etc. Oxygenated terpenes (among all terpenes) and hydrocarbons are present in this plant in abundance out of all the components in its volatile oil (Rather et al. 2017; Adewumi et al. 2020). In its essential oil, total 32 compounds had been reported to be found from Uttarakhand Himalaya, isolated and evaluated by GC and GC/MS method, among which oxygenated sesquiterpenes in 33.83% and davanone in 30.8% were the main compound. Besides this two, monoterpene hydrocarbons in 25.90%, sesquiterpene hydrocarbons in 20.54%, and oxygenated monoterpenes in 15.15% were found. Other major components found were β-elemene, β-pinene, β-myrcene, δ-cadinene, τ-muurolol, germacrene-D, trans-caryophyllene, cymene, limonene, linalool, 1,8-cineol, sabinene, etc. (Haider et al. 2014). Some previous studies in this region had shown that essential oil of *A. indica* were lacking the component davanone; even not present in traces (Shah and Rawat 2008). Besides these components, Artemisia ketone, ascaridole, borneol, transverbenol, alpha thujone, p-cymene, chrysanthenyl acetate, cubebene, caryophyllene oxide, terpineol, eucalyptol, isoascaridole, camphor, etc. were also found to be present in its volatile oil (Satyal et al. 2012; Rashid et al. 2013). Diverse solvent extracts had been isolated from the leaf of this species and assessed by HPLC-MS and HPLC-DAD method which showed flavonoids like casticin,

Table 3.1 Traditional use of *A. indica* in different places

Places	Parts used	Uses	Reference
Ilam, eastern Nepal	Whole plant	Treatment of fever, diphtheria, malaria, scabies, gonorrhea, measles, hyperthermia, sore throat, food poisoning, helminthic and lice infections	Bhattarai (2020)
Norkek biosphere, Meghalaya, India	Tender shoots	Fried and eaten as vegetable	Singh et al. (2012)
Northern Pakistan	Leaves	Used in medicines, especially for ear problems	Afzal et al. (2009)
Xishuangbanna, China	Whole plant	Mosquito repellent, mostly in dengue	Gou et al. (2020)
Tejpur, Assam	Whole plant	For malaria and associated symptoms like joint pain, shivering, weakness, fever, headache, and sweating	Namsa et al. (2011)
Nepal	1. Young leaves 2. Dried leaf and flowers	1. Consumed with rice and barley 2. As insecticides and for treating skin ailments	Rashid et al. 2013; Nigam et al. (2019)
Chuadanga, Bangladesh	Leaves	Treatments of leukorrhea, i.e., white discharge in urine of females	Rahmatullah and Biswas (2012)
Western Himalaya	Whole plant	For treating dyspepsia, hepatic ailments, and chronic fevers	Adewumi et al. (2020)
Swat, Pakistan	Aerial parts	Used as anthelmintic	Ahmad et al. (2013)
Darjeeling, India	Whole plant	Cure asthma, amoebic dysentery, helminthic infections, several skin, and stomach problems	Tiwary et al. (2015)
Khimi, Central Nepal	Especially the young leaves (besides, the whole plant)	Use in medicines	Sigdel et al. (2013)
Okinawa, Japan	Whole plant	As food plant	Niwano et al. (2009)
Gilgit-Baltistan, Pakistan	Different parts of whole plant	As foods, fuels, ornaments and for medicinal use	Hussain (2019)
Arunachal Paradesh, India	Young leaves	Consumed as vegetable	Joram et al. (2021)
Bagmati watershed, Nepal	Leaves	As insecticides to repel moths and other insects in order to prevent infestation of foods, clothes, furniture, etc.	Joshi and Joshi (2004)

cirsilineol, eupatin, and chrysoplenetin in it. These are all polymethoxy flavonoids (Tasdemir et al. 2015). In *A. indica*, exiguaflavanone-A, exiguaflavanone-B, maacklain, 2-(2,4-dihydroxyphenyl)-5,6-methylenedioxybenzofuran, and artemisinin were isolated and discovered to show the antimalarial activity as major

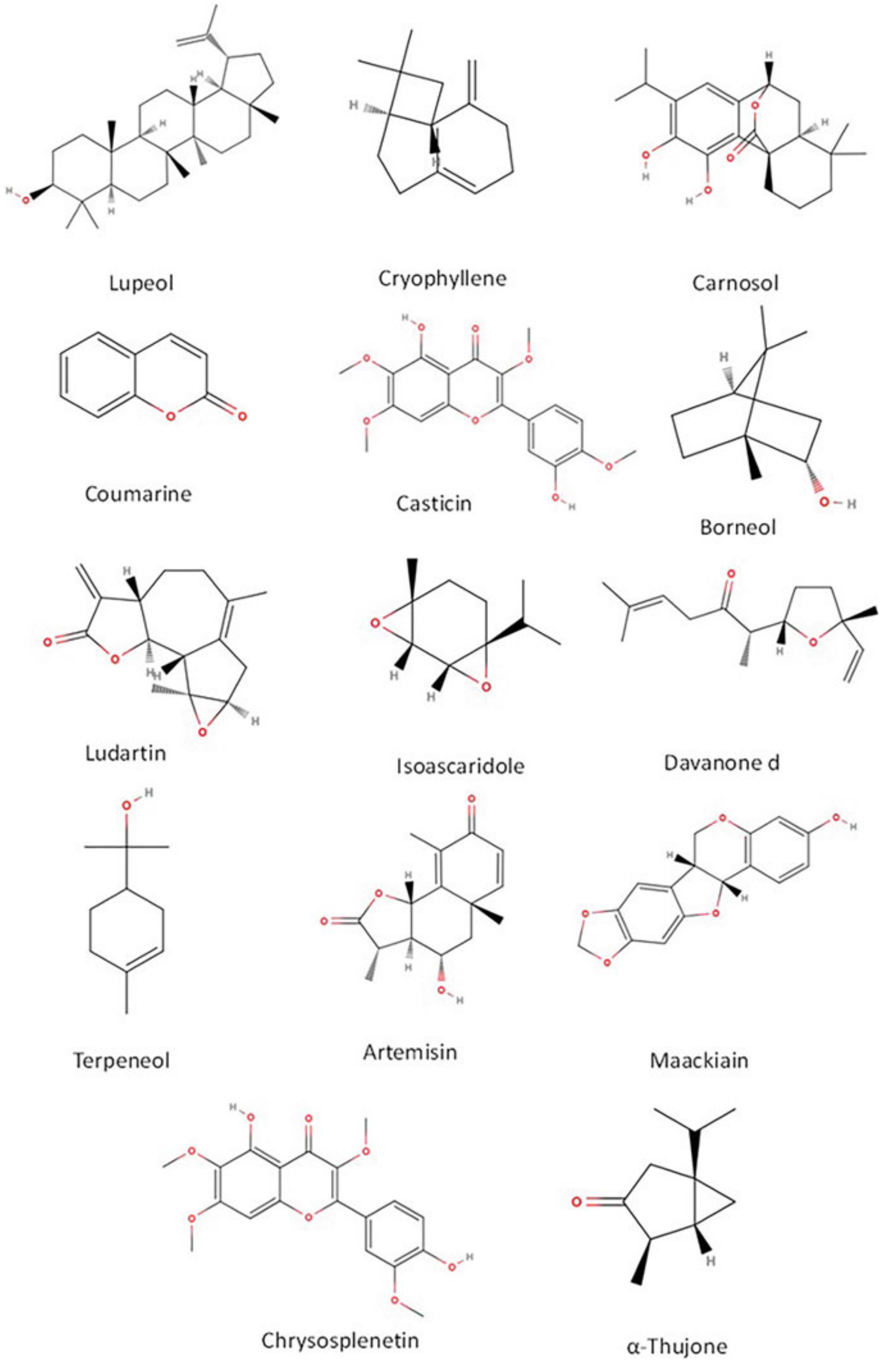

Fig. 3.1 Structures of the Phytochemical Found in *A. indica*

compound responsible for its antimalarial activity (Chanphen et al. 1998; Mannan et al. 2011). From the root and shoot, various compounds had been isolated and identified through bioassay-guided fractionation method such as 5-hydroxy-3,7,4-′-trimethoxyflavone, 6-methoxy-7,8-methylenedioxy coumarin, cis-matricaria ester, lupeol, maackiain, ludartin, cis-matricaria ester, and trans-matricaria ester (Zeng et al. 2015). Various components, isolated from various parts of the plant, are shown below with its pharmacological attributes in Table 3.2.

3.4 Pharmacological Activities

This medicinal plant is industrially very crucial as it exhibits diverse pharmacological properties from its different parts. Some of these activities are mentioned below in brief (Fig. 3.2).

3.4.1 Antimalarial Activity

It is used majorly in malaria, caused by protozoa *Plasmodium sp*., mostly by *Plasmodium falciparum* (Saxena et al. 2003), as antipyretic to reduce the fevers. An effective antimalarial drug artemisinin, derived from the leaves of its species which is an endoperoxide sesquiterpene lactone (Mannan et al. 2011). This artemisinin had been produced through different cultures such as callus, hairy shoot, and root cultures. One of these cultures had been experimentally proven to show increased amount of artemisinin. In such experiments with hairy root cultures of *A. indica* in liquid medium, it was found that artemisinin content increased (0.042%) in its transformed roots after transformed by T- DNA of *Agrobacterium rhizogenes* strain (Mannan et al. 2008). Another research on *A. indica* showed other two components—exiguaflavanone A and B—to have in vitro antimalarial effect. These components were isolated and purified by the crude MeOH extracts, obtained from the air-dried stem. Then their antimalarial activities were evaluated by their effective concentration (EC_{50}) values (Chanphen et al. 1998).

3.4.2 Anticancer Activity

Cancer is the serious worldwide public health issue, mostly because of its lacking in early detection methods. So anticancer activities generally help to prevent or suppress the carcinogenic development (Chanda and Nagani 2013). Study on 50 μg/mL ethanol extract of leaf of *A. indica* in MTT, trypan blue exclusion assays, and morphological assessment showed that these extracts had inhibited more than 50% of human breast adenocarcinoma (MCF7) growth, human cervix adenocarcinoma

Table 3.2 Various components with its different pharmacological activity, isolated from different parts of *A. indica*

Components	Plant parts	Pharmacological activity	Reference
Lupeol	Shoot	Antiprotozoal, antitumor, apoptotic	Zeng et al. (2015); Gallo and Sarachine (2009)
Caryophyllene	Oil from aerial parts	Hypolipidemic, analgesic, anti-cancer, anti-inflammatory, preventing alcoholic steatohepatitis and osteoclastogenesis	Baldissera et al. (2017); Jassal et al. (2019)
Carnosol	Leaf	Antidiabetic and anti-hyperlipidemic; antioxidant; anti-microbial; antidepressant; anxiolytic	Khan et al. (2017); Nahid et al. (2017); Khan et al. (2016)
Coumarin	Root	Antitumor, anticancer, anticoagulant, antibacterial, anti-inflammatory, apoptotic	Zeng et al. (2015); Xu et al. (2015)
Casticin	Aerial parts	Anti-inflammatory, antitumor, anticancer, immunomodulatory, anti-hyperprolactinemia	Chan et al. (2018); Jassal et al. (2019)
Borneol	Oil from aerial parts	Antibacterial, antifungal, antioxidant, anticancer, antidepressant	Rashid et al. (2013); Hou et al. (2017)
Ludartin	Shoot or aerial parts	Antitumor, apoptotic, anti-inflammatory, recovery in spinal cord injury	Zeng et al. (2015); Xu et al. (2019)
Isoascaridole	Leaf	Cytotoxic, allelopathic, insecticidal, analgesic, antinociceptive activity	Satyal et al. (2012); Jaffal and Abbas (2019)
Davanone	Oil from aerial parts	Insect repellent, fumigant, antispasmodic	Hu et al. (2019); Jassal et al. (2019)
Terpineol	–	Anti-diarrheal, gastro-protective, anti-spasmodic, anti-hyperalgesic activity	Sadraei et al. (2015); Souza et al. (2011); Oliveira et al. (2016); Negreiros et al. (2019)
Artemisin, maccklain, exiguaflavanone	Stem, leaf	Antimalarial	Chanphen et al. (1998); Mannan et al. (2011)
Chrysoplenetin	Leaf	Antimalarial, anti-parasitic, anti-cancer, antioxidant, inhibition of enterovirus 71 replications	Tasdemir et al. (2015); Ferreira et al. (2010); Zhu et al. (2011)
α-Thujone	Aerial parts	Pro-apoptotic, cytotoxic, antiangiogenic, synergistic effects	Torres et al. (2016); Lee et al. (2020)

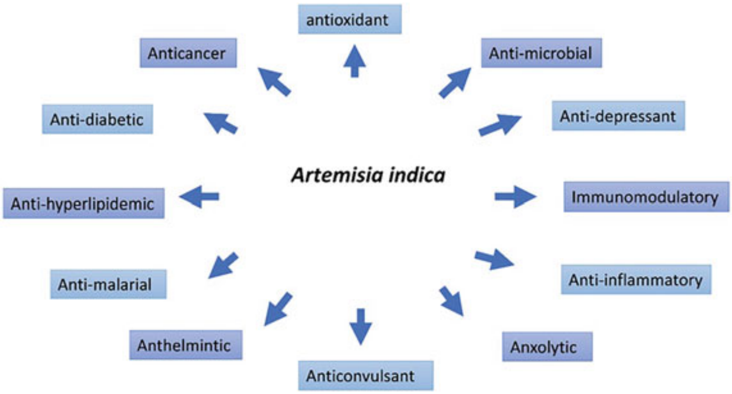

Fig. 3.2 Different pharmacological activities of *A. indica*

(HeLa), and human hepatocarcinoma (HepG2) cell lines (Tiwary et al. 2015). Another study on aerial parts of *A. indica* had been done by sulforhodamine-B assay to know its cytotoxic effects on leukemia (THP1), lung (A-549), liver (HEP-2), and colon (Caco-2) cancer cell lines. This study revealed that essential oil, extracted from these extracts, had significantly inhibited these cell lines' growth in the dilution range of 10–100 μg/mL with 19.5 μg/mL IC_{50} value for Caco-2, 10 μg/mL IC_{50} value for THP-1, 15.5 μg/mL IC_{50} value for HEP-2, and 25 μg/mL IC_{50} value for A-549 (Rashid et al. 2013). Other reports suggest that ethyl acetate extract of this species showed anticancer activity by decreasing the mitochondrial membrane potential and by inducing the DNA damage against lung (A-549), colon (Colo-205), human breast adenocarcinoma (MCF-7), and BHY and Miapaca cancer cell lines. Ludartin and lupeol had been found in this study to be the major component, responsible for this activity (Zeng et al. 2015).

3.4.3 *Antidiabetic and Antihyperlipidemic Activity*

Diabetes is another major issue (a metabolic disorder) in the world now as insufficient blood sugar regulation creates serious health concern. It is generally distinguished by chronic hyperglycemia, i.e., high blood sugar, because of the disabilities in insulin action and secretion (Salehi et al. 2019). An evaluation study on these activities of *A. indica* in 50 mg/kg diabetic Sprague-Dawley rats induced with streptozotocin had been performed. This study showed that 200 and 400 mg/kg b.w. hydroethanolic crude extracts and 200 mg/kg b.w. chloroform extracts of aerial parts of the plant had reduced the blood glucose levels considerably. It showed antihyperlipidemic (high lipid levels in blood) activities by reducing the cholesterol levels, serum creatinine, lipoproteins, and triglyceride levels (Ahmad et al. 2014). In reports of Jassal et al. (2019), oleanolic acid and carnosol had been found to have antidiabetic activities, whereas caryophyllene had found to treat hyperlipidemia, i.e., high lipid in blood (Jassal et al. 2019). 1–100 mg/kg b.w. carnosol, present in chloroform extracts of *A. indica*, was found in recent studies to lower the blood glucose levels, cholesterol, triglycerides, low-density lipoproteins, and creatinine levels in diabetes-induced rats (Khan et al. 2017).

3.4.4 Anthelmintic Activity

Helminths, the parasitic worms, create the most common infections (helminthic infections) in men. So anthelmintic drugs destroy or expel these parasitic worms which are present in large numbers, majorly in gastrointestinal (GI) tract (Das et al. 2011). Many experiments had been performed to show this activity in *A. indica* plant. One such investigation on crude aqueous, chloroform, and methanolic extracts of this species had been done against the healthy Indian earthworm, *Pheretima posthuma* where 2.5 mg/mL chloroform and methanol extract had shown efficient anthelmintic effect against the earthworm. The former one showed paralysis and death time of 9.67 and 20.67 min respectively, whereas the later one showed 19.67 and 25.33 min for paralysis and death respectively (Sarnim et al. 2013). Another study was done to scientifically prove its activity with 3.75, 6.25, 12.5, 25, and 50 mg/mL concentrations, accompanied by positive control with 10% albendazole and negative control with PBS. This resulted in the highest anthelmintic activity of *A. indica* at 50 mg/mL concentration of ethanolic extracts by different assays such as egg hatch inhibition, larval mortality, and adult worm mortality (Khan et al. 2015).

3.4.5 Antidepressant and Anxiolytic Activity

Antidepressant drugs have been used to decrease the symptoms of psychological disorders, especially the depressive disorders, by rectifying the chemical imbalances of vital neurotransmitters (common link of communication between nerve cells) in the brain that can improve the behavior and mood during these disorders. They generally increase the levels of neurotransmitters (e.g., selective serotonin reuptake inhibitors) around the nerves (Ogbru 2021). An anxiolytic drug has been used to treat anxiety disorders almost in the same way. Some investigations on nonvolatile components of *A. indica* had been done in mouse models to understand its efficacy on the function of central nervous system (CNS). The outcome of these investigations showed that oleanolic acid, carnosol, and ursolic acid, isolated from this species, had induced the anxiolytic (through light or dark box paradigms and elevated plus maze tests) and antidepressant (through forced swim and tail suspension tests) activities in mouse without any signs of toxicity (Khan et al. 2016).

3.4.6 Antimicrobial Activity

Antimicrobial activity is activity of all the active agents that can cease the microbial growth or can inhibit or destroy their colonies or may kill them directly (Elmogahzy 2020). This species has thus shown effectively this antimicrobial activity, especially antibacterial and antifungal activity. Study on antimicrobial activities of *A. indica*, *Tecoma stans*, and *Medicago falcata* in vitro had shown that chloroform, ethyl acetate, and butanol extracts of *A. indica* have 15–20 mm inhibitory effects towards *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Escherichia coli* bacteria, whereas it showed 12–14 mm inhibitory activities against bacterium *Salmonella typhi*. Chloroform and n-hexane extracts of *A. indica* had been shown antifungal activities against *Fusarium solani* and *Aspergillus flavus*, respectively, by completely ceasing their growth (Javid et al. 2015). Another investigation to understand the antimicrobial activity of *A. indica* was done on the essential oil, extracted from the aerial parts of the plant. Total 43 phytoconstituents had been found through GC-MS and GC-FID analysis, among which 42.1% artemisia ketone, 8.6% germacrene, 6.1% borneol, and 4.8% cis-chrysanthenyl acetate were the major components to show notable antibacterial activities, mostly against gram-negative bacteria like *Pseudomonas aeruginosa* and *klebsiella pneumonia* and antifungal activities against fungal strains such as *Pseudomonas chrysogenum* and *Aspergillus niger* (Rashid et al. 2013). Leaves of *A. indica* had also been reported to show antileishmanial activity against the protozoan parasite *Leishmania* sp. (which creates leishmaniasis), due to the presence of artemisinin compound in it (Ganguly et al. 2006).

3.4.7 Anti-Inflammatory Activity

Many reports suggested that this species has ability to reduce inflammation. Inflammation generally occurs in response to the cell death, degeneration, cancer, ischemia, and tissue injury or due to the invasion of microbes in the body (Azab et al. 2016). Research on anti-inflammatory action of methanol extract of aerial parts of *A. indica* by carrageenin-induced rat paw edema, a well-established model of assessing chronic inflammation, was done. This research had revealed that methanolic (100, 200, and 400 mg/kg) extracts had notably inhibited the carrageenin-induced paw edema in rats. Flavonoids had been reported to be responsible for this anti-inflammatory activity as it can inhibit the prostaglandin synthesizing enzymes (Mansouri et al. 2015; Sagar et al. 2010). Other reports suggested that saponins, tannins, casticin, and terpenoids (like carnosol, caryophyllene), present in *A. indica* extracts, showed anti-inflammatory activity because of its effect of inhibition on inflammation (Ruwali et al. 2015; Jassal et al. 2019).

3.4.8 Immunomodulatory Activity

Modulation of immune system (defense system of our body) denotes any change in the immune response such as expression, stimulation, inhibition, or amplification of any phase of the immune response. So immunomodulators are used to modify to alter this immune response of the system (Abood et al. 2014). Major information is reported about its immunomodulatory action but in vitro experiments are few. One experiment on methanolic fresh aerial parts of this plant had been performed through B and T lymphocyte proliferation assay in lymphocyte culture of chicken. The results suggested that 200 μg/mL extracts had significantly increased the regulation of B cell proliferation at 11.76% and T cell proliferation at 12.018% in the presence of LPS (B cell mitogen) and Con A, respectively (Ruwali et al. 2015). Casticin had been reported as one of the most responsible phyto-constituent for this activity in *A. indica* (Jassal et al. 2019).

3.4.9 Antioxidant Activity

Prevention of developing reactive oxygen species and their reactions, thereby inhibition or limitation of oxidation of nutrients like proteins, lipids, is called antioxidant activity (Guclu et al. 2021). These reactive oxygen species can also bring about necrosis, apoptosis, and oxidative stress. Thus, antioxidants can prevent all these distress from these harmful substances. Methanolic extracts of leaves of *A. indica* had been evaluated in vitro by DPPH free radical scavenging assay and revealed to consist antioxidant activity because of the existence of phenol and flavonoid in significant quantity (Nahid et al. 2017). Essential oil, collected from its aerial parts, was also reportedly found to have antioxidant activities, after studying through hydroxyl and DPPH radical scavenging assays (Rashid et al. 2013).

3.4.10 Anticonvulsant Activity

Anticonvulsant drugs, also known as anti-epileptic or anti-seizure drugs, have been used to prevent the convulsions or seizures by either decreasing the excitation or enhancing the inhibition. *A. indica* was investigated for its anticonvulsant activity and found as an effective drug for it. Few studies had been done on non-volatile compounds such as ursolic acid, oleanolic acid, and carnosol which had been assessed for this effect on GABA-A receptors in mouse models of convulsions, induced by pentylenetetrazole (PTZ). The result of this assessment showed that 10 mg/kg carnosol, 30 mg/kg ursolic acid, and 100 mg/kg oleanolic acid had effectively increased the span of onset and reduced the span of clonic-tonic seizures and also gave 100%, 83.37%, and 66.7% protection, respectively. In this assessment, 1 mg/kg diazepam had been used as reference drug (Khan et al. 2016).

3.5 Studies Related to Safety and Toxicity

Medicinal plants or natural herbs have been the chief remedy for almost 100 years ago to treat numerous diseases, and 25% of the medicines (those are recently used/ modern medicines) are primarily utilized by these herbs. Generally, these herbs have been regarded safe because of its long history of use in traditional medicines, but still nowadays this safety has been a major concern for both of the general public and the national health authorities. On the other hand, toxicity is the capability of substances to cause toxic or harmful effects in living beings. It can be acute, chronic, subacute, and subchronic type (Mensah et al. 2019). So besides of safety, toxic doses of these herbs must have assessed and are also the major concern. Extracts of *A. indica* have also specific safe and toxic doses of showing particular pharmacological activities. No such toxicity of this plant was found, but in some cases dermatitis or different allergies can occur in people (Foster and Duke 2020). Some reports suggested that crude hydro-methanolic extracts at 200 mg/kg body weight and 400 mg/kg body weight; chloroform extracts at 200 mg/kg body weight of *A. indica* had shown to decrease the blood glucose levels. So, these doses were safe and did not produce any harmful changes or effects in the diabetic rats induced by streptozotocin, but the extract at 2000 mg/kg body weight dose had shown few irritations and escape behavior in rats (Ahmad et al. 2014). Other studies on anthelmintic activity of this species, 6.25 mg/L methanol and chloroform extracts and 2.5 mg/L chloroform extracts were found to show significant positive effect against *Pheretima posthuma*, but the toxic doses were not evaluated that much (Sarnim et al. 2013). In an in vitro study, 0.3–1.6 mg/mL methanolic extracts had also shown 54.72% cytotoxicity in chicken lymphocytes, and 0.2 mg/mL extracts had shown complete cell viability (Ruwali et al. 2015).

3.6 Conclusions and Future Recommendations

Humans rely on medicinal plants for their daily need for years and investigations on these plants have been in attention more for scientists in recent days. *Artemisia* is one of such genera that is very beneficial medicinal plant, but the species, *A. indica*, is not that much explored till now. So, this chapter covers its history of traditional uses in different places for different diseases and its photochemistry, vast pharmacological activities, and clinical studies with safety and toxicity. Various phytochemical components have been isolated from the plant and identified which has enormous health benefits. Several studies on the extracts of *A. indica* have shown that it has numerous pharmacological properties such as antimalarial, antitumor, anticancer, anthelmintic, antihyperglycemic, anti-inflammatory, anticonvulsant, antidepressant, and many more. Many in vitro and in vivo experiments are mentioned regarding to its different pharmacological properties. This plant is generally is considered only as a weed and has been neglected but many more medicinal uses, and experiments should be performed and established on it. In recent times, research interests have been shifted towards the exploration of biologically active components or natural components for the health benefits so various phytochemical components from different plant parts of *A. Indica* should be assessed more to know and understand it's health benefits. To use it more efficiently and before the clinical applications, the toxicity or safety levels or doses should also need to be evaluated. When this plant has already gained attention in the world because of its traditional uses to combat malaria, this information summarized in this chapter thereby is proposed to act as a reference tool to the people interested in this plant and to others for understand the importance of this beneficial plant, also for performing several experiments and research on it to understand it more.

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