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REVIEW

Phytochemistry and pharmacological activity of the genus artemisia

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Abstract Artemisia and its allied species have been employed for conventional medicine in the Northern temperate regions of North America, Europe, and Asia for the treatments of digestive problems, morning sickness, irregular menstrual cycle, typhoid, epilepsy, renal problems, bronchitis malaria, etc. The multidisciplinary use of artemisia species has various other health benefits that are related to its traditional and modern pharmaceutical perspectives. The main objective of this review is to evaluate the traditional, modern, biological as well as pharmacological use of the essential oil and herbal extracts of *Artemisia nilagirica, Artemisia parviflora,* and other allied species of Artemisia. It also discusses the botanical circulation and its phytochemical constituents viz disaccharides, polysaccharides, glycosides, saponins, terpenoids, flavonoids, and carotenoids. The plants have different biological importance like antiparasitic, antimalarial, antihyperlipidemic, antiasthmatic, antiepileptic, antitubercular, antihypertensive, antidiabetic, anxiolytic, antiemetic, antidepressant, anticancer, hepatoprotective, gastroprotective, insecticidal, antiviral activities, and also against COVID-19. Toxicological studies showed that the plants at a low dose and short duration are non or low-toxic. In contrast, a high dose at 3 g/kg and for a longer duration can cause toxicity like rapid respiration, neurotoxicity, reproductive toxicity, etc. However, further in-depth studies are needed to determine the medicinal uses, clinical efficacy and safety are crucial next steps.

Keywords Artemisia · Phytochemical constituents · Essential oil · Sesquiterpenes · Pharmacological activity · COVID-19 · Toxicological studies

Introduction

The genus Artemisia belongs to the family Asteraceae, which is one of the most prominent disseminated genera comprising of 500 diverse kinds found in Northern temperate regions of North America, Europe, and Asia (Bora and Sharma 2011). The generic name 'Artemisia' is derived from 'Artemis,' which means Diana, a Greek Goddess. *Artemisia vulgaris*, L. was employed as an essential remedy for women's sickness in folk medicament. The genus has been certified for its remedial, curative, and therapeutic medicinal virtues, employed to synthesize essential oil used in medicine, food commodities, and cosmetics (Teixeira 2004; Verma et al. 2006; Ahuja et al. 2011, 2018; Pal and Ghosh 2018). *Artemisia nilagirica* regionally designated as "Indian wormwood" pertains to the Asteraceae family (Suresh et al. 2011). It is popularly known as nagdona, which propagates up to 150 cm on nitrogenous soil in mountainous districts of India (Joshi et al. 2016). The leaves are

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5–20 cm in height, peachy, soft, dark green on apex pale green with tiny white hairs on base. It is the medicinal plant that has been described to be pre-owned over ten decades employed to treat a large number of ailments; their signs and symptoms like inflammation, diabetes, malaria, anxiety, depression and several other microbial illnesses (Mohanty et al. 2018). The plant has exploited to possess several biochemical constituents i.e., volatile oils and essential oil that is considered for the cure of diverse kinds of ailments and disabilities (Kishore et al. 2001; Singh et al. 2015; Mishra et al. 2017). It contains a sesquiterpene lactone and flavonoids used as antimicrobial, insecticidal, along with anticancer activities, also applicable to cure neurological problems, dermal infections, inflammation, and to treat epileptic disorders (Banerji et al. 1990; Shinde et al. 2016). *A. nilagirica* has confirmed to have ayurvedic as well as homeopathic remedial properties (Uniyal et al. 1985). The juice of leaflets of this plant has been used for the treatments of intestinal worms, threatened abortion, vomiting, and rheumatism (Badoni et al. 2010; Panda et al. 2018; Hijazi and Salhab 2010). Besides this, the genus artemisia species mentioned in traditional pharmacopeias of different ethnic groups. The numerous species like *A. cappilaries, A. Sacrotum, A. absinthium, A. herba alba, A. annua, A. vulgaris, A. tridentata, A. argentea, A. ludoviciana, A. Mexicana,* etc posssess impotrant therapeutic properties (Yamahara and Kobayashi 1989). Mugwort leaves and stems are used therapeutically as an acrid pungent assimilative tonic, uterine stimulant and antirheumatic (Balunas and Kinghorn 2005). Few species of the genus artemisia recommended for the treatment of gastrointestinal problems, hypertension (Zeb et al. 2018), also possess potent immunomodulatory, antihypertensive, anticancer, and anti-inflammatory properties (Lian et al. 2018; Mohanty et al. 2018). Mugwort contains secondary metabolites like flavonoids, terpenoids, saponins, and polysaccharides, etc. Arglabin is a sesquiterpene lactone found mostly in all species of Artemisia, exhibits noticeable anticancer effects against varying tumor cell lines (Adekenov et al. 1982). Artemisinin isolated from *Artemisia annua* known as "qinghaosu" is sesquiterpene lactone endoperoxide used for the prevention and cure of malaria and cancer. Several analogs such as artesunic acid, artelinic acid, arteether as well as artemether can be semi synthesized and are extremely proficient against malaria induced by multidrug-resistant *Plasmodium falciparum* (Jain et al. 2000; Abolaji et al. 2013). Artemisinin is present in leaves and flowers of the plant at a minimal amount; its dehydrated weight renders from 0.01 to 0.8%. Various procedures can be applied to increase the synthesis of artemisinin, hence, to yield it in an excess concentration to make it readily and smoothly approachable for the benefit of mankind.

In this review, we have focused on the chemical constituents, traditional uses, diverse pharmacological importance of *A. nilagirica*, *A. parviflora,* and some other allied species of genus artemisia, and our previously published article on different valuable medicinal plants (Sharma et al. 2019) encourages us to write this article. The valuable pieces of information provided in this review will help the researcher to design a safe formulation for the cure of different ailments.

Traditional uses of *Artemisia nilagirica*

Artemisia nilagirica plant is traditionally used for the cure of illness such as digestive problems, morning sickness, irregular menstrual cycle, typhoid, epilepsy, renal problems, bronchitis, and malaria, etc. (Suresh et al. 2011). The extracts of *A. nilagirica* proves an extensive range of antibacterial effects on the assessed microorganisms. It has also practiced to diminishing as well as restrain the pangs of childbirth, systematize women's menstrual irregularities, also be used as an abortifacient (Tahir et al. 2015). *A. nilagirica* was proclaimed for efficient nematicidal activity against *Meloidogyne incognita* that is a plant-parasitic roundworm (Kalaiselvi et al. 2019).

Chemical constituents of *Artemisia nilagirica*

The phytochemical assessment of *A. nilagirica* showed the presence of different phytoconstituents namely tannins, alkaloids, flavonoids, terpenoids, amino acids, glycosides, and quinines, etc. (Arokiyaraj et al. 2012; Rani et al. 2012). Numerous secondary metabolites like terpenoids, flavonoids, polysaccharides as well as saponins have been characterized as well as authenticated by using High-performance liquid chromatography (HPLC), Gas Chromatography–Mass Spectroscopy (GC–MS), and Nuclear Magnetic Resonance (NMR) (Xie et al. 2008; Avula et al. 2009).

Artemisa parviflora

Artemisia parviflora Buch is a non-aromatic, erect and tall perennial herb with versatile sessile, linear cuneate leaves, greenish-white flower heads in racemes (Rana et al. 2003). Leaves are linear-oblong much reduced terminally, panicles are terminating in the branchlets. Capitulum is cream-colored. Glabrous phyllaries and sterile disc florets are present.

Traditional uses of *Artemisia parviflora*

This plant has been traditionally employed as an appetizer, antiviral, diuretic, wound healer, anti-inflammatory,

antioxidant, and antifebrile medicine, for treatment of sores, injury, wounds, leprosy, cough, asthma, and vaginitis (Suresh et al. 2010; Ahameethunisa and Hopper 2012; Koul et al. 2017; Malik 2017). It is also reported as a fodder plant of Uttarakhand, India (Singh et al. 2008), an entire plant can be utilized to mitigate fever (antipyretic) (Bhat et al. 2013). It is also associated with the ethnoveterinary drug as an anthelmintic agent (Gupta et al. 2010). A decoction formulation of the leaves buds of the plant can be consumed with stock animals and can be applied for the treatment of roundworm infections (Kumari et al. 2009). It is frequently availed as a traditional European nostrum for the cure of amenorrhea, dysmenorrhea, and also employed as a choleretic agent (Aziz et al. 2018).

Chemical constituents of *Artemisia parviflora*

The essential oil obtained through aerial regions of *A. parviflora* from Pauri Garhwal (Uttarakhand, India) was commenced to perceive β-caryophyllene (15.3%), camphor (11.4%), germacrene D (14.7%), artemisia ketone (7.8%), 1,8-cineole (5.8%) (Haider et al. 2010; Tewari et al. 2015). The chemical constituents of *A. parviflora* Buch have been examined through Gas chromatography (GC), Gas chromatography–Mass spectroscopy (GC–MS) (Rana et al. 2003). Twenty-two chemical constituents isolated from *A. parviflora* accounts for more than 72% of the oil obtained, (Brenda et al. 2007). The medicinally active constituents were β-caryophyllene (15.3%), germacrene-D (14.7%), camphor (11.4%), ketone derivatives (7.8%), 1,8 cineole (5.8%), α-copaene (2.6%), alcohol derivatives (2.6%), terpene-4-ol (2.3%), caryophyllene oxide (1.2%), α-pinene (1.1%), sabinyl acetate (1.1%), α-humulene (1.1%). The plant also possesses sesquiterpenes and coumarin such as articanin, flavone-jacosidin, and scopoletin. (Pandey and Singh 2017; Paramakrishnan et al. 2012). In consideration of Suresh et al. (2012), it was suggested that phytochemical compositions of *A. parviflora* Roxb were reported to be flavonoids, tannins, coumarins, phenols, alkaloids sterols/terpenoids, germacrene D (Brown 2010; Amirmohammadi et al. 2014; Salehi et al. 2018; Goel et al. 2019).

Chemical constituents of genus artemisia species

Constitutional analysis of the composition of medicinal constituents of genus artemisia stated that a notable alteration in the concentration of chemical constituents is due to seasonal and atmospheric adjustments (Costa et al. 2009; Padalia et al. 2014). The genus artemisia possesses numerous therapeutic components, some important medicinally active constituents of this genus are mentioned in following Table 1 (Rashmi et al. 2014; Stappen et al. 2014; Sonker et al. 2015; Farahani et al. 2017; Hussain et al. 2017).

The various non-volatile, volatile, flavonoids, phenolic acids, coumarin derivatives, monoterpene, and sesquiterpene constituents of Artemisia species were informed (Wallaart et al. 1999; Aberham et al. 2010; Khan et al. 2016; Ahuja et al. 2018; Nigam et al. 2019) given in the Fig. 1 compound **1–16**, Fig. 2 compound **17–31**, and Fig. 3 compound **32–87** respectively.

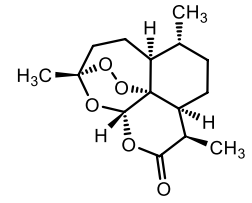
Pharmacological studies; uses in traditional medicines of genus artemisia

Infusions of leaves are employed as hemostatic to extenuate the burning sensation in conjunctivitis. The herb is also considered as an emmenagogue, anthelmintic and stomachic (Irum et al. 2017). The roots of grass acclimated as a tonic as well as an antiseptic. This medicinal herb also manifests other important therapeutic activities like antimicrobial, antiulcer, anticancer, antioxidant, asthmatic insecticidal, larvicidal, and anti-inflammatory (Ng 2004;

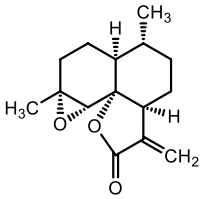
Table 1 Chemical compositions of some medicinally active constituents of genus artemisia essential oils

Compound	Relative content	Compound	Relative content
β-Myrcene	0.2	α-Phellrene	2.1
β-Pinene	0.9	Pinocarvone	3.7
α-Humulene	0.3	(*Z*)-Citral	2.1
α-Pinene	1.1	Sabinene	14.3
γ-Terpinene	0.3	Germacrene D	2.1
Caryophyllene	1.3	Camphor	22.8
Curcumene	0.4	Eucalyptol	2.3
Caryophyllene oxide	0.6	Camphene	2.7
DL-Limonene	1.1	α-Thujone	14.6
(*E*)-Citral	1.1	*trans*-Caryophyllene	16.7
Total identified	91.1		

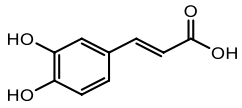
Fig. 1 Some non-volatile constituents of Artemisia species



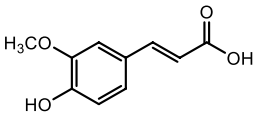
Artemisinin (**1**)



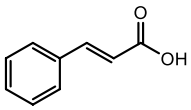
Arteanniun B (**2**)



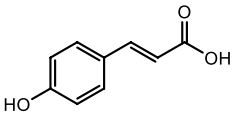
Caffeic Acid (**3**)



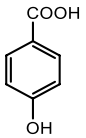
Ferulic acid (**4**)



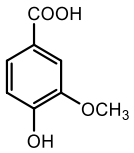
Cinnamic acid (**5**)



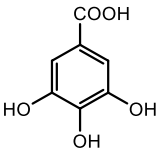
p-coumaric acid (**6**)



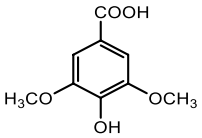
p-hydroxybenzoic acid (**7**)



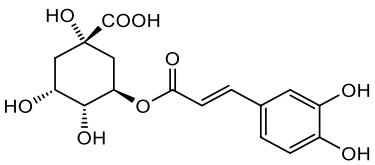
Vanillic acid (**8**)



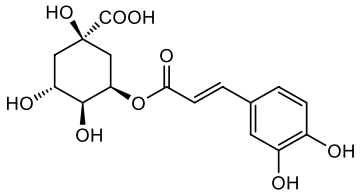
Gallic acid (**9**)



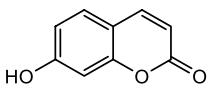
Syringic acid (**10**)



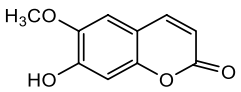
Chlorogenic acid (**11**)



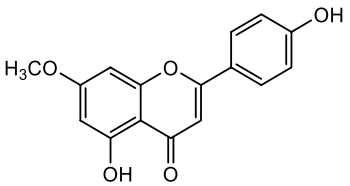
Neochlorogenic acid (**12**)



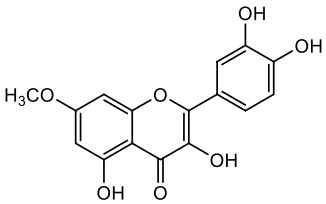
Umbelliferone (**13**)



Scopoletin (**14**)



Genkwanin (**15**)



Rhamnetin (**16**)

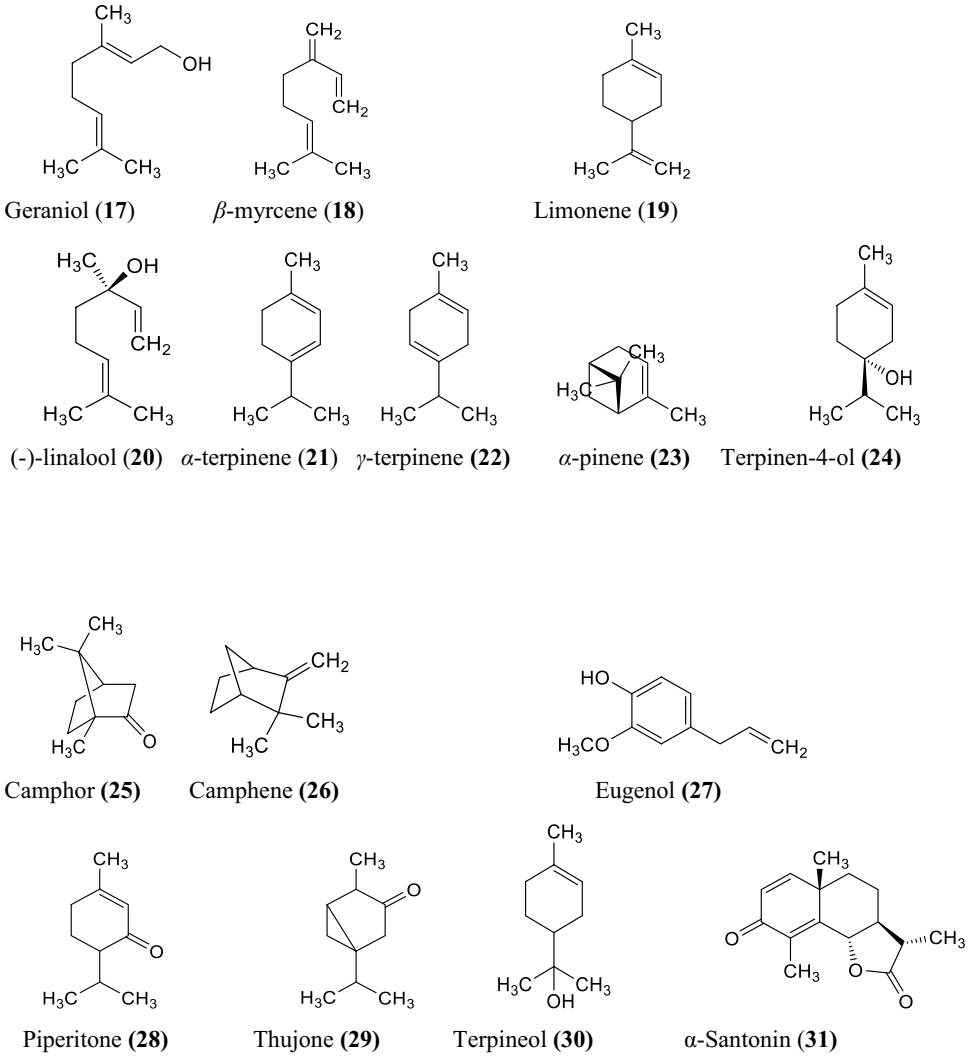


Fig. 2 Some volatile constituents of Artemisia species

Ahameethunisa and Hopper 2010; Paneerselvam et al. 2012; Naik et al. 2014; Balasubramani et al. 2018).

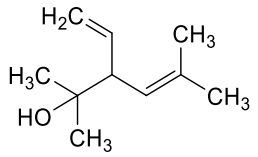
The various bacterial races, namely *Salmonella*, *Pseudomonas*, *Staphylococcus* may induce several kinds of ailments. *Pseudomonas aeruginosa* accounts for respiratory tract contamination, toxemia in patients suffering from cystic fibrosis and annihilation of the immune organization (Esen et al. 2001; Rahimi et al. 2011).

Therapeutic uses of artemisia and its allied species

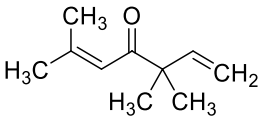
The mugwort plant showed several therapeutic applications in folk medicine that involves gastrointestinal tract like ulcer indigestion and hepatic problems (Gilani et al. 2005; Gruenwald et al. 2008; Nadeem et al. 2013). The plant is also applied in the treatment of worm infection, epilepsy, anxiety, insomnia, autonomic neurosis, general irritability, and neurasthenia, etc. It is not used during breastfeeding (Gruenwald et al. 2008; Gupta et al. 2014). The essential oil of the plant is considered to have a variety of pharmacological actions, with an extended spectrum of bioactivity, due to the presence of multiple functioning metabolites of the subsidiary chemical constituents, which promote their operation through a different mode of action (Walter and Memory 2003; Silva 2004). It also proved to be a pain killer in conjunction with acupuncture treatment, and in China, it is often employed for moxibustion (Yoshikawa et al. 1996). A powder leaves or paste is used for skin problems and also implicated as a poor alternative for cinchona for reducing the episodes of malaria fever (Haider et al. 2003; Judzentiene and Buzelyte 2006).

Utility benefits of Artemisia species in food technology

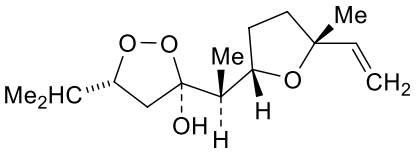
At present, there has been an increasing demand regarding the feasible utilization of medicinal plants in their natural



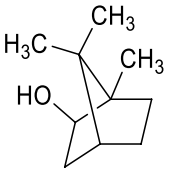
Santolina alcohol **(32)**



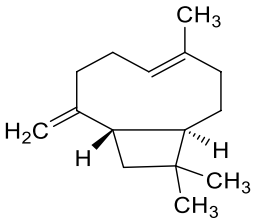
Artemisia ketone **(33)**



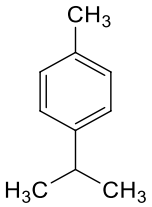
Sesquiterpene proxy hemiketal **(34)**



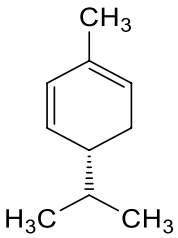
Borneol **(35)**



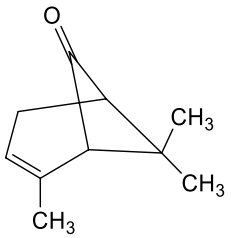
Caryophyllene **(36)**



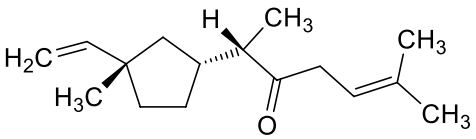
p-Cymene **(37)**



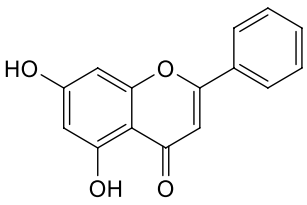
α-Phellandrene **(38)**



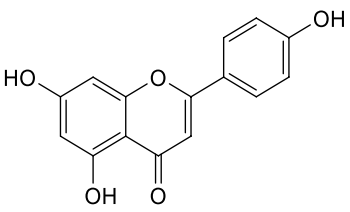
Chrysanthenone **(39)**



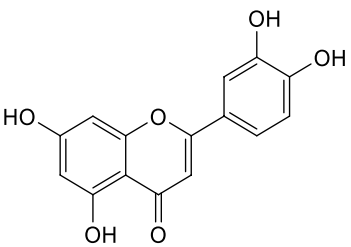
Davanone **(40)**



Chrysin **(41)**



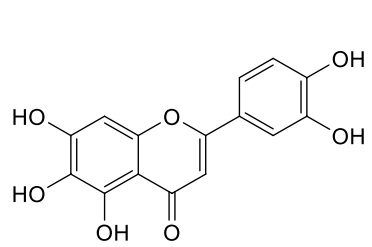
Apigenin **(42)**



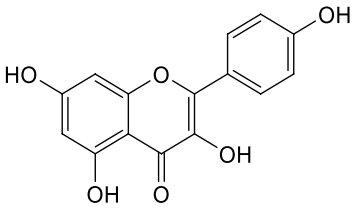
Luteolin **(43)**

Fig. 3 Some chemical constituents of genus artemisia i.e. flavonoids, phenolic acids, coumarin derivatives, monoterpene, and sesquiterpene

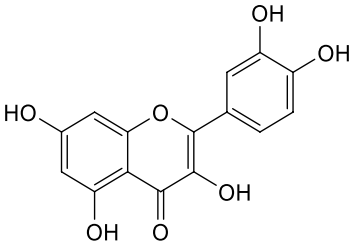
forms for pest control in the agriculture field which is less hazardous to the surroundings as well as for human health (Wang et al. 2006; Hussain et al. 2008). The essential oil of mugwort has been suggested to decrease or suppress the development of several kinds of insects, microbial parasites, and might be applied to insulate foods from spoilage.



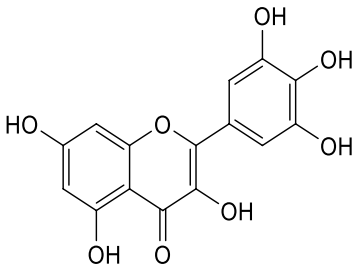
6-Hydroxy luteolin **(44)**



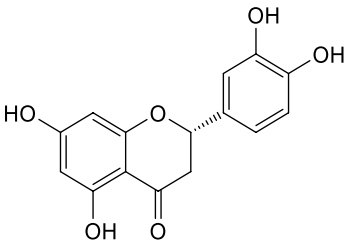
Kaemferol **(45)**



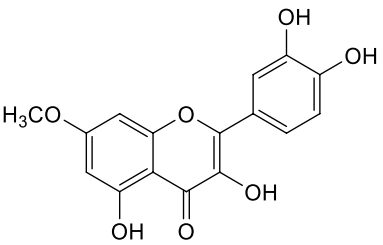
Quercetin **(46)**



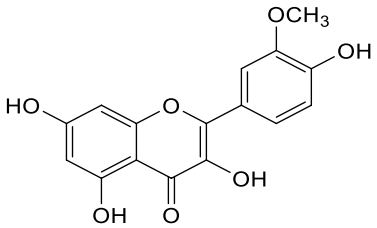
Myrcetin **(47)**



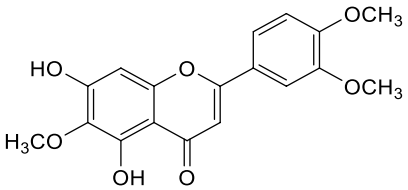
Eriodictyol **(48)**



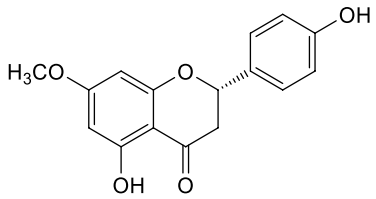
Rhamnetin **(49)**



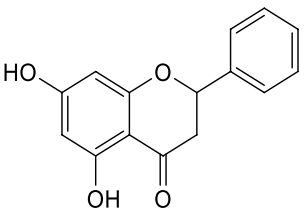
Isorhamnetin **(50)**



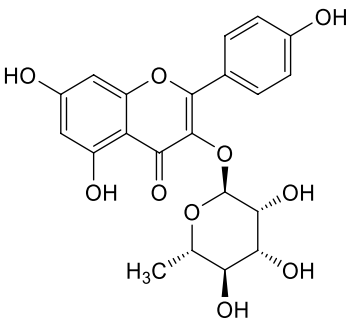
Eupatilin **(51)**



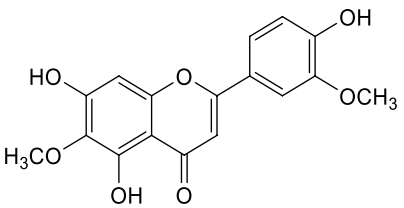
Sakuranetin **(52)**



Pinocembrin **(53)**

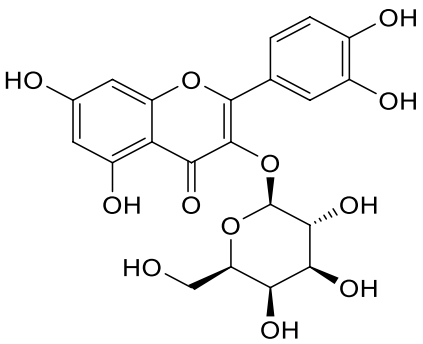


Kaempferol-3-*O*- rhamnoside **(54)**

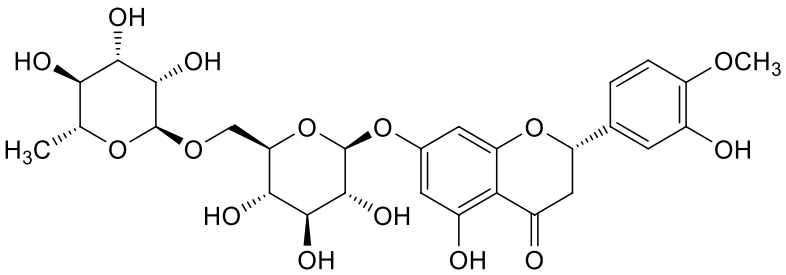


Jaceosidin **(55)**

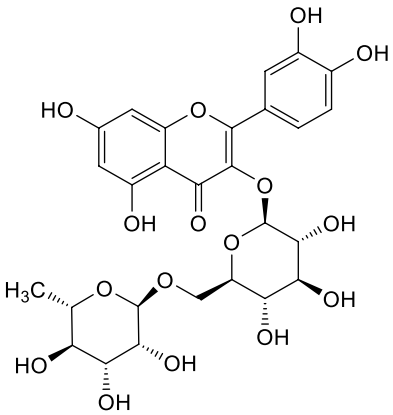
Fig. 3 (continued)



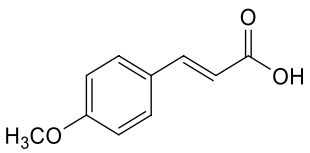
Hyperoside **(56)**



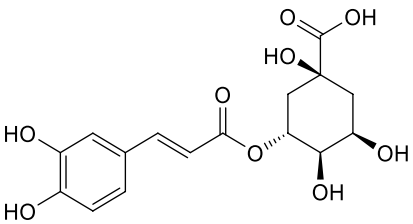
Hesperidin **(57)**



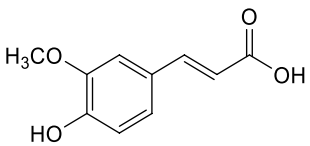
Rutin **(58)**



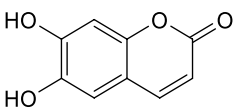
4-methoxycinnnmaic acid **(59)**



Chlorogenic acid **(60)**

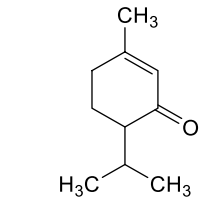


trans-ferulic acid **(61)**

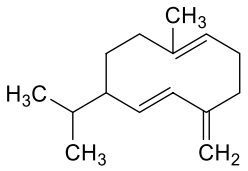


Esculetin **(62)**

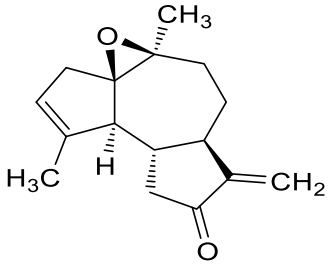
Fig. 3 (continued)



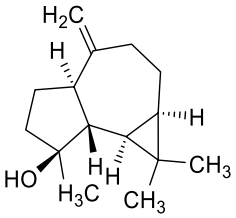
Piperitone **(63)**



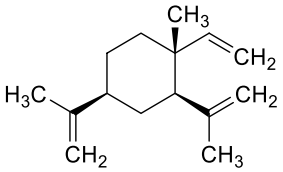
Germacrene D **(64)**



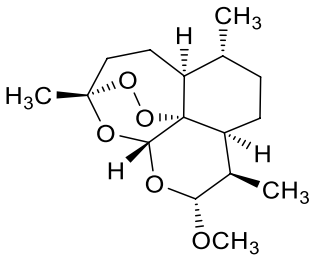
Arglabin **(65)**



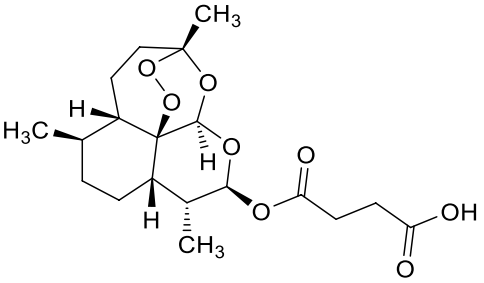
Spathulenol **(66)**



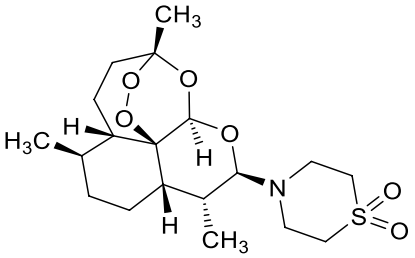
β-elemene **(67)**



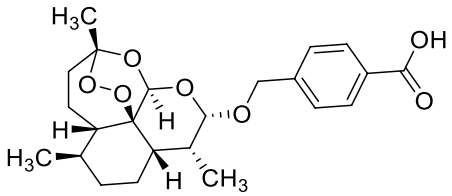
Artemether **(68)**



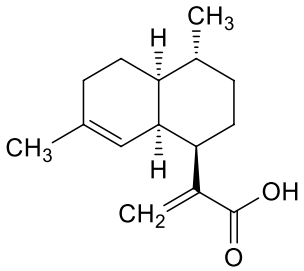
Artesunic Acid **(69)**



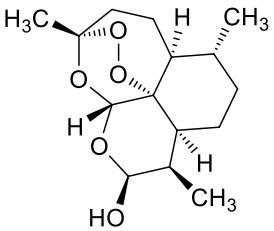
Artemisone **(70)**



Artelinic acid **(71)**

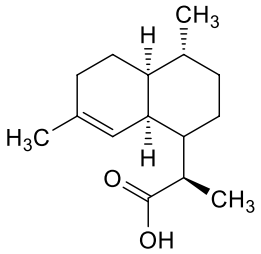


Artemisinic acid **(72)**

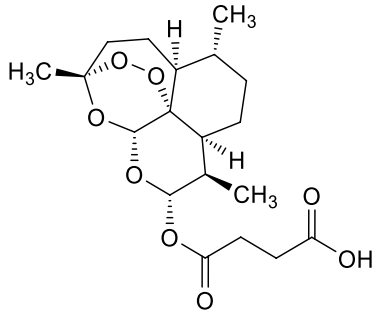


Dihdroartemisinin **(73)**

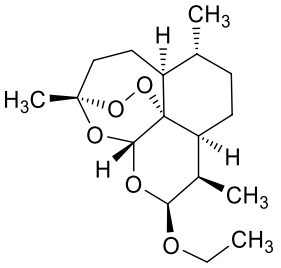
Fig. 3 (continued)



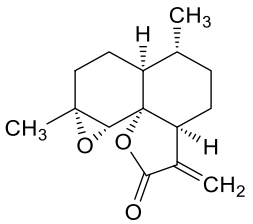
Dihydroartemisinic acid **(74)**



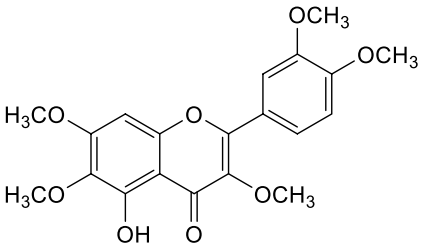
Artesunate **(75)**



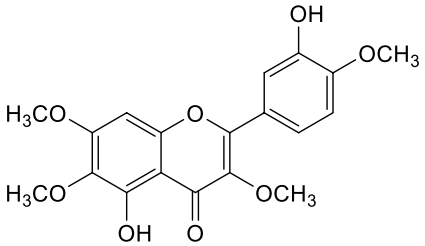
Arteether **(76)**



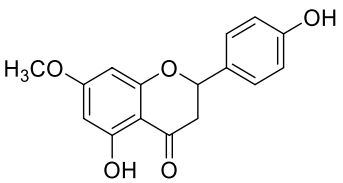
Arteanniun B **(77)**



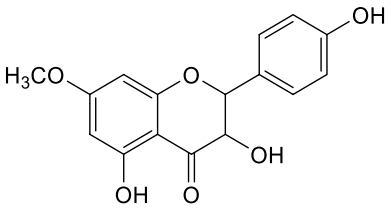
Artemetin **(78)**



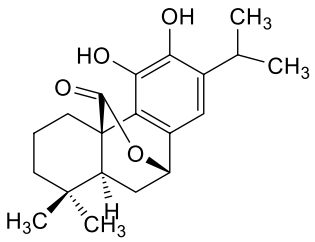
Casticin **(79)**



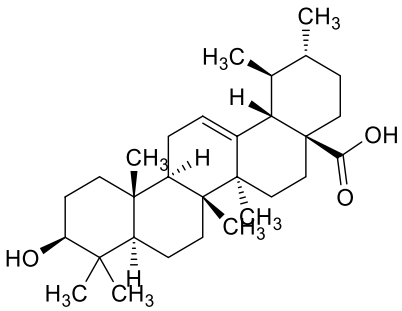
Sakuranetin **(80)**



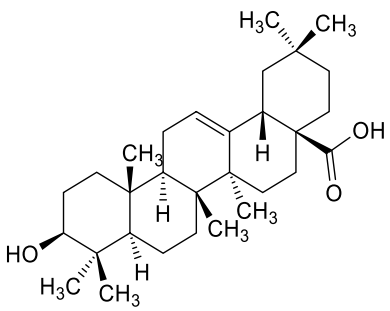
7-methoxyaromadendrin **(81)**



Carnosol **(82)**

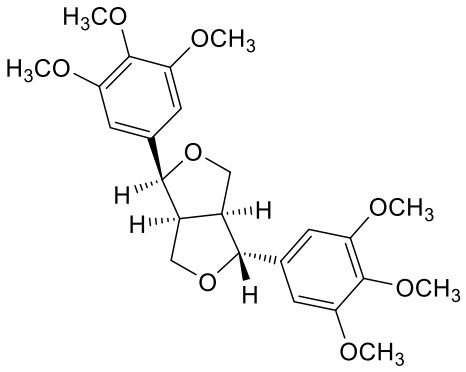


Ursolic acid **(83)**

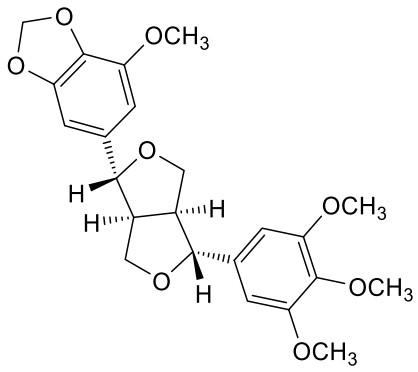


Oleanolic acid **(84)**

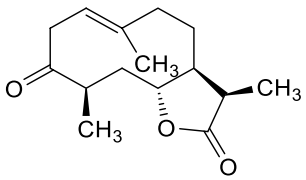
Fig. 3 (continued)



Epiyangambin **(85)**



Sesartemin **(86)**



Ketopelenolide B **(87)**

Fig. 3 (continued)

Mugwort essential oil exhibits fumigant repellent activity against different microbial strains involving *Staphylococcus aureus, Salmonella typhimurium, Cida albicans, Escherichia coli, Staphylococcus epidermidis, Enterococcus faecalis,* and *Enterobacter cloacae* applying disc diffusion technique collated with the positive control (ketoconazole, ceftazidime). The essential oil can develop a zone of inhibition larger than the standard drug, therefore, recommending its utilization as an antimicrobial compound. The potent antimicrobial property of mugwort essential oil is due to 1,8-cineole, camphene, and α-thujone, whereas the antineoplastic property is because of artemisinin (Sun et al. 1992; Blagojevic et al. 2006; Jasinskas et al. 2014).

It has been reported that mugwort incorporating natural supplements and possesses potent antioxidant activity (Juteau et al. 2002; Erel et al. 2012). It is prominently preferred that the extracts of phenolic flavonoids parts of the *A. vulgaris* have found efficient antioxidant activity (Wright 2002; Albayrak et al. 2010). The rich amount of flavonoid indicates an immense level of antioxidant activity (Matvieieva et al. 2019). It is also known that some flavonoid constituents are used in the treatment of neurodegenerative disorders, Alzheimer's disease (Pradeep and Rengaswamy 2016) and also manifest antihyperlipidemic effects (Dib and Alaouri-faris 2019). The important oil obtained from the stem part of mugwort has an influential larvicidal activity against *Aedes aegypti* when used in small concentration, therefore, scrutinized as a natural larvicidal compound against some carrier-mediated illness and for pest management in food technology (Govindaraj and Kumari 2013). Mugwort essential oil is also confirmed for its insecticidal effect for *Tribolium castaneum* (Herbst), *Collosobruchus maculates* (F.), and *Rhyzopertha dominica* (F.) (Tigno et al. 2000; Sharifian et al. 2013).

Chemical compositions of mugwort (*Artemisa vulgaris*) essential oil

The robust fragrance scent of *A. nilagirica*, *A. vulgaris,* and their species are principally due to the immense amount of volatile terpene and its active components of the essential oil (Abad et al. 2012). The chemical ingredients of *A. vulgaris* include flavonoids, coumarins, volatile oils, sesquiterpene, lactones, inulin, and traces of alkaloids. The major components of essential oils are camphene, 1,8 cineole, α-thujone, germacrene D, β caryophyllene, and camphor (Jerkovic et al. 2003) are given in Table 2, and extraction of mugwort oil is represented in Table 3.

Table 2 Phytochemical analysis of *A. nilagirica* extracts

S. no.	Test	Chloroform	Diethyl ether	Ethanol	Hexane	Methanol	Petroleum ether
1	Phlobatannins	−	−	−	+	−	+
2	Glycosides	−	−	−	−	−	−
3	Flavonoids	++	+	++	++	++	+
4	Saponins	−	−	+	−	+	−
5	Amino acids	−	−	+	−	++	−
6	Carbohydrates	−	−	−	−	+	−
7	Alkaloids	++	++	++	++	++	+
8	Volatile oils	−	−	−	+	+	−
9	Phenol	++	+	++	+	++	+
10	Tannins	−	+	++	−	++	−
11	Terpenoids	++	++	++	++	++	++
12	Quinines	+	+	+	+	+	+
13	Hydrolysable tannins	−	−	−	−	−	−

(−) = Absent, (+) = Present, (++) = Abundant

Table 3 Extraction of oil from asunder segments of mugwort (*A. vulgaris*)

Origin/parts	Procedure	Equipment	Yield (%)	References
China/leaves stems	Hydrodistillation	Clevenger	–	Wang et al. (2006)
Sebia/aerial parts	Hydrodistillation	Clevenger	–	Blagojevic et al. (2006)
North Lithuania/ aerial parts	Hydrodistillation with hexane diethyl ether combination	–	0.2–0.4	Judzentiene and Buzelyte (2006)
Turkey/aerial parts	Hyrodistillation	Clevenger	0.40	Erel et al. (2012)
Italy/aerial parts	Hydrodistillation	Likens-Nickerson apparatus	–	Mucciarelli et al. (1995)
Iran/aerial parts	Steam distillation	Clevenger	1.4	Alizedah et al. (2012)
Nepal/leaves	Steam distillation	Clevenger	–	Bhatt et al. (2007)
Cuba/aerial parts	Hydrodistillation	Clevenger	0.1	Pino et al. (1999)
India/aerial parts	Hydrodistillation	Clevenger	0.16–0.5	Haider et al. (2003)
Vietnam/aerial parts	Hydrodistillation	Clevenger	0.32–1.14	Thao et al. (2004)
India/stem	Hydrodistillation	Clevenger	–	Govindaraj and Kumari (2013)
Iran/aerial parts	Hydrodistillation	Clevenger	0.25	Bamoniri et al. (2010)

Pharmacological activities

Antioxidant activity

Free radicals are those compounds that contain unpaired electrons, are extremely reactive species such as many reactive oxygen species (ROS) usually are the outcomes of routine cellular biotransformation in the biological systems (Qadir et al. 2014; Zhang et al. 2018). ROS is a complete range of large riposte molecules that are produced from oxygen metabolism (Dhanapal et al. 2016). Antioxidants maintain the equilibrium of radicals in cells, which prohibit oxidative stress against different ailments (Szerlauth et al. 2019). However, the excess formation of reactive oxygen species (ROS) is due to severance of the exquisite balance in the middle of the antioxidant system, its production is accountable for the oxidative damage which results in the deterioration of cellular macromolecules like enzymes, lipids, deoxyribose nucleic acids (DNA), and proteins (Halliwell and Gutteridges 1984; Msaada et al. 2015). This imbalance can be used for the diagnosis of numerous disorders like necrosis, swelling, Parkinson's disease, Alzheimer's sickness, high blood pressure, hyperglycemia, atherosclerosis, heart-related problems, and immunological perturbation (Morris et al. 2013; Wang et al. 2019). ROS can cause necrosis due to their strength to enlarge cell growth, endurance molecular wandering. Moreover, it can also responsible for DNA impairment, which evinces in the form of genetic

complications that prompt tumorigenicity and ensuing tumor development (Storz 2005). Malignancy is one of the fatal diseases predominantly in public health aspects in both progressing as well as the progressed world (Prakash et al. 2013). In conjunction with this, current perspectives of cancer therapy, for example, immunosuppression, radiotherapy, chemotherapy and surgery, are integrated with a vast mortality rate despite substantial development in cancer therapy of cytostatic compounds (Sidaoui et al. 2016). Furthermore, the results of the presently available procedure for the diagnosis of several cancers are clear, mainly when cancer has attained the metastatic phase and cellular progression of cancer has been done (Seo et al. 2003; Mojarab et al. 2009).

Antioxidants afford a cellular protective mechanism against oxidative stress within the human body. They pertain to the potential to extinguish reactive oxygen species by furnishing hydrogen atoms or electrons, chelating transitional metal ions, invigoration of enzymes, namely superoxide dismutase (SOD), catalase (CAT) glutathione peroxidase (GPx) as well as preventing the oxidizing entities. However, these protective techniques are sometimes inadequate due to the large pathological condition; hence, antioxidant additives play an essential role in encountering oxidative detriment (Gul et al. 2013). Medicinal plants have rescued association in contemporary times due to their elevating abundant biological characteristics appearing apperception of their provenance, functioning structural variations (Sen and Samanta 2014). Medicinal plants are attaining significant consideration because of their remarkable antioxidant potential with lesser side effects (Auddy et al. 2003). They accommodate a vast range of chemical compositions, which may impart their effect specifically or corroboratory to cure the diseases integrated with oxidative stress, ameliorate health (Bhatt et al. 2007, 2013). The polyphenolic preparation of extract from leaves of *A. annua,* and *A. absinthium* L. was estimated as a modality of natural antioxidants (Skowyra et al. 2014). Leaves of *A. annua*, extract for antioxidant activity have been performed by interpolating different solvents, i.e., chloroform, hexane, ethyl acetate, methanol–water. The antioxidant potential is evaluated by estimating total phenolic and flavonoid content (TPC and TFC), ferric reducing antioxidant power (FRAP), Trolox equivalent antioxidant capacity (TEAC), 2,2-Diphenyl-2-picrylhydrazyl Hydrate (DPPH) radical scavenging activity, and lipid peroxidation. The extreme TPC, TFC, TEAC, DPPH radical scavenging, and little lipid peroxidation effects were carried out in methanol (CH_3OH) extracts, although aqueous extract evinces exorbitant ferric reducing antioxidant strength demonstrating CH_3OH to be the highly suited suitable extract (Temraz and El-tantawy 2008; Iqbal et al. 2012; Katiyar et al. 2012; Qadir et al. 2014; Pereira et al. 2018; Sembiring et al. 2018). The aqueous ethanolic extracts of *A. nilagirica* asserted for estimation of in-vitro antioxidant activity, superoxide scavenging activity, total flavanol content, total phenolic content, hydrogen donating activity and reducing power assay, etc. (Devmurari et al. 2010; Khezrilu and Heidari 2014; Pal and Ghosh 2018).

Antimicrobial activity

It has well established that the diethyl ether extract of the leaves of *A. nilagirica* demonstrated antimicrobial properties against the soil-borned plant pathogen i.e., *Phytophthora capsici*. The disc diffusion method has been applied to perform the antimicrobial activity. The results showed that the mycelial development of *P. capsici* entirely suppressed by a concentration of 100 ppm of the oil in the carrot agar vehicle and shown in Table 4.

The inhibitory effect against *P. capsici* is due to the presence of thujones about 41.9%. It has been illustrated that similar activity has been done by utilizing cedar leaf oil and *A. nilagirica* oil (Shafi et al. 2004). The plant extracts have shown extended activity against *Pseudomonas aeruginosa*, *Staphylococcus typhi*, *Escherichia coli*, *Yersinia enterocolitica*, *Bacillus subtilis*, *Cida albicans, Staphylococcus aureus,* and *Proteus vulgaris*. It has been reported that *P. aeruginosa* exhibited the largest zone of inhibition at 16, 17, 19 mm at 100, 150–200 µg concentrations serially. *B. subtilis, S. typhi* displayed inhibition zones of 14, 16 and 18 mm, pursued by *S. aureus* with 13, 15, and 18 mm at three separate concentrations (100, 150, and 200 µg). *Escherichia coli* showed the zone of inhibition (14, 15 and 17 mm) at 100, 150 and 200 µg, serially. The microbial characteristics of *A. nilagirica* were reported by numerous investigational groups; it possesses potent antibacterial activity towards *Bacillus subtilis*, *Staphylococcus aureus,* and *Klebsiella pneumonia* (Rao et al. 2006).

Table 4 Antimicrobial action of plant extracts from *Artemisia nilagirica* (Clarke) Pamp (Parameswari et al. 2019)

Bacterial	The concentration of the leaf extract (µg)				Standard
	50	100	150	200	
Cida albicans	3	6	8	10	12
Staphylococcus aureus	11	13	15	18	20
Escherichia coli	12	14	15	17	19
Bacillus subtilis	12	14	16	18	40
Yersinia enterocolitica	–	–	–	–	16
Pseudomonas aeruginosa	13	16	17	19	43
Proteus vulgaris	–	–	–	–	13
Salmonella typhi	12	14	16	18	33

Antifungal activity

The in-vitro antifungal effect of essential oils of *A. nilagirica* along with *Juglans regia* var. *kumaonica* against *Drechslera sorokiniana* (Sacc.) Subram. was found to be more efficacious than *J. regia* var. *kumaonica* in prohibiting the spore pullulating mycelial enlargement inhibition (Chowdhury et al. 2008). Some researchers have also evaluated the antimicrobial, antifungal actions by selecting leaves of *A. nilagirica*. Besides that, the essential oil obtained from this plant has anti dermatophytes action against *Epidermophyton floccosum, Trichophyton violaceum*. Essential oil intermixed in polyethylene glycol proclaimed potency as the herbal antifungal compound in different dermatomycosis problems in guinea pigs. The extract persuades the effect within 14 days of pertinence; the minimum inhibitory concentration of oil has 200 ppm (Kishore et al. 2001).

Antibacterial activity

The phytochemical assessments of extracts the analysis expressed the presence of flavonoids, terpenoids, phenols, alkaloids, quinines, and tannins (Tajehmiri et al. 2014; Hiremath et al. 2011; Parameswari and Devika 2014; Addo-Mensah et al. 2015; Bereksi et al. 2018; Mamatova et al. 2019). Despite this, saponins and amino acids were found in methanol and ethanol extracts whereas carbohydrates specifically lie within methanol extracts, and glycosides hydrolyzable tannins were not found in the extracts. The susceptibility test showed the suppression of phytopathogens in hexane extracts. The phytopathogen of petroleum ether extract resulted in less suppression (8–10 mm) in correlation to other extracts (10–14 mm). The phytochemical assessments of entire extracts with petroleum ether revealed that it contains alkaloid derivatives (Erdogrul 2002; Shafaghata et al. 2009). Therefore, it is recommended that digression of alkaloid abundance in petroleum ether may be the source of reduced stimulation in phytopathogens. The minimum inhibitory concentration (MIC) analysis result of alkaloids against pathogens (Torres et al. 2002; Raghavendra et al. 2008) such as gram-positive and gram-negative bacteria denoted the availability of a wide range of antibiotic components. The methanol extracts demonstrated maximum suppression at the minimal concentration for the majority of the clinical pathogens as compared to other extracts. The MIC of methanol extract limits from 32 to 64 µg/ml for *Enterobacter aerogenes, Salmonella typhi, Escherichia coli, Yersinia enterocolitica, Bacillus subtilis, Pseudomonas aeruginosa, and Proteus vulgaris*. The phytochemical assessment of menthol extract demonstrated the existence of the majority of the components like terpenoids, alkaloids, flavonoids, phenols, amino acid, and tannins. Besides this, it has evidenced that alkaloids, amino acids, flavonoids, phenols, and tannin are recommended to be active antimicrobials (Brandao et al. 1997; Chakraborty and Brantner 1999; Shaheen et al. 2003; Chowdhury et al. 2008). Extracts of *A. nilagirica* intimated a wide range of antibacterial effects on the assessed microorganisms. Hexane extract demonstrated maximum prohibitory efficacy for the phytopathogens, as compared to methanol extract on *Staphylococcus aureus*, *Escherichia faecalis, and Klebsiella pnumoniae* (Ahameethunisa and Hopper 2010). Some specific reports reveal the antibacterial effects of *A. nilagirica* leaf extract and showed that *Escherichia coli* was more active than *Klebsiella pneumoniae* (gram-negative bacteria) whereas against gram-positive bacteria *Bacillus subtilis and Staphylococcus aureus* was found to be less active. The activity result suggests that the *A. nilagirica* extracts have shown profound activity as compared to the root extract of *Aristolochia indica* (Rao et al. 2006; Suresh et al. 2011).

Antiulcer activity

A peptic ulcer is increasing worldwide due to the emanation of unhygienic food and contaminated dietary supplements that adversely influence the health of human beings. *Helicobacter pylori,* one of the major causative microorganisms of duodenal ulcers, accounts for an inflammatory effect in gastric mucosa by enhancing the formation of cytokines, therefore, developing ulcer production (Zapata-Colindres et al. 2006; Marcus et al. 2013; Mohanty et al. 2018). Freeze-dried ethanolic extracts obtained from upper segments of *A. nilagirica* were ascertained for gastric antiulcer effects on rats. Ulceration was actuated by ethanol–hydrochloric acid and a 500 mg/kg concentration of extract defended the animal from gastric ulcer response. It has been stated that the 500 mg/kg concentration has a paramount level of gastric protection, mucus content was enhanced in proteins, which give rise to antiulcer action. Cimetidine was used as a control, which was not able to manifest any response on mucus secretion in the animal model (Suresh et al. 2011; Oliveira et al. 2014). *A. nilagirica* possesses many essential oils, as discussed earlier and these oils have an antiulcer effect as well as gastroprotective action, which was evidenced by its in-vitro study on rats (Moraes et al. 2009; Baananou et al. 2013). It was also authenticated that extracts of *A. nilagirica* on ulcer produced rats showed to prevent the ulcer formation by increasing the mucus concentration (Braquet et al. 1988; Mohanty et al. 2018).

Larvicidal activity

There has been a report that synthetically prescribed drugs in the market over a while has a resistance. Thereupon there is a requirement of another form of drugs such as herbal or ayurvedic formulation to overcome such types. *A. nalagirica*

has already been conversated to incorporate numerous essential oils and other prominent therapeutically active chemical constituents, depending on these parameters, investigation was performed to analyze the larvicidal effect of this plant. It was ascertained that plant extract of *A. nilagirica* confirmed for noteworthy action against *Aedesal bopictus* and extract of *A. nilagirica* has been found beneficial larvicidal activities (Verma et al. 2006). The methanolic extract of artemisia has little effect on the protoscolices of hydatid cysts. Moreover, hydatidosis is a usual zoonotic sickness developed by the larval phases of *Echinococcus granulosus* (Faizei et al. 2015).

Antiasthmatic activity

Asthma is a disease of highly prevailing respiratory disorder that arises due to the susceptibility of adherent allergens existing in the atmosphere (Agrawal and Mehta 2008). Bronchial asthma is a complicated sickness, outlined by acute sensitiveness of trachea and bronchi to several stimuli characterized by acute, recurrent, chronic attacks of the prevalent shrinking of airways. Clinically, asthma is depicted by airway interruption that implicates inflammation and over the responsiveness of the pulmonary airways bronchial and is generally reversible (Cazzoletti et al. 2010). Asthma complies in children is due to respiratory tract infection, common cold, or viral infections (Singh et al. 2019). ROS is involved with the pathological process of asthma by actuating bronchial hyperreactivity inducing histamine liberation from mast cells mucus exudation from epithelial cells of the airway (Mali and Dhake 2011). Free radicals are assumed as an efficient instigating agent of various illnesses like bronchial asthma. Free radicals can ease detriment to intact biological membranes by infiltrating their glycoconjugates, proteins, lipids, and nucleic acids (Sahiner et al. 2011). *A. nilagirica* recommended as an antiasthmatic agent and was proved in Wistar rats to which ovalbumin solution ingested (Dorsch et al. 1987). These rats have manifested a potent therapeutic effect, which was shown by a low count of WBC (monocytes, neutrophils), less formation of nitrate ion, therefore diminishing the inflammation in lung regions of asthma induced animal model (Drazen 1997; Huntley and Ernst 2000). The in-vivo antiasthmatic reports confirmed that the *A. caerulescens* plant extract of aqueous suspension at a concentration of 200 mg/kg found potent activity as compared to a positively control-treated group that is ketotifen (Medici et al. 1989; Moran et al. 1989; Dyson and Mackay 1980; Kabra et al. 2000).

Anticancer activity

Devmurari and Jivani (2010) reported the anticancer activity of methanolic extract of *A. nilagirica* in Swiss albino mice, and the result was found to contain significant activity when compared to standard drug vincristine. Whereas the aqueous extract of *Solanum nigrum* along with species of genus artemisia such as *A. vulgaris*, *A. nilagrica*, *A. parviflora* produces a prohibitory action on cell development, colony accumulation of the human breast, prostate, colorectal cell lines. The cytotoxicity in cancer cells was due to internucleosomal DNA fragmentation, caspase-3-mediated Poly (ADP-ribose) Polymerase (PARP), ribose polymerase cleavage. The in-vitro results showed the methanolic extract of *A. nilagirica* has antineoplastic actions specifically in the breast, colon, and prostate (Devmurari and Jivani 2010; Devmurari et al. 2010; Nawab et al. 2011). The *A. nilagirica* fraction of ethyl acetate-hexane against DLD-1 human cancer cell lines showed good activity. HPLC-ESI-QTOF-MS/MS discovery ascribes the recognition of cytotoxic agents that are to be implied for further preclinical testing (Sahu et al. 2018). Consumption of methanolic leaf extract of *A. vulgaris* is considered to execute a wide impact in all the phases of hepatocellular carcinoma (HCC). Hence, there has needed to elaborate the investigations for the employment of plant-originated agents as an effective anticancer compound in opposition to HCC for a peculiar drug evolution process (Emami et al. 2009; Nair and Varalakshmi 2011). Besides, artemisinins bioactive analogs can also be used as an antitumor agent against various types of cancerous cells, with lesser toxic effects on normal cells (Efferth 2015, 2017; Zhang et al. 2018; Numonov et al. 2019). The research on the bioactivity of different constituents of Artemisia species constituents has a good therapeutic against the treatment of cancer (Pezzuto 1997; Taherkhani 2015). Artemisia produces anti-angiogenic actions in tumor cell lines, and the methanolic extract of *A. absinthium* inhibits the growth of MCF-7, MDA-MB-231 cell which at different concentrations for nearly 3 days at a dose of 20 g/ml and 25 g/ml caused 50% suppression in MDAMB-231 and MCF-7 cells respectively with control (Shoaib et al. 2017; Ahamad et al. 2019). It was also expressed that some extracts of artemisia varieties evaluated manifested a prominent effect on ER-a-positive T47D cells and had a dual impact (stimulatory or prohibitory) on cell dissemination. Nevertheless, evaluation at concentration underneath 100 mM or for 24 h accentuates cell progress, evaluating with artemisia spp. extracts at concentrations beyond 100 mM for 72 h remarkably prohibited cell distribution. All extracts represented similar anti-cancer activity in a dose time-dependent pattern in HS578T cells. Whereas at lesser concentration growth of T47D cells, the prevent the growth of T47D cells at larger concentrations (> 100 mg/ml) for 72 h were notably higher than those of HS578T cells (Kaji et al. 1990; Wolin et al. 2010; Rabe et al. 2011; Choi et al., 2012; Choi et al. 2013a, b). The cytotoxic effects of *A. fragrans, A. incana*, *A. absinthium*, *A. spicigera,* and *A. vulgaris.* root, stem, leaf, and flower extracts

on human embryonic kidney normal cell line (HEK293), and breast cancer cell line (MCF7) was determined using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay at concentrations (62.5, 125, 250, 500 µg/ml). Methanol extracts of leaf, stem, flower, and the root of *A. vulgaris* and *A. absinthium* displayed remarkable anticancer activity, and the flower part showed greater cytotoxicity on MCF7 cell with an IC_{50} of 221.5 > 500 µg/ml. Whereas the cytotoxic effect of *A. absinthium, A. vulgaris, A. incana* against MCF7 was 10–40% higher than HEK293 cells. *A. spicigera* and *A. fragrans* were not able to demonstrate any cytotoxic effects on both cell lines while *A. vulgaris* and *A. absinthium* might have a higher new anticancer compound (Kaji et al. 1990; Nibret and Wink 2010; Zahi et al. 2010; Gordanian et al. 2014).

It was also found that *A. sacrorum* Ledeb has five types of flavonoid contents, namely kaempferol, Jaceosidin, luteolin, quercetin, and quercitrin. Two flavonoids obtained from the dichloromethane portion and other flavonoids from the 95% ethyl ether portions were analyzed for anticancer effects on human SK-Hep 1 hepatoma cancer cells human and HeLa cervical cancer cells. Two flavonoids have possessed significant anticancer activity against the HeLa cells line (Yuan et al. 2016). It was found that antiproliferative properties have been ascertained for some varieties of the genus artemisia. In that report, they observed the cytotoxic and apoptotic effects of *n*-hexane, dichloromethane, ethyl acetoacetate, *n*-butanol, water, and methanol extract of *A. armeniaca* on two myeloid cell lines, apoptosis-proficient HL60 cells, apoptosis-resistant K562 cells, and J774 cells as a control (Mojarrab et al. 2013). Several researchers revealed the identification of 130 constituents from the stem leaf of *A. monosperma* essential oil has an apoptotic cell in the human melanoma A375 cell line in-vitro anticancer effect on colorectal breast cancer cell lines by polyacetylene dehydrofal carindiol. Capillin (1-phenyl-2,4-pentadiyne), one more polyacetylene present in *A. monosperma*, was validated to persuade apoptosis in various human cancer cell lines like pancreatic MIA PaCa-2, colon HT29, lung carcinoma A549 cells, epidermoid carcinoma of the larynx HEp-2 (Stavri et al. 2004; Formisano et al. 2012; Khan et al. 2012; Solowey et al. 2014). Based on the above study artemisinin and its spinoffs have also been introduced as possible cancer treatments that affect multiple pathways. They are known to arrest the cell cycle, induce apoptosis, and slow cell proliferation. At lower concentrations, artemisinin is associated with the symbol of oncosis-like cell death. However, when the concentration increases, it promoted apoptosis in cells. The accumulation of artemisinin inside lysosomes and mitochondria has also been found to play a role in cell death (Du et al. 2010). As per the literature, the alkylating activity of artemisinin is due to the presence of the endoperoxide bridge in the structure of artemisinin that reacts with the heme group and iron. Artemisinin is capable to arrest the cell cycle, induce apoptosis, and slow cell proliferation. The accrual of artemisinin inside lysosomes and mitochondria has also been found to play a role in cell death (Konstat-Korzenny et al. 2018).

The cytotoxicity of the different part extracts of *A. absinthium* was tested on the breast cancer cell lines (MDA MB-231 & MCF-7) by MTT and lactate dehydrogenase (LDH) assay. The cytotoxic research along with proteome analysis indicate that extract stuffed polymeric nanoparticles (NPs) proficiently prohibits cell proliferation and persuade apoptosis also cell cycle arrest in the G0/G1 stage in both the breast cancer cell lines through appreciably regulating the expression of the key proteins concerned to the proliferation, apoptosis, tumor suppression and vesicular trafficking. (Mughees and Wajid 2019).

Antihyperlipidemic activity

Hyperlipidemia occurs due to lipid biotransformation induced by the increase of plasma concentration of various lipid lipoprotein that results in cardiac disease. It is accounted for as elevated serum total cholesterol, triglycerides, very-low-density lipoproteins, low-density lipoproteins, high-density lipoproteins (TC, TG, VLDL, LDL, HDL) which are responsible for congestive heart failure, cardiac arrest, myocardial infarction, cardiac strokes, atherosclerosis, coronary artery syndrome pancreatitis (Konda et al. 2013). Hypercholesterolemia is commonly accredited to be the crucial hazardous aspect of the progression of cardiovascular disorders. It has been assessed that hypercholesterolemia is the source of the augmented development of ROS. Oxidative stress produced by ROS imparts a principal role in the diagnosis of atherosclerosis as well as in coronary heart disorder. Considerable attention has been paid to naturally occurring compounds and their role in up-gradation for health fitness. The cholesterol-reducing property of comestible plants has been well measured and numerous plants have found profitable in, mitigating plasma cholesterol extent and raising the safety parameters (Kruth 2001). The *A. vulgaris* extract in hypercholesterolemic rats showed a remarkable reduction in β-hydroxymethylglutaryl-CoA reductase (HMGCoA) action with these excess fat diets treated animals control ones (Khan 2015). Therefore, it can be concluded that *A. vulgaris* extract produces hypolipidemic, anti-inflammatory, antioxidant properties and might be used for the treatment of atherosclerosis as well as cardiovascular-related diseases (Zhao et al. 2011; El-Tantawy 2015). It has been observed that the aqueous extract of roots has an explicit hypolipidemic effect in cholesterol diet-persuaded hyperlipidemia in rats (Rajendran et al. 1996; Yokozawa et al. 2003). Aqueous extract of the root can exhibit

hypolipidemic activity same as the HMG-CoA reductase inhibitors such as rosuvastatin (Blois 1958).

Antiepileptic activity

Epilepsy is a prevalent mental ailment; common manifestations are seizures or convulsions. A disequilibrium between the aggravating overwhelming neurotransmitters is liable for the principal cause of seizures (Santilna et al. 2014). It influences around 7 million population in India and 50 million globally; around 40% of them found to be women (Kumar et al. 2012). About 50–80% of people living with epilepsy are manageable with presently receivable anticonvulsant drugs, but these medications are still not capable enough to cure convulsions entirely in about 10–20% of the patients with epilepsy (Nsour et al. 2000). Most of the prescribed drugs by registered medical practitioners availed as antiepileptic compounds have deleterious influence sometimes life-threatening human situations are also realized by patients who are victims of epilepsy (Mittal et al. 2011; Sharma et al. 2013). That's why there is a great demand to innovate an alternative subsidiary antiepileptic agent from naturally occurring sources with potent therapeutic effects and lesser side effects (Smith and Bleck 1991; Nsour et al. 2000; Loscher and Schmidt 2006). The anxiolytic and anticonvulsant activities of the plant *A. vulgaris* was performed using the elevated plus-maze test and the Marble-Burying test (EPMMBT) diazepam 2 mg/kg used as standard. The methanol extracts produce antiseizure activities, elevating the time of quiescence for the initiating of the initial convulsion in all the assessments (Almeida et al. 2013). It has been noticed that ethanol extract of some species of the genus artemisia such as *A. capillaris* Herba (AC) has remarkable anticonvulsant action in electroshock as well as pentylenetetrazole (PTZ) seizure model. In comparison to diazepam, AC (100–200 mg/kg) did not modulate the locomotor performance and proceeding duration on the rota-rod, which denotes that it is unable to produce hangover, myorelaxation as well as not be sleep-inducing. Such dissimilarity between AC and diazepam is advantageous, stipulating that sleep induction and sedation is a general adverse effect of a few of the GABAergic neuronal anticonvulsants. Esculetin (ECT), therapeutically active medicinal constituents present in AC, imparting an anticonvulsant effect same as in the case of AC, which designates that the effect of AC is as an outcome of ECT (Novack et al. 1978; Bum et al. 2001; Obniska et al. 2006; Woo et al. 2011). This has also been observed that ursolic acid, carnosolole, anolic acid intimated remarkable anticonvulsant effects against PTZ-induced seizures in mice. Oleanolic acid, carnosolursolic acid developed a dose-reliant enhancement in the duration of onset of tonic–clonic seizures, as a result, reduced the time of seizures (Khan et al. 2016).

Antimalarial activity

Malaria is one of the biggest life-intimidating diseases caused by Anopheles mosquitoes affecting a large number of populations globally (Barradell and Fitton 1995; Carter and Mendis 2002). It was studied that the effectiveness of antimalarial activity declared by selecting six different leaf extracts of *A. nilagirica* in solvents (*n*-ethanol, petroleum ether, hexane, chloroform), besides this, methanol aqueous organic leaf extracts of *A. nilagirica* (Clarke) Pamp was found to be effective for Plasmodium *falciparum* (malarial parasite) (Czechowski et al. 2019). The antiplasmodial activity obtained the highest 50% inhibitory concentration (IC_{50}) after 32 h of gestation. This study reveals that the methanolic extract of leaf of *A. nilagirica* showed an in-vitro antiplasmodial effect on *Plasmodium falciparum* strain (FCR-3). In addition to this, the characterization of the medicinally active component from leaf extract may contribute to a molecule for malaria; their in-vivo studies also proved (Suberu et al. 2013). It can be concluded that *A. vulgaris* leaf extract has potent antimalarial activity against the *Plasmodium yoelii*. Due to resemblances between *P. yoeli* and human malaria parasites like *Plasmodium vivax, Plasmodium falciparum,* and *Plasmodium yoelii* can be utilized as another in-vivo model for human malaria (Carlton et al. 2002; Kodippili et al. 2011).

The antimalarial effect of the organic extract of *A. vulgaris* was for both antiparasitic and its other actions and at different doses (250, 500, 1000 mg/kg). There has been performed 4-day suppressive assay when extract has applied orally at 500 mg/kg, 1000 mg/kg doses to mice then it was found that there has been remarkably prohibited parasitaemia by 65.16% and 51.46%. The *A. vulgaris* extract to administered to mice for 14 days (assay of sub-chronic toxicity), no ostensible symptoms of toxicity were seen. Hepatotoxicity serum glutamic-pyruvic transaminase (SGPT) has been estimated in respect of serum glutamic-oxaloacetic transaminase (SGOT) levels, renotoxicity (in respect of creatinine serum urea), haematotoxicity in respect of entire white blood cells and red blood cells (WBC and RBC), as well as differential leukocyte counts, were also precluded. Finally, *A. vulgaris* leaf extract was considered to be orally proficient, non-lethal and it can be an inexpensive origin of plant antimalarial (Kalkanidis et al. 2002; Mirjalili et al. 2007; Bamunuarachchi et al. 2013).

On another way, artemisinin obtained from *A. annua* is a potent antimalarial agent against chloroquine-resistant malaria. Root level study was taken into consideration to ascertain the antiparasitic action of an *A. vulgaris* in ethanolic leaf extract (AVELE) against *Plasmodium berghei* ANKA murine malaria model against falciparum malaria (Bamunuarachchi et al. 2013). Dichloromethane extracts of both species of *A. spicigera* and *A. scoparia were* reported

to contain an antimalarial effect with IC_{50} at 0.7780.999 mg/ml for *A. spicigera and A. scoparia*. *A. spicigera* was found more potent rather than *A. scoparia* (Afshar et al. 2011). The hydroalcoholic aqueous extracts of *A. annua* L. were prominently found to be effective on malaria and can be utilized by inhabitants on a worldwide level to diagnose this disease, particularly in endemic regions where there is not sufficient budget to purchase potent new therapeutically active medicines (Mueller et al. 2000; Zime-Diawara et al. 2015).

The most extensively consumable, utilized antimalarial therapy is artemisinin-based combination therapies (ACTs), which are seen to be unadulterated, authentic, natural. Genuine artemisinin is found in combination form and isolated from the various genus of the artemisia plant prime one is *A. annua* (Weathers et al. 2014; Weathers and Towler 2014). Evaluating artemisinin along with sodium borohydride gives rise to dihydroartemisinin, which was considered to be an even more competent persuasive antimalarial agent than artemisinin (Basco and Le-Bras 1993; Weathers et al. 2011). Dihydroartemisinin persuades as the basis for the raise of oil–water-soluble analogs (Snow et al. 2001; De Ridder et al. 2008). Most of these analogs are dihydroartemisinin derivatives (Wongsrichanalai et al. 1997). The effectiveness of artemisinins analogs has been assessed by the in-vitro method with different strains of *Plasmodium falciparum* (Payne 1987; Su and Miller 2015). It has observed that the drug concentration required to prohibit 50% of the parasite's activity, the IC_{50}, artemisinin has persistently been considered 2–5 times less efficacious than its analogs dihydroartemisinin, artesunate, and artemether (Hassan et al. 1996; Delabays et al. 2001; Medhi et al. 2009). Thereupon, larger doses of artemisinin are needed to attain a similar antimalarial activity. WHO endorses ACTs as the fundamental basic remedy for easygoing and apparent *Plasmodium falciparum* malaria, additionally for chloroquine-resistant *Plasmodium vivax* malaria (Barradell and Fitton 1995; Snow et al. 2005). Artemisia herbal medications have also been recommended for elimination as well as avoidance of different malarial strains (Carter and Mendis 2002; WHO 2019). *A. indica*, which has flavonoids such as sakuranetin, 7-methoxy aromadendrin, also showed extreme antiprotozoal activity (Ribeiro et al. 1997).

Anti-inflammatory activity

The leaf extract obtained from the plant manifested to protect the human red blood cells (HRBC) with 74.63% at 20 µg/ml concentration and minimum hemolysis seen about 25.37% in a hypotonic solution as compared to standard drug diclofenac (Ghisan et al. 1991; de Souza et al. 2016). Finally, by employing a UV–Visible spectrophotometer hemoglobin concentration of the supernatant was assessed at 560 nm (Anosike et al. 2012). It was proved that the extract selected from the leaves of *A. nilagirica* (Clarke) Pamp was effective for in-vitro anti-inflammatory activity and the leaf extract displayed utmost conservation scanty hemolysis of the HRBC (74.63%, 25.37%, serially) at a cumulation of 200 µg/ml in hypotonic suspension. Moreover, at a cumulation of 50 µg/ml, the extract manifested extreme hemolysis of 52.89%, 47.11%, serially, and was collated with the reference drug that was < 91.18% protection 16.68% hemolysis. The extract demonstrated membrane stabilization by suppressing hypotonicity and lyses of the erythrocyte membrane (Chou 1998). Furthermore, immobilization of the extract can immobilize lysosomal membranes, which play an important role in inflammatory responses by decreasing the lysosomal ingredients of triggered neutrophil-like bactericidal enzyme proteases (Murugasan et al. 1981). It also can hamper these proceedings, which may induce or elevate the intracellular ingredients (Iwueke et al. 2006).

Hepatoprotective activity

A maximum number of the drugs, food water components are metabolized in the liver. Vital tasks of the liver concerns with the metabolism of fats, carbohydrates, proteins along with their detoxification process. Besides this ejection of bile, the collection, as well as detoxification of various drugs and xenobiotics, proceeds through the liver. The hepatic reticuloendothelial system (RES) clears stimulated clotting factors, proteolytic enzyme/inhibitor complexes, and fibrin–fibrinogen cleavage proceeds (Bansal et al. 2014). Liver-related diseases are one of the biggest health disorders in the world; the pathogenesis of hepatic ailments as well as the role of oxidative stress inflammation are well accomplished (Malhi and Gores 2008; Tacke et al. 2009). By decreasing the chain reactions of oxidation inflammation steps could be a significant and useful therapeutic approach for the prohibition of liver abrasion and damage. In-vivo model is used for the exploration of new hepatoprotective compounds that have prescribed rodent model of liver injury caused by carbon tetrachloride (CCl_4), a chemical hepatotoxin that produces a free radical-mediated hepatocellular harm reparation (Weber et al. 2003; Upur et al. 2009; Amat et al. 2010). Qualitative as well as quantitative phytochemical analysis of the aqueous extract of *A. absinthium* L. (AEAA) was implemented with the help of thin-layer chromatography and spectrophotometric assays which assess in-vivo hepatoprotective action of the aqueous extract of *A. absinthium* L. (AEAA). The action of AEAA inhibits acute liver abrasion, which may be due to its immunomodulatory and antioxidative properties (Amat et al. 2010). The hydroethanolic extract of *A. scolari* preserves the structure of the hepatocellular membrane which is because of the acetaminophen-prompted up-gradation in serum glutamic oxaloacetic transaminase

(GOT) and glutamic pyruvic transaminase (GPT) extents in rats and mice. Thus, this study concludes the conventional utilization of the *A. scoparia* plant in hepatobiliary ailments. Hydroalcoholic extract of *A. dracunculus* reinstated the elevated serum enzyme extents, reduced liver antioxidant markers, strived, and proficient antioxidant activity under in-vitro situations demonstrating that it has hepatoprotective antioxidant efficiencies in CCl_4-intoxicated rats (Mankani et al. 2005; Gilani and Janbaz 1993). The hepatoprotective property of hydro-alcoholic extracts of aerial parts of *A. dracunculus* (HAAD) caused by extenuated lipid peroxidation improved protection of the hepatocytes against reactive oxygen species (ROS) (Lopez et al. 2017). The histopathological reports also proved the effectiveness of the plant extract. In addition to this, the antioxidant activity of *A. dracunculus* supports the therapeutically and medicinally active constituent of this plant as well as recognizing their functioning pattern (Kordali et al. 2005; Zarezade et al. 2018). The efficacy of the crude extract and aerial segments of *A. vulgaris* have been identified against lipopolysaccharide (LPS) and galactosamines (D-GalN) induced hepatitis in mice. These experiments proved the conventional use of *A. vulgaris* for numerous liver-related diseases (Gilani et al. 2005). Different xenobiotics studies confessed to elicit hepatotoxicity, produced by paracetamol (*p*-hydroxy acetanilide or PHA) and carbon tetrachloride (CCl_4) on the animal model which showed mechanisms of actions for liver impairment. Water-soluble polysaccharides, polypeptides, organic acids, and flavonoids for the liver protective actions of *A. capillaris* has also elucidated (Han et al. 2006; Choi et al. 2013a, b; Jiao et al. 2016).

Antitubercular activity

Tuberculosis (TB) is disease-causing mortality globally around 9 million population and affecting 2 million people yearly (Elhassan et al. 2013; Ngadino et al. 2018). *Mycobacterium tuberculosis* is one of the fatal diseases involving a large number of the human population and drug resistance also occurs (Jimenez-Arellanes et al. 2014). A large number of secondary plant metabolites are confirmed to retain antitubercular activity (Negi et al. 2010). It was seen that methanolic extracts of *A. capillaries* and hydroquinoneursolic acid have shown inhibitory actions against many strains of *Mycobacterium tuberculosis* (MTB by using MGIT™ 960 resazurin assay. Phytomolecules have been additionally assessed by transmission electron microscopy (TEM). Hydroquinone (HQ) and ursolic acid (UA) stops the growth of both vulnerable resistant species of *M. tuberculosis* (Jyoti et al. 2016). Some antimycobacterial activity reports that 20%, 40%, 70%, and 96% ethanolic extracts of the root of *A. absinthium* decrease 100% growth inhibition of *Mycobacterium tuberculosis* strains with 96% ethanolic extract. However, the mechanism of the plant is needed for prevention as well as control of disease (Hojageldiyev et al. 2019).

Antihypertensive activity

The antihypertensive activities of *A. scoparia* (AS) on hypertensive rats (ASHR) showed splendid activity (Cho et al. 2015). *A. persia* (AP) is used in folk medicine for antihypertensive potency. The aqueous methanolic extracts of *AP* are used for obtaining cardiovascular effects, for blood pressure (BP), cardiac rate (CR) of normotensive ephedrine induced hypertensive rats. High blood pressure was decreased by a single sip of ephedrine (40 mg/kg/IM) to uplift BP 20–30 mmHg. Aqueous methanolic extracts were given at a dose of (300, 400, and 500 mg/kg) by gavage process excellent results for the systolic blood pressure of normotensive rats observed at 400 mg/kg afterward 20 min consummation while others don't influence diastolic BP or HR compared with enalapril (30 mg/kg). Oral consummation of AP extracts next 20 min systolic BP in normotensive hypertensive rats, on the contrary, the aqueous extract of AP extenuated the BP of hypertensive rats much faster as that of enalapril (Ghisalberti et al. 1998; Esmaeili et al. 2009; Ahmed et al. 2017). Another variety of the genus artemisia that is *A. pallens* has successfully been reported in Ayurveda for the treatment of high blood pressure (Pavithra et al. 2018). Moxibustion is a conventional and East Asian medical treatment that contains *A. vulgaris* with acupuncture treatments (Kim et al. 2010; Zhou et al. 2018). One more distinct species of the genus artemisia that is *A. herba-alba* recognized for its therapeutic medicinal characteristics, it was consumable in an easy way and available in both traditional as well as in contemporary medicine. *A. herba-alba was* utilized as a folk remedy for the prevention of arterial hypertension (Mohamed et al. 2010; Samaha et al. 2019).

Antidiabetic activity

World Health Organization (WHO) describes diabetes as a disturbance in the metabolism of carbohydrates, fats protein; generated by the deficit of insulin deliverance, or decreased susceptibility of the tissue to insulin (Kavitha and Dattatri 2013). Allopathic medications are not enough, therefore naturally occurring medicinally active plants impart a crucial role in the cure of diabetes mellitus (Dabe and Kefala 2017). The aerial root extracts of *A. dracunculus* were evaluated for antidiabetic effect in streptozotocin (STZ) promoted diabetic rats. It showed a promising and remarkable antihyperglycemic effect when compared with standard drug glibenclamide at a dose of 0.25 mg/kg. The plant was capable of enacting antidiabetic, along with antihyperlipidemic properties (Samyal et al. 2011). The antidiabetic efficacy of *A. amygdalina* being effective in hyperglycemia

may successfully control metabolic disorder and endorse its medicinal therapeutics and conventional uses (Sidhu and Sharma 2013; Ghazanfar et al. 2014). *A. dracunculus* L. was found to contain a hypoglycaemic effect by numerous investigators (Ribnicky et al. 2009; Wang et al. 2011). Wang et al. (2011) ascertained a particular *A. dracunculus* L. plant for its prominent insulin susceptibility as well as insulin resistant (IR) signaling in insulin-resistant KK-Ay mice but are unable to describe the appropriate cellular mechanism (Coman et al. 2012).

Antiparasitic activity

Parasites cause different types of tropical illnesses like malaria, helminthiasis, onchocerciasis, schistosomiasis, lymphatic filariasis, trypanosomiasis, leishmaniasis. It affects around 1–2 billion people, which gives rise to a million death each year (Wink 2012; Nikpay and Soltani 2018). Furthermore, these fatal and harmful parasitic diseases, numerous ectoparasites adversely influence salubrity as well as the normal health of human beings, which accommodate slice, fleas, mites, bed bugs, various myiasis causing Diptera (Nussbaum et al. 2007; Peters and Pasvol 2007). Several human parasites are spread and expended by arthropod mediators, which also might be a goal regarding subsidiary metabolites containing insecticidal properties (Le et al. 2018). *Hymenolepis nana* is a usual intestinal tapeworm, which adversely and skeptically influences the life of human beings. Drugs used against this disease are niclosamide, nitazoxanide, praziquantel (PZQ). An aqueous extract *A. absinthium* against *H. nana* was examined in-vitro, 15 mg/ml of the extract as a test, and 1 mg/ml of PZQ as standard showed significant anthelmintic activity. The in-vivo examination of *A. absinthium* was carried out, mice have distributed into untreated, PZQ treated (400–800 mg/kg). Before and after evaluation, egg per gram of feces (EPG) was noted; the decreased rate ratio of the (EPG) worm was counted. The promising outcome obtained was comparable with praziquantel promoted worm paralysis, inanimation, lipid congregation, etc. decrease in the EPG worm encumbrance was observed and noted. *A. absinthium* has been found to give promising results, comparable to PZQ, additional studies imparting separate extracts, active constituent concentrations across diverse parasites might be accompanied (Beshay 2018). Herbs have been successfully applied and selected for centuries against endoparasiticides. Food–Drug Administration along with the National Administration of Drugs, for Food Medical Devices (FDA, ANMAT) monitored a few of the plants considered in various research for *Artemisia absinthium*, black walnut nut, wormwood as medicinally approved fruitful herbs with vermicide action (Griselda et al. 2016; Osorio and Garcia 2019). The hydroalcoholic extract of *A. absinthium* set forth a promising and prodigious antileishmanial activity after 48–72 h. The IC_{50} for the alcoholic extract of *A. absinthium* was reported at 56 mg/ml and 51 mg/ml cumulations of amastigote sand promastigotes. The decrease in NOs has been observed at 100 and 50 mg/ml (Aberham et al. 2010). The previous one was attained at 60.8–58.8 ng/ml next 24–48 h and later on for 72 h (Rahiminejad et al. 2018).

Artemisia herba-alba has proclaimed the anthelminthic effect as it has decreased egg shedding worm encumbrance in the infected birds in the same way as that of albendazole. The herbal extract improved feed conversion ratio (FCR) around further infected groups (positive control albendazole treated group) and it was observed that no detrimental actions were found on the liver and kidney, of treated poults. These results suggest that *A. herba-alba* could be utilized and availed for the management and prevention of heterakid (nematode worm) infection. Efforts for the separation and identification of the medicinally active ingredients accountable for such activities are still in the development process (Pohlit et al. 2011). Later on, investigations have tried to find out the precise mode of action (Seddiek et al. 2011). Parasitic infections in a different manner (food, water, vegetables) can influence the lives of human beings, and cause gastrointestinal problems, malnutrition disorders, anemia, allergies frequently even life denunciatory. The employed terms for treating all of these complications comprise herbal medicine, medicinal plants, anthelmintic drugs, antinematoda, anticestoda, antitrematoda induced infections are also prevented by the same (Porrini et al. 2011; Bahmani et al. 2014). Some investigations regarding the crude extracts of *A. absinthium* were found to be effective in in-vivo enlargement, progress, and improvement of the parasite that is syphacia. *A. sieberi* was proposed as one of the huge imposing medicinal active constituents possessing plant against the coccidiosis in the chickens that are contaminated with *Eimeria acervolina,* and *Eimeria tenella* except for *Eimeria maxima* microorganism (Arab et al. 2006; Youssefi et al. 2011).

Artemisinin (ART), and their several derived analogs possess antimalarial and antischistosomal compounds originated from *A. annua* L., ART, and against another parasitic protozoan (Ataei and Delnavaz 2019). ART and their numerous analogs are used as protozoan parasites in in-vitro, and in-vivo, incorporating, Trypanosoma spp, Leishmania spp, Babesia spp, *Cryptosporidium parvum*, *Naegleria fowleri*, *Giardia lamblia*, *Neospora caninum*, *Toxoplasma gondii*, *Eimeria tenella,* and *Acanthamoeba castellanii,* etc. considered as auspicious substitutes for prohibiting non-malarial protozoan infections in developing nations (Loo et al. 2017). *A. absinthium* has proficient flavors, thus has very potent actions in animals including ruminants (Beigh and Ganai 2017). The chemical constituent ivermectin have investigated and identified and later on was considered as a strong newly emerged antiparasitic compound at Merck

Shape and Dome Research Laboratories (MDRL), afterward chemically altered avermectin known as ivermectin, have been developed and found to be efficacious against parasitic infection (Burg et al. 1979; Campbell et al. 1979; Chabala et al. 1980). Ivermectin is a semisynthetic compound and has a good therapeutic index as well as safety (Campbell et al. 1983; Campbell 2012; Tambo et al. 2015).

Antidepressant activity

Several investigational reports have demonstrated the medicinal property of phenolic compounds, chlorogenic acid, syringic acid, caffeic acid, ferulic acid, vanillic acid, kaempferol, rutin, luteolin, quercetin, and catechin in the cure of mental illness. Since these secondary metabolites are considered as the phenolic agents emerged from *A. dracunculus* and *Stachys lavulifolia*. Antidepressant properties of the extracts were examined in the forced swimming test (FST) along with the tail suspension test (TST) (Ahangar et al. 2011; Akkol et al. 2019). An open field test was performed to examine the usual locomotor actions in ice complying treatment with the extracts. Remarkable activity between the phenolic contents of the extracts was not observed, whereas *S. lavulifolia* demonstrated good activity due to excess flavonoid contents. Animal treated with extracts reduced the immobility duration in FST, as well as TST, collated to the vehicle group excluding any promising impression on the locomotor action of animals (Aslam 2016). Moreover, *S. lavulifolia* at 400 mg/kg concentration demonstrated enhanced efficacy in both tests connoted to *A. dracunculus* (Khosravi et al. 2017). Some important research reports contributed prodigious substantiation on the antidepressant resembling the action of both extracts, which could be concerned with flavonoids as the prime constituents of the extracts (Jahani et al. 2019).

The ethanolic extract of *A. annua* L. the essential oil (AEO) attained by hydrodistillation, both with serene leaves for the forced swimming test (FST), the open-field test (OFT) are evaluated for antidepressant activity. *A. annua* essential oil or raw ethanol extract extended the calmness duration in the FST extenuated another function (ambulation, rearing, exploration, and grooming) in the OFT in livestock, along with AEO and pentobarbital used as a standard drug as satisfactorily, however, the essential oil has shown a noticeable action. Inspecting these results, this is probabilistic to propound that *A. annua* crude ethanol extract essential oil is responsible for the suppressor of the central nervous system (CNS) (Perazzo et al. 2008).

Numerous findings of some of the recently performed discoveries intimate the antidepressant effects of *A. absinthium* in the FST and TST model of depression. *A. absinthium* remarkably attenuated the quiescence duration in FST as well as TST. The extract has been found capable to express auspicious and providential outcomes but disparate extents of antioxidant effects in some models are also considered. Further investigations are required to determine its appropriate mechanism (Mahmoudi et al. 2009). *A. absinthium* has been proved to accomplish antidepressant action in a mouse model of tail suspension forced swimming tests (Rahman et al. 2017). Chlorogenic acid separated and taken away through *A. capillarie*s has demonstrated to acquaint appreciable antidepressant activity (Park et al. 2010; Khan et al. 2016).

Gastroprotective activity

Gastritis is indicated by the indication such as irritation, inflammation, or abrasion of the gastric epithelium and eventually can cause cancer (Kangwan et al. 2014; Kuipers 2015). Gastrointestinal inflammation is biochemically sevenfold sophisticated as well as intricated, might be gendered through oxidative bunts issuing as a result of enormous stress, surplus drinking, or the exploiting of certain drugs (Fakhoury et al. 2014). The generation of reactive oxygen species (ROS), namely oxygen ions, peroxides, and free radicals, might be a grave hurdle in gastrointestinal homeostasis so far as their huge chemical reactivity (Tian et al. 2017). In that case, ROS formation can give rise to gastric mucosal harm, to that lipid peroxidation is abundantly extended (Rezaie et al. 2007). Lipid peroxides generally degraded to malondialdehyde (MDA), 4-hydroxynonenal (4-HNE), and concentrations, unfold ROS-reliant gastric bunt. It has been ascertained in some research reports that a concentration of the aqueous leaves extracts of *A. herba alfa* against aspirin-induced ulcer where the extract was seems to be healing of ulcer (Abushwereb and Tolba 2016).

It was investigated by some researchers about the gastroprotective activity of an isopropanol extract from the aerial segments of *A. princeps* (IPAP) and designed as a gastroprotective floating tablet of IPAP (IPAP-FR) and obtained gastroprotective results against the excessive gastric mucosa secretion (Kim et al. 2017). The medicinally active constituent that is scoparone (6,7-dimethoxycoumarin), a coumarin-derived component obtained from *Hericium erinaceus* with *A. capillaries*, confirms an efficacious gastroprotective impact on gastric secretion induced by HCl/ethanol in rats (Son et al. 2015). Aqueous extract of *A. capillaris* (AEAC) against the gastric mucosal lesion (Yeo et al. 2018). The therapeutic potency of AEAC was seen by employing the gastric ulcer index and histological assessments, the mucosal impairment was indeed commanded by therapy with 200 or 400 mg/kg AEAC. It has not possessed acid-nullifying property in-vitro unable to stop histamine release in HMC-1 mast cells. In gastric mucosa, AEAC, furthermore, outstandingly deprived lipid peroxide production by superoxide dismutase (SOD) stimulation. AEAC also helps in the formation of

proinflammatory cytokines, namely interleukin-1β (IL-1β), interleukin-6 (IL-6) via nuclear component kappa B (NF-κB) downregulation (Soufli et al. 2016; Haq et al. 2019). The results suggest that AEAC prohibits inflammation continues as well as perpetuates oxidant/antioxidant homeostasis, in a gastro-protection to HCl/ethanol-instigated gastric and can be availed as a proficient drug for gastritis and gastric ulcer.

Antiviral activity

In our review, we have briefly concise the antiviral properties from various naturally occurring resources and herbal remedies in contrast to a few distinguished viral microorganisms accompanying coronavirus (CoV), hepatitis B virus (HBV), measles virus (MV), dengue virus (DENV), enterovirus 71 (EV71), hepatitis C virus (HCV), coxsackievirus (CV), human immunodeficiency virus (HIV), influenza virus, herpes simplex virus along with respiratory syncytial virus (RSV) (Karamoddini et al. 2011; Lin et al. 2014). Here, we have principally emphasized coronavirus disease 2019 (COVID-19), as it is extremely and severely exploring conditions globally at present. Severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV) is an offbeat and unique virus that has stirred up enormously and profoundly globally, word wide to this current era (Cheng et al. 2007). There is no antiviral remedy or vaccines that have been achievable as long as for prevention of this contingent as well as fatal ailment, which can be prevented by obeying social distancing and taking adequate and preliminary precautions exclusively (Yang et al. 2020). The corona viridae dynasty, an enwrapped RNA virus dynasty, in addition to copious specifically, human coronaviruses (HCoV), HCoV causes respiratory problems such as bronchiolitis, bronchitis, and pneumonia, with decreased immunity (Geller et al. 2012). Dissemination of coronaviruses on account of infected drained superficies has been presumed accompanying auto-exegesis of the mucous integument of the mouth, nostrils along with eyes, reiterating the ponderability of comprehensive and sightedness discerning of coronavirus stubbornness on defunct superficies (Kampf et al. 2020). Vero E6 (BJ001, BJ006) sorts of SARS-CoV treated with *A. annua* that is a Chinese medicinal herb (Li et al. 2005; Cheng et al. 2007). Some crucial and conspicuous species of *A. annua* in conjunction with *Pyrrosia lingua* and *Lindera aggregate* demonstrated the anti-SARS-CoV activity (Yang et al. 2020). Adscititious, several kinds of anti-coronaviral compounds described and recognized out of possession of Traditional Chinese Medicine (TCM) herbs, albeit the mode of functioning of these newly identified compounds, were not accomplished till date. The extracts prepared from *A. annua* plant might be given in the form of infusion to accomplish an abundant range of antiviral properties notably against coronavirus, dengue virus, and herpes simplex virus (Mesa et al. 2015). Moreover, global studies reported that many medicinal herbal ingredients have revealed antiviral activities against coronaviruses and their primary mechanism of action seems to be through the inhibition of viral replication (Jassim and Naji 2003). China has commonly used traditional Chinese medicinal herbs for the treatment of SARS effectively in many cases. However, there is no substantial evidence yet on the clinical effectiveness of these for Covid-19 infected patients (Luo et al. 2020). The genus artemisia revealed that traditional herbal remedies that emerged for this genus are productive and worthwhile against SARS-CoV infectious ailments (Haq et al. 2020).

Miscellaneous activity

The genus artemisia plants contain sesquiterpene that seems too effective in female-related sexual problems. Mugwort remedial treatment is pleasant secure for menopausal apart from hormone restoration therapy. Mugwort treatment decreases hyperactivity disorder, found to be safe and intact for the children when compared to amphetamine or methylphenidate treated therapy (Adams et al. 2012). Artemisia plants also bear a noteworthy as well as prodigious action against numerous tropical ailments such as schistosomiasis, leishmaniasis, and Chagas disease, etc. (Lutgen 2019).

The ethanolic aqueous extracts of *A. nilagirica* and *A. parviflora* have been employed for the anti-Alzheimer effect. A different test for catalepsy (bar test), locomotor action (actophotometer test) muscle mobility (rotarod test) proves for antiparkinsonian effect, and also possesses impressive and emphatic neuroprotective activities (Sengupta et al. 2011; Rios et al. 2016). *A. absinthium* was employed in the formulation of the drink, presently have been restricted in a maximum number of nations because of neurotoxicity (Lachenmeier and Uebelacker 2010; Lachenmeier 2010). Arglabin was separated as an extract from *A. myriantha,* possessing efficacious immunomodulatory effects (Bottex-Gauthier et al. 1993; Adekenov 2016).

Extracts obtained from *A. annua* L. (EAA) plus methotrexate-leflunomide were employed for the treatments of rheumatoid arthritis (RA) (Min et al. 2016). Extracts of *A. afra* was correlated with medication therapy of tuberculosis (TB) and some commonly arises manifestations of TB (Semenya and Maroyi 2013). Haemoptysis is suppressed by some reports of investigators (Han et al. 2018). *A. scoparia Waldst. Kit* (Asteraceae) is employed even as an effective remedy for some serious diseases such as hepatitis, jaundice, inflammation of gall bladder & this plant in conjunction with other herbs have been applied for the inhibition of cholagogue (Ryu et al. 2018). This plant also capable of eliciting significant insecticidal activity. Decoction has been successfully formulated from this plant used topically

to cure infectious wounds in Pakistan (Negahban et al. 2006; Tareen et al. 2010).

One species of this genus *A. herba-alba* was also confirmed to function as a vermifuge by lowering the egg and worm load of *Heterakis gallinarum* eggs in *Haemonchus contortus* and infected birds. (Ninditya et al. 2020).

A. verlotiorum Lamotte, (Asteraceae), an entire plant might be used for the cure and prevention of leucorrhoea, tonic emmenagogue, dermal infections, fever, influenza (Sussman 1980; Wong Ting Fook 1980; Adjanohoun et al. 1983; Fakim 1990; Gurib-Fakim et al. 1993, 1996a, b). The chemical constituents obtained from this pant also employed as hemostatic, stomachic, to control dysmenorrhea, metrorrhagia, antispasmodic and skin ailments. The leave contents of the plant suggest an essential oil which contains abundant chemical constituent like germacrene that obtained in the yield of around 23.6% (Gurib-Fakim et al. 1996a, b, 1997). *A. annua* plants kill the parasites integrated with malaria and dengue fever. Explorers commenced by imparting artemisia extract against the parasite larvae originated from the mosquito's kin *Anopheles stephensi* female (malaria) together larvae originated from *Ades aegypti* which disseminates dengue fever. The extract of *A. annua* demonstrated the tenacious larvicidal effects, remedy for fever, liver gall bladder disorders, now it is being assessed for flatworm infection as well as contamination produced by schistosomiasis (Biesen 2010; Hossain et al. 2014; Noori et al. 2014; Darvishpor et al. 2018; Zeb et al. 2018). It is also estimated by some explorers that a particular methanol extract of *A. pallens* mitigates APAP (Acetaminophen) persuaded renal poisoning in rats via showing its anti-inflammatory as well as antioxidative properties (Honmore et al. 2014). *A. capillaris* plant is also used to control atopic dermatitis (AD) that is an inflammatory, chronically relapsing, and non-contagious stage. It is also employed as medication for treating pruritic and skin related problems (Ha et al. 2014).

Toxicological studies of artemisia

Ogbole et al. (2014) performed acute toxicity studies of hexane leaf extract of *Artemisia annua* using rats at a dose of 1000, 2000, 2500 mg/kg intraperitoneally. They measured and observed different parameters like food and fluid intake, which was decreased, whereas urine and fecal output increased. Hematological parameters viz red blood cells, white blood cells, hemoglobin, mean corpuscular volume, packed cell volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelets, and lymphocytes showed some significant changes. The lethal dose (LD_{50}) of the extract was found to be 2750 mg/kg body weight. Overall studies showed low toxicity in short time treatment. It was declared that *A. parviflora* did not elicit any kind of harmful manifestations or demise in the acute toxic toxicity study, revealing that an $LD_{50} > 1$ g/kg body weight (Paramakrishnan et al. 2012). On the other way, *A. nilagirica* oil has been disclosed to be more toxic, evincing 100% mycelia inhibition of all test fungi (Sonker et al. 2015).

The ethanolic extracts of aerial parts of *A. abyssinica* and *A. inculta* were studied for acute and chronic toxicity was done by Qureshi et al. (1990). In *A. inculta* extract showed no signs of toxicity however at a dose of 3 g/kg it showed CNS stimulation, rapid respiration, which might be due to the presence of bitter principles in the extract. During chronic toxicity studies, two animals were found to have eye inflammation; otherwise, no signs of any abnormality; and mortality was observed as compared to the control. This plant extract did not show any signs of a spermatotoxic effect. *A. abyssinica* treated animals did not show visible toxicity, whereas at 3 g/kg some decreased locomotor activity. Chronic treatment with this extract, four female mice were found to be anemic. Alopecia was noticed for one male in its genital region, and one male animal suffered from forelimb inflammation and constipation. However, no significant and no weight gain and acute mortality were observed up to 3 g/kg p.o but a significant spermatotoxic effect was observed.

In-vitro and in-vivo animals and human clinical studies revealed that the genus artemisia has artemisinin that showed reproductive toxicity and neurotoxicity which include hearing loss, ataxia, and tremor. This was confirmed when a 20 mg/kg/day of artemether was given i.m. to groups of 3 male Beagle dogs for 5 and 30 days, respectively. Symptoms of neurotoxicity were observed from test day 23 onwards that includes hypochromic, microcytic anemia. After 5 days neuropathic alteration like neuronal and secondary axonal damage occurs in the cerebellar roof, pontine and vestibular nuclei, and in the raphe/paralemniscal region. Neuronal damage was found in all animals at 40 and 80 mg/kg following i.m. treatment. At 20 mg/kg it showed minimal effects in 5/8 dogs only, demonstrating that this level was close to tolerated exposure (Nontprasert et al. 1998; Classen et al. 1999; Medhi et al. 2009). A comparison of neurotoxic potential of the artemisinin and its derivatives using adult swiss albino mice model for 28 days via oral and the parenteral routes. Neurotoxicity or death in 50% of animals (ED_{50}) was observed by the intramuscular route for artemether and artesunate at 300 mg/kg/day compared to 50 mg/kg/day.

When oral administration of the artemether showed an increase in neurotoxicity and mortality compared with the aqueous suspension, $ED_{50} = 150$ mg/kg/day. These results indicated that once-daily oral administration of artesunate or artemether is relatively safe, presumably because the CNS is exposed transiently, whereas regular introduction either from depot i.m. injection of an oil-based drug or constant oral

intake carries produces higher neurotoxic potential (Nontprasert et al. 2000).

The artemisinin also showed genotoxicity and reproductive toxicity the genotoxic profile of in-vitro bacterial mutagenicity and an in-vivo bone marrow micronucleus test were conducted in mice. Concentrations of up to 300 g per plate in the bacterial assay, and doses of up to 845.6 mg/kg in the micronucleus test were shown to be without effect, and the compound can thus be regarded as devoid of genotoxic activity. Dihydroartemisinin, the principal metabolite of artemisinin showing embryo death and abnormalities in early pregnancy in-vitro and in-vivo experimental models. Oral administration of artemisinin can adversely affect post-implantation development at different periods of pregnancy (Boareto et al. 2008; Longo et al. 2006; White et al. 2006).

Some allied species of genus artemisia

Some important medically, as well as therapeutically active species of the genus Artemisia, is very briefly enumerated below.

Artemisia absinthium L.: Popularly called "wormwood," is a yellow-flowering plant found throughout numerous areas of Europe Siberia, is entrusted for its antiparasitic properties is used as a medication to cure indigestion and anorexia. The aerial segments are prompted to formulate various gastric herbal formulations, in dietary complements, also involved in alcoholic potations, for instance, absinthe preparations, those are delighting a rejuvenation (Lachenmeier 2010).

Artemisia arborescens L.: ("great mugwort," "arborescent mugwort") is physically in appearance capricious progenies (or amalgamation of species) with grey-green to silver leaves. It is indigenous to the varied dwellings of the Mediterranean area, where it exists as a shrub enlarging near about one meter in length. As reported by famous folklore, it was employed as anti-inflammatory medicine (Ballero et al. 2001).

Artemisia campestris L.: This is a perpetual subtle aromatic herb abundantly allocated in the south premises of Tunisia, frequently indicated as "tgouft". The leaves of this plant are broadly utilized as traditional remedies as a maceration formulation and satisfies its anti-inflammatory, antimicrobial anti-rheumatic as well as antivenin aspects (Hamed et al. 2014).

Artemisia douglasiana Besser.: In Argentina, it is substantially known as "California mugwort", which is fortuitously harvested in the Cuyo premises is consumed as a folk remedy confessed to receiving the prevalent name of "matico." The favored proper application of the decoction of leaves of "matico" is applicable in treating gastrointestinal problems and peptic ulcers (Ariza-Espinar and Bonzan 1992).

Artemisia dracunculus L.: ("tarragon") is a perennial herb, that has a detailed chronicle of consummation in culinary conventions. It also occupies a vast scope of health prosperity; hence this has been extensively employed as herbal remedy. Two well-reported cultivars (Russian and French) are employed broadly vary in ploidy extent, physical appearance chemistry. The photochemicals as well as medicinal ingredients, are meticulously described in the existed research, mainly emphasizing its essential oil constitution, which provides its characteristic flavor (Obolskiy et al. 2011).

Artemisia abrotanum L.: ("southernwood") was prescribed as an ancient remedy for diagnosing a range of ailments involving upper respiratory tract problems. Contemporarily, this perpetual plant is successfully applicable for culinary along with cosmetic prospects (Gruenwald 2000).

Artemisia scoparia Waldst. & Kit.: ("Redstem wormwood") is a slightly perfumed annual herb that is distributed globally prevailing all over the globe, especially in southwest Asia regions as well as central European regions. The accomplishment of *A. scoparia* might be accredited to phytotoxins and essential oils, spare to another non-soaring secondary compounds. It has been entrenched that aerial pieces of *A. scoparia* manifested a soaring essential oil that possessed great therapeutic importance. It pertains to antibacterial, insecticidal, antiseptic, antipyretic, anticholesterolemic, vasodilatory, diuretic, cholagogue, and purgative characteristics; this is also applicable for the cure as well as recovery from gall bladder inflammation, jaundice along with hepatitis (Kooy and Sullivan 2013).

Artemisia spicigera C.: Koch, is called provincially in Turkey as "yavsani", is highly distributed in Eastern Central Anatolia areas, is conventionally employed for the cure of dermatological problems and ulcerative sores (Afshar et al. 2015).

Artemisia vulgaris L.: Frequently called "mugwort", is a perpetual weed found in North America, Europe-Asia, and Philippines, which is pertinent for its antihypertensive properties. It was also found to retain diverse characteristic medicinal aspects, namely anthelmintic, carminative, antispasmodic, and anti-inflammatory activities; as well as cure of onerous menstruation (dysmenorrhea) in the treatment of labor pain or miscarriage (Melguizo-Melguizo et al. 2014).

Conclusion

Artemisia and its allied species have been traditionally and ethnopharmacologically used to treat many diseases such as

diarrhoea, dysentery, cholera, diabetes, hypertension, inflammation, intestinal spasms, and liver diseases. Artemisia species contain diverse compounds whose principal chemical constituents are polyphenols and essential oils. The result showed a substantial conceivable quantitative and qualitative variation between essential oil contents of *A. nilagirica* and *A. parviflora*. These oils have been found to play an essential role in uncoupling of electron transport chain in a variety of bacterial species and can be used for food preservation and cosmetic preparations. They also contain coumarins, acetylenes, sesquiterpene, lactones, and a large number of phytoconstituents viz alcohols, phenols, flavonoids monoterpenes, and sesquiterpene derivatives. These species possess different pharmacological activities such as antineoplastic, antimalarial, insecticidal, antispasmodic, anti-inflammatory, antioxidant, antibacterial, antifungal, antiepileptic and analgesic properties. Acute studies showed that the plant to be nontoxic or low toxic, whereas chronic use of the plant causes toxicity. In this review, we have tried to abridge the pertinent findings, rational approaches, and innovative development regarding the ethnopharmacological activities of genus artemisia and novel therapeutic compounds that emerged out from this genus which are used to control and cure various types of common as well as lethal kinds of human diseases. It has been seen that *A. annua* is under clinical trial against COVID-19 disease, presently vast research is going against the treatment of this pandemic. If proved by researchers then chemical entities obtained from this genus will be cost effective, readily available, marvellous and will posssess persuasive therepeutic effect for combating against COVID-19. This review can be used for further research investigations as well as clinical purposes in the development of novel medicinally efficacious and safer plant derived drugs for curing several kinds of illnesses.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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