Advances in Bioresearch
Adv. Biores., Vol 12 (4) July 2021: 316-333

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.12.4.316333

Advances in Bioresearch

REVIEW ARTICLE

An updated review on pharmacognostical characteristics and pharmacological activities of *Artemisia annua*

Varsha Raj*[a], Manveer Singh[b], Munesh Kumar Mani[a], Navneet Verma[a]
[1]Faculty of Pharmacy, IFTM University Lodhipur Rajput, Moradabad -244102 Uttar Pradesh, India
Corresponding author-varsharaj01@gmail.com

ABSTRACT
The essential oils present in medicinal or aromatic plant, have a varied range of medicinal properties because of they contain the range of active constituents, having the various pharmacological action. Plant Artemisia annua (A. annua) belongs the widest annua Asteraceae family, has the large number of therapeutic utility in human ailments, such as antioxidant antimicrobial and insecticidal study have been carried out for the different species of the A. annua. On the subject of insecticidal and antimicrobial properties we have concluded here the potency of essential oils adjacent to the insect and microbes, while, only some species have been investigated for the antioxidant activity.
KEYWORDS: *Artemisia, chemical composition, essential oil, insecticidal, antimicrobial, antioxidant.*

12.04.2021 Revised 26.06.2021 Accepted 11.07.2021

How to cite this article:
V Raj, M Singh, M K Mani, N Verma. An updated review on pharmacognostical characteristics and pharmacological activities of *Artemisia annua*. Adv. Biores. Vol 12 [4] July 2021. 316-333

INTRODUCTION

Medicinal and aromatic plants are the significant resources of the secondary metabolites, having the large range of utility towards in the direction of to control of plant and human diseases, pharmaceutical industry as well as in cosmetics preparations [1]. Inside the kingdom plante, family Asteraceae is gifted from the plants which are fully loaded from the property of essential oil-yielding plants. Among these kinds of plants, the *A. annua* got the top place due to its biological characteristics. *A. annua* having the small shurbs and herbs, occurred in northern temperate areas and contain approx 500 species from North America, European countries and South Asia[2]. *A. annua's* species are commonly known as Annual wormwood, sweet wormwood, sweet annine and sweet sagewort. Due to the availabilty of sesquiterpene lactones and terpenoids, the majority of species have bitter tastes and intense aromas, which may depress the herbivores and had the specific benefits [3]. The *A. annua* species have large and diverse applications to control the human as well as plant disease. It is also utilized in the pharmaceutical industry. *A. annua* is renowned therapeutic plant for its antimalarial property due to availabilty of its active constituents artemisinin (also known as Qinghaosu), which is sesquiterpene lactone (a cadinane-type) contain the endoperoxide bridge. Presently it is the most efficacious and potent compound alongside chloroquine, for Plasmodium falciparum (that cause the cerebral malaria) and other malaria-causing parasites [4]. Alongside antimalarial effects, *A. annua* has also other biological actions such as anti-inflammatory, antibacterial, angiotensin converting enzyme inhibitory effect and antitumor activity [5].

PLANT DESCRIPTION

A. annua is the yearly herb inhabitant to Asia, mainly in China. Naturally, it is found as the vegetation's component in the northern areas of Suiyuan and Chahar areas in China, at 1000 to 1500 m above from the sea level; recently it is cultivated in various countries as well as in the United States, Australia, Africa and tropical areas. *A. annua* having the aromatic leaves which having the length up to 3 to 5 cm and these alienated by intense cuts into 2 or 3 tiny leaflets. Flowers and leaves both have the five celled filamentous trichomes as well as ten-celled biseriate trichomes. From the ancient time in traditional Ayurvedia as

well as in Homeopathic medicinal system, *A. annua* is used as a folk medicinal plant which having the potent anti malarial property. As per the earlier literatures, inside China and Korea, it was used in the form of aqueous preparation of the dried herb which was useful against the various ailments such as the skin diseases, malaria, fever, hemorrhoids and jaundice [6, 7].

Recently the Pharmacopoeia of the People's Republic of China officially lists the dried herb of *A. annua* as a remedy for fever and malaria, at a daily dose of 4.5–9 g of dried herb prepared as an infusion [8]. This is the herbal preparation that has been used for clinical trials. *A. annua* is also described to have anti-hyperlipidemic, anti-plasmodial, anti-convulsant activity [9].

Research showed that the *A. annua* was also highly effective against the malaria's patients infected from the *Plasmodium falciparum, Plasmodium vivax*, mainly and those one who showed the chloroquine resistant. Since 2001 WHO highly recommended the Artemisinin and its derivative based combination therapies for the malaria treatment, consequently they are utilized in all over the world as an Anti malarial drug [10].

The significance of artemisinin has lead to various synthetic as well as semisynthetic compound, looms to its formation to complement its derived from the *A. annua*. The most successful modern approach is the chemical conversion of artemisinic acid in to artemisinin, which one is produced by the *Saccharomyces cerevisiae* strain [11].

Additionally to this dynamic compound, *A. annua* has too an appealing dietary profile with due to the availability of vitamins, amino acids, minerals as well as essential beneficiary nutrients which is required for the health [12]. From the time when it is discovered, the *A. annua* is the exclusive topic of widespread research due to its chemical constituents. Over the 600 active secondary metabolites has been recognized from the plant [13], together with the various triterpenoids, sesquiterpenoids, steroids, monoterpenoids, coumarins, flavonoids, benzenoids and alkaloids [14-16].

Thankfulness to this fortune, the plant *A. annua* has a huge number of the different biological goodness for example it is well explored for the hepatoprotective, antitumor, antifungal, anti-asthmatic, antioxidant and anti-inflammatory activities [17].

All these reports assured the potency of *A. annua* as an aspirant for the medical, food, nutraceutical, cosmetic and pharmaceutical industries.

Aim of the current review is, to explore the details of different identified chemical compounds of *A. annua* as well as to explain the various phytochemical and pharmacological activities showed by this plant and its active compounds further than the malaria [17].

Botanical classification of the plant

Kingdom: Plantae
Clade: Angiosperms
Clade: Eudicots
Clade: Asterids
Order: Asterales
Family: Asteraceae
Genus: *Artemisia*
Species: *Artemisia annua*
Binomial name: *Artemisia annua* L.

Fig.1. *Artemisia annua (A. annua)* **[1**8]

PHARMCOGONOSTICAL CHARACTERISTICS

Leaves of *Artemisia annua* are widely used for the treatment of malaria and as anti-inflammatory in most part of the world and in most of herbal drug market, leaves are being sold along with the aerial parts as Qinghao [19] . Therefore, macroscopic and microscopic characters of the aerial parts are described below:

Macroscopic characteristics

An aromatic annual herb 0.9 to 1.95 m in height with deeply grooved branches. Variation generally present in the leaves and aerial parts. The leaves margins are not entire but the base is asymmetrical. The leaves are light green to dark green in color and strongly aromatic in smell and slight bitter in taste [20]. The lamina is completely divided into two separate segments called leaflets. The leaflets are arranged in pairs. [21].

(The leaves are arranged in pinnately as well as shapes of the leaves are lanceolate to oblong plus several deeply cut segments are present. The both outer and inner surfaces are glabrous along with a thin brittle texture. The leaves are dorsiventral histologicallly) [21].

The leaves contain anomocytic stomata with numerous glandular and non-glandular trichomes on both the surfaces with little stalk. Spongy parenchyma contains 4-6 layers of loosely arranged cells. Reticulate xylems are lignified and present in the ventral surface of the leaf [21].

Microscopic charactestics

Artemisia annua leaf includes stomatal number of upper epidermis (32-47) and lower epidermis (62-66); stomatal index of upper epidermis (0.05-0.08) and lower epidermis (4-9); palisade ratio (35.5-5.75); Vein islet number (3-5) and Vein termination number (6-8). The average values of moisture content (9.2w/w), total ash (8.3w/w); acid insoluble ash (0.91) as well as alcohol (6.2w/w) and water (3.8) soluble extractives of *Artemisia annua* leaves were determined (10). The aerial parts of *Artemisia annua* (Asteraceae), have been used in Iranian traditional medicine. Composition of the essential oil, which was obtained from the aerial parts of *Artemisia annua* collected from Ilam-Iran, was determined by GC-MS. In total, twenty-five components (91.27 % of essential oil) were identified. Major constituents were α-pinene (7.33 %), camphene (5.68 %), sabinene (4.78 %), β-myrcene (22.41 %), 1,8-cineole (17.17 %) and camphor (20.41 %) [22].

Active chemical ingredients found in *Artemisia annua*

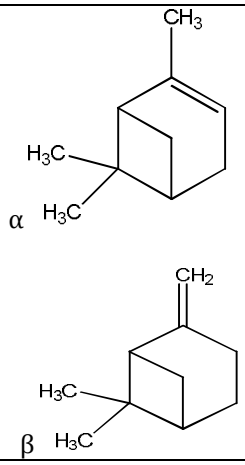
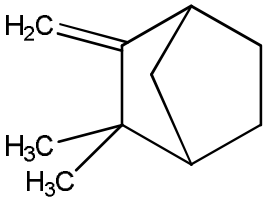
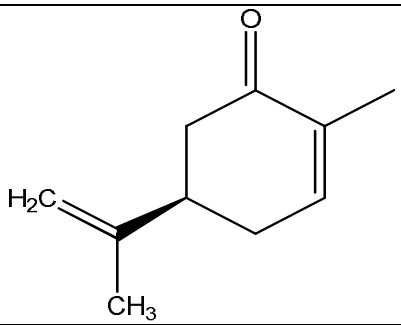
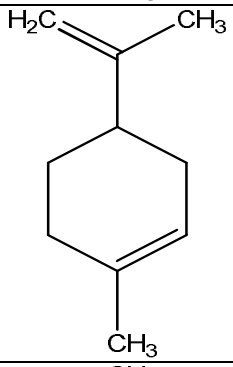
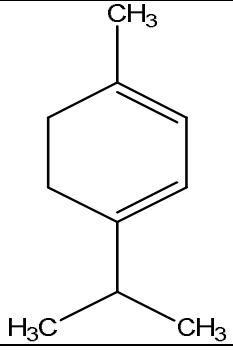
The chemical composition of *Artemisia annua* consists of volatile and non-volatile constituents. The volatile components are mainly attributable to essential oils with the content of the latter being 0.2–0.25%. The main compounds, which account for about 70% of the essential oils, appear to be camphene, β-camphene, isoartemisia ketone, 1-camphor, β-caryophyllene and β-pinene. In addition, other minor ingredients, such as artemisia ketone,1, 8-cineole, camphene hydrate, and cuminal are also found in the volatile parts of *Artemisia annua* [23].

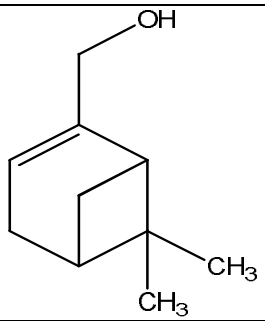
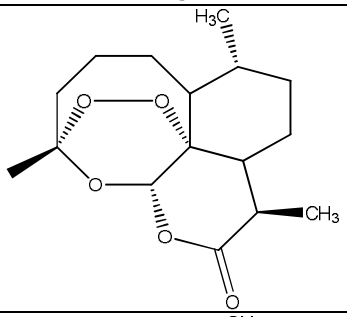
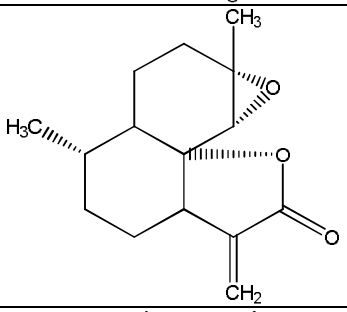
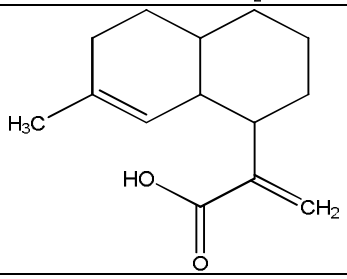
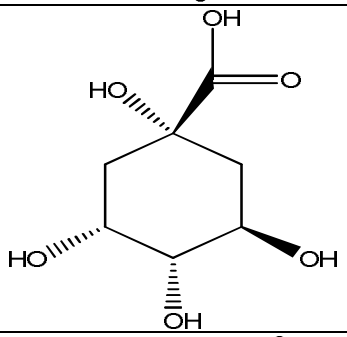
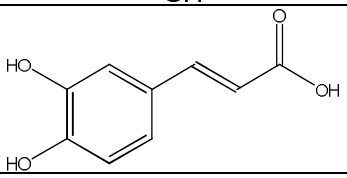
The main non-volatile ingredients include sesquiterpenoids, including artemisinin, artemisinin I, artemisinin II, artemisinin III, artemisinin IV, artemisinin artemisic acid, artemisilactone, artemisinol and epoxyarteannuinic acid . flavonoids and coumarins, together with proteins (such as β-galactosidase, β-glucosidase), steroids (e.g. B-sitosterol and stigmasterol) are the main chemical constituents of *A. annua* [23].

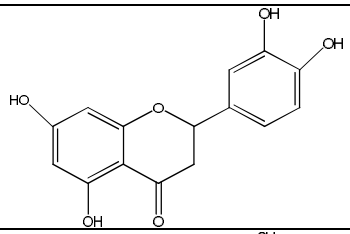
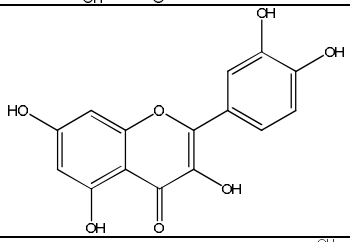
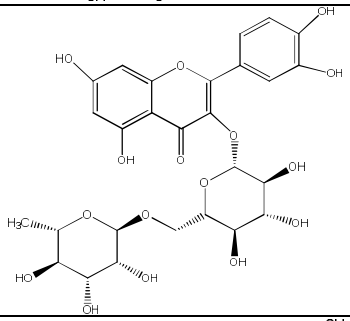
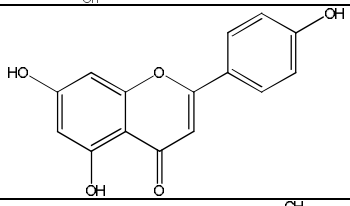
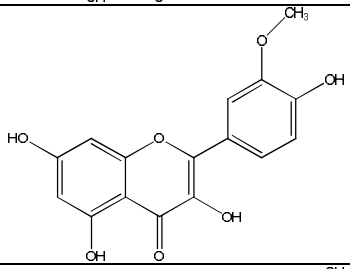
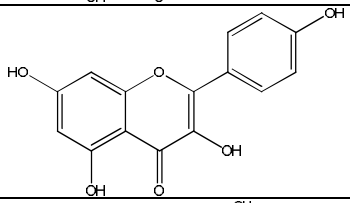
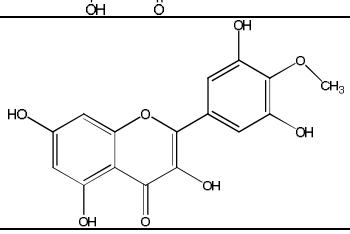
The area subsequently placed under various production arrangements. [The planted area was in Kenya (nearly 65%) followed by Uganda (19%) and Tanzania (north, over 16%). Both small and large farms were involved. In 2006, 7,500 farmers were reportedly involved, but area was not revealed. Currently the plant is widely cultivating in many places of Ethiopia [24].

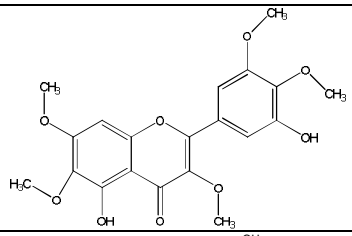
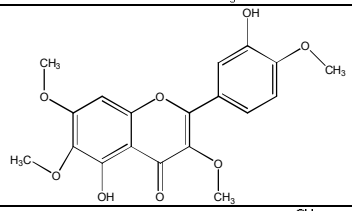
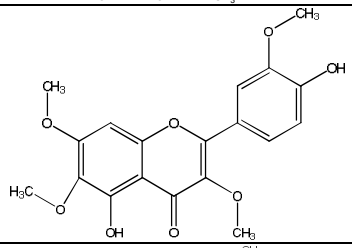
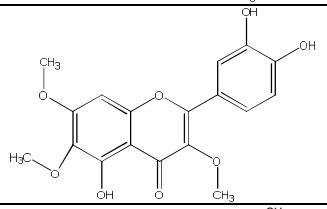
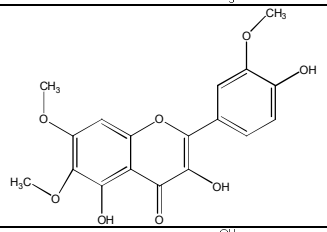
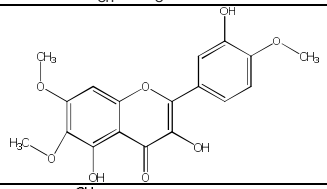
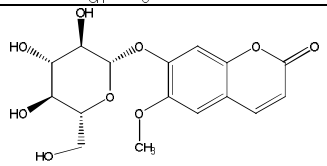
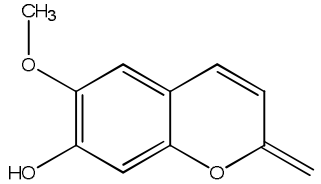
Table No.1 The chemical structure and biological activity present in *A. annua*.

Molecule	Structure	Activities	References
1,8-cineole		Insecticidal, expectorant, anti-inflammatory, antibacterial, antitumor, antifungal	[25-31]
α-and β- pinene		Antimicrobial, anti-hypertensive, antinociceptive, anti-inflammatory, for flavor and fragrance purpose and as a food additives	[32-35]

			
Camphene		Insecticidal, antitumour, anti-inflammatory, anesthesia, neuroprotective	[36-52]
Carvone		Anti-inflammatory, anti-hyperlipidemic, anti-microbial, anti-carcenogenic, chemopreventive, anti-hypertensive, immunomodoulator	[52-56]
Limonene		Antioxidant, antigenotoxic inhibition of angiogenesis, antitumor	[57-59]
α-terpinene		Antioxidant	[60]

Myrtenol		Mutagenic, neuroprotective, Analgesic, antitumor, anti-inflammatory,antioxidant, antiaging, anti-diabetic, protects against the lungs disease, LDL (Low Density Lipoprotein)	[61-64]
Artemisinin		Antiviral,antitumor, antimalarial, antiparasitic, anti-inflammatory, antifibrotic	[65-69]
Arteannuin B		Antiviral,antitumor, larvicidial, anti-inflammatory,	[70-74]
Artemisinic acid		Regulator of adipocyte diferentitations	[75]
Quinic acid		Antioxidant, lipolytic, antiobesity, antiviral, inhibitor of hepatic glucose-6-phosphate translocase	[76-79]
Caffeic acid		Antiviral, antimicrobial, anti-inflammatory, antitumor, antialzimer, anti- diabetic, cardiovascular protector	[80-87]

Luteolin		Antitumor, antioxidant, anti-inflammatory,nervous system protector, cardiovascular protector	[88-93]
Quercetin		Antioxidant, vasodilators effect, antinflammatory, antitumor, cardiovascular protector, neurodegenerative diseases protector, antiviral	[94-101]
Rutin		Antioxidant, cytoprotective antinflammatory, immunomodulator, neuroprotective, neurodegenerative, antidiabetic, hypotensor, an antiviral	[102-105]
Apigenin		Antioxidant, antinflammatory, antitumor , antimicrobial	[106-110]
Isorhamnetin		Antioxidant, antinflammatory, neuroprotective, antidiabetic	[111-117]
Kaempferol		Antioxidant, antinflammatory, neuroprotective, antitumor	[118-121]
Mearnstein		Antioxidant	[122]

Artemetin		Hypotensor, antitumor, antioxidant, anti-inflammatory	[123-127]
Casticin		antitumor, antioxidant, anti-inflammatory, antiageing	[128-130]
Chrysosplenetin		Antiviral	[131]
Chrysoprenol D		Antiinflammatory, antitumor, antioxidant	[132]
Cirsilineol		Immunosuppressive, antitumor	[133-136]
Eupatorine		Antitumor	[137-139]
Scopolin Scopoletin	 	Antinociceptive, anti-inflammatory, antioxidant, antipyretic, cooling effect, antiallergic	[140-145]

THERAPEUTIC POTENTIAL OF *A. ANNUA*

As per the traditional and folk medicinal system the various pharmacological investigations has been carried out scientifically to confirm its potential and efficacy in cure of various diseases [146].

Antihypertensive activity

The earlier literature reveled that the diabetic rabbits and rats were (body weight approx 100-390 mg kg^{-1}) regularly feed the aqueous extract of the *A. annua* (aerial part) in specific dose for 2-4 weeks regularly, the results showed the significant reduction in blood pressure. This pharmacological action prevent the risen level of glycosylated haemoglobin also showed the hypoliposis action, additionally it prevent the loss of body weight in diabetic animals. It was also estimated that the administration of *A. annua* extract in 100-200 mg kg^{-1} were significantly prevent the phenylephrine-induced contraction as well as showed the effective endothelium-dependent relaxation in rat's aortic rings inside the Krebs's solution [146].

Antimicrobial activity

The essential oils collected from the *A. annua* explored the vital antimicrobial activity during this experiment. The essential oil showed the significant antimicrobial potency against all the experimented microbes, excepted *Pseudomonas aeruginosa*, no antimicrobial activity has been observed. The research showed that the maximum inhibitory activity against the fungal microbes *Saccharomyces cerevisiae* as well as the *Candida albicans* , showed the (Minimal Inhibitory Concentration) MIC = 2 mg/ml and MIC = 2mg/ml respectively [147]. The essential oil showed the moderate inhibitory activity against the *Escherichia coli* and *Staphylococcus aureus*, the MIC value was found 64 mg/ml and 32 mg/ml respectively [148].

Anti-inflammatory activity

Research stated that the aqueous methanolic extract of *A. annua* showed the significant anti-inflammatory activity when investigated by using the egg albumin and carrageenan induced rat paw edema screening models (for acute condition) and grass pith and cotton pellets induced screening models (for chronic inflammation). At a dose 200mg/kg, the *A. annua* showed the good anti-inflammatory activity in the carrageenan and albumin induced screening models, showed the MIC value 55.44% and 53.16% respectively [149].

At the dose of 200 mg/kg, in the chronic inflammatory screening models the *A. annua* extract explored the 60% declination in granuloma weight. During this, the Diclofenac Sodium (non-steroidal anti-inflammatory agent) is act as standard drug and the efficacy of the plant extract was compared with the standard drug.

Phytochemical screenings also reveled that the presence of flavonoid, triterpenoids, coumarin and polyphenols in the *A. annua* extract, which prevent the progression of maximum edema response in acute as well as chronic anti-inflammatory screening models [149].

Antioxidant activity

Various research study showed that the plant *A. annua* had the potent antioxidant activity due its available chemical constituents specifically the phenolic compounds [150].

Another study reveled that the plant *A. annua* posses the antioxidant activity because of the major compound such as flavonoids, coumarins and terpenes, it is importantly stated that a flavonoid which named is chryprenol D(Molecular formuls is $C_{18}H_{16}O_8$), has been recognized as major molecule which play significant role in the antioxidant activity for this plant[151].

Another research showed that the essential of *A. annua* had the potent antioxidant activity whih is based on the 2,2-diphényl-1-picrylhydrazyle (DPPH), Oxygen Radical Absorbance Capacity (ORAC) 2,20 -azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) diammonium salt),assays and metal chelating ability using the ferrozine assay [150, 152].

Additionally the animal feed with the *A. annua* extract diet showed the progressive changes in the functioning of NQO1 (NAD(P)H: quinone oxidoreductase 1), which is act as important marker antioxidant enzyme, in the cause of various significant organs such as Large intestine, Small intestine, Stomach, Kidney.

Collectively, these high level different antioxidant activities concluded the results that *A. annua* is a richer source of the antioxidants which may favor its therapeutic utilization, it's utility as a highly effective herbal tonic by humans and other living beings [153].

Antimalarial activity

Research showed that Artemisinin and its derivatives are the principle constituents which are majorly responsible for the antimalarial activity. They showed their therapeutic effect because of the interfering in the catabolic pathway of plasmodial hemoglobin as well as by preventing the heme polymerization [154, 155]. Result obtained from the *in- vitro* studies showed that, in malarial parasites the artemisinin is

capably blocked the proteolytic activity of the digestive vacuole. Additionally the *ex vivo* research revealed that, inside the parasites the administration of artemisinin with the hemoglobin accumulation, prevent the hemoglobin degradation. In research artemisinin has been explored as a potent inhibitor of the heme polymerization activity regulated by the *Plasmodium falciparum* histidine and *Plasmodium yoelii* lysates [156, 157].

Although other plants of this family, which do not contain artemisinin, such as *A. apiacea* *A. herba alba*, *A. abrotanum, A. absinthium, A. ludoviciana*, and specifically *A. afra* jewel from the good antimalarial property, later on it is used for the antimalarial activity in South Africa and tanzania[158].

Antiparasitic activity

Antiplasmodial Activity

In area of central Africa, Malaria patients are treated from the *A. annua* tea, at a particular dose (as per the Chinese pharmacopoeia), showed the potent anti-malarial activity.

During this experiment 5 malaria patients received the *A. annua* tea showed a rapid recovery from parasitemia in two to four days. One another trial which carried out with the 48 malaria patients confirmed the recovery from parasitemia in 44 patients during 4 days. Both clinical trials explored the clear improvement and recovery in the malarial symptoms [150].

Anti-Helminthic property

From the data, each year In 78 nations, around 250 million populace are infected from Schistosomiasis, in which 280,000 people were died approximately every year and in sub-Saharan Africa nation approx 172 million peoples get infected from it. The ailment is occurred by the trematode worms (genus Schistosoma) with 6 species (S. mansoni, S. haematobium, S. japonicum, S. intercalatum S. malayensis and S. mekongi,). In which S. mansoni and S. haematobium are the major causing agents for the intestinal and urinary schistosomiasis, correspondingly, that abundantly found in Africa (230). Artemisinin and its derivatives having the higher potency to deduct the total worm rates which does not depend on the route of drug administration, also seen the higher deduction rates for female as compare with male worms.

In addition the Artemisinin derivatives are also majorly reduced the worm eggs burden as well as granulomata which is caused by the worm egg inside the liver of animals(host)[150].

Artemisinin and its derivatives were also found to be active against a number of nematodes. In an in vitro study, artemether treatment caused cuticular changes on adult Toxocara canis similar to those induced by albendazole sulfoxide with faster onset of action [159]

A research performed on *Neospora canum*, a kind of protozoal parasite that causing the infection inside the mammals very commonly, causing the reason of abortion in cattle was also carried out. The cultured cells (Vero cells mouse peritoneal macrophages or vero cells) were infected with *Neospora caninum tachyzoites* and treated by artemisinin at the concentrations 20, 10, 1, 0.1, 0.01 µg/ml respectively. On the 11 days of the experiment at the concentration 20 or 10 µg/ml artemisinin compleletly abolished the all kind of microscopic foci of the *N. caninum* . The same result has been observed at 1 µg/ml on the 14 days of the experiment. In shorter duration at the 0.1 µg/ml conentration artemisinin decrease the intracellular proliferation of *N.caninum tachyzoites* ($p < 0.05$) [13, 14].

Others nematodes on which Artemisia and its derivative have been investigated include *Haemonchus contortus* in animals and plant nematodes (Globodera, Meloidogyne spp., Xiphinema index, rostochiensis) [160].

Anticancer activity

Several research showed that Artemisinin showed excellent anti-cancer property when it is experimented for *in vitro* trial. The endoperoxide group present in the Artemisinins is totally responsible for its anticancer as well as antimalarial property. There is no clinical trial has been performed for the *in-vivo* study. Such as Hydrogen peroxide (H_2O_2), artemisinin also react with ferrous iron (Fe2+) for the formation of radical species. Artemisinin-derived radical species related to anti-parasitic as well as anti-cancer activities [161, 162].

Artemisinin derivatives bear the good anti-cancer property, which is significantly risen when the iron compounds were merging inside the cell culture medium. Artemisinin and transferrin (ART-Tf) complex, which is iron containing transport protein human, is dynamically taken up by cancer cells via the endocytosis pathway which is mediated by transferrin receptor (TfR) and it is explore remarkably greater anti-cancer activity than the unconjugated artemisinin. Resembling ART-Tf, artemisinin-peptide conjugates which are framed to target TfR too explored the highly effective and specific anti-cancer property [161, 163].

These researches showed the significance of iron metabolism in to find out the efficacy of artemisinin derivatives in inhibiting the cancer cells. Derivatives of Artemisinin, stimulate the cancer cells's planned cell death by trigger the cytochrome C-regulated or intrensic pathway for the apoptosis, while the preliminary protein artemisinin derivatives which are targeted for the apoptosis process in human carcinogenic cells have not recognized till the date. Even though the formation of free radicals starting from the reaction between artemisinin and iron, is recognized as the major mechanism for its anticancer property, there are some other mechanisms, vital for the cancer survival and proliferation which are influenced by artemisinin [164, 165].

Antiviral activity

The data obtained from the research via *in vitro* and *in vivo* method for *A. annua* extract and its derivatives, showed that the plant having the good antiviral activities and act as a potent anti-viral agent. Experimented viruses (both DNA and RNA viruses) on which antivirus activity has been performed, so effectively act on both type of viruses [166].

A. annua (methanolic extract) was experimented in a syncytium inhibition assay; depend on the reaction between the HIV-1 and the CD4 cell membrane of T-lymphocytes [167].

An *in vitro* research has explored that tea infusion of *A. annua* has good anti-HIV property. The availability of HIV-malaria co infection in malaria prone areas has the chances of anti-HIV activity of *A annua* traditionally utilized for malaria treatment. It has been demonstrated that artemisinin was not the primary compound which is responsible for the anti-HIV activities.

From the *In vitro* study, *A. annua* tea infusion study is observed highly active, the IC50 values found below the 2.0 μg/mL, however artemisinin was found inert at the 25 μg/mL [16]. Nevertheless, in vitro models of NL3.4 HIV-1 infected PBMCs showed that 10 μM of artemisinin inhibited HIV-1 replication by 60% [168].

As per the latest research it is explored that the *A. annua* tea infusion had the power to work against the HIV infection. In this experiment *A. afra* species were utilized (not contain the artemisinin). In this study there were two different samples with different format were utilized (in which one was an infection sample format and the other one was the co-cultivation sample format). Both experimental samples were also investigated for cellular toxicity, for the human cells which were tested inside the experiment. No evidence has been showed for the cellular lethality at the highest concentrations from the experiment. It is the experimental study which was gives primarily the proof for the *in vitro* anti-HIV capability of *A. annua* tea infusion [169].

Immunosuppressive activity

In the preclinical study, *A. annua* (ethanolic extract) showed the immunosuppressive property against the splenocyte proliferation, cconsequently the *A. annua* was used in the treatment of various autoimmune diseases as well as considered as a potent immunosuppressant for the future research. The extract obtained from the plant was purified and phytochemicaly evaluated. Suppressive property of the plant extract was observed against the calmodulin by the increase in the fluorescence production of calmodulin [170].

Anti-diabetic activity

A. annua (aqueous extract) showed the considerable anti hypoinsulinemia and anti-diabetic in the animal (at the dose 28.5 mg/kg) during the preclinical study. The phenomena which is responsible for this property is may be due to, it make the proper secretion of insulin from the β cells of pancreas as well as by α cells inhibition or it may be occurred by increasing in the insulin activity.

Additionally, now days a well significant connection is established between the inflammatory response, oxidative stress as well as insulin activity. It provides the details about the potency of antioxidant to prevent against the harmful effects of hyperglycemia condition as well as the progression of glucose metabolism. Commonly, the flavonoids are the main components which responsible for the antioxidant potency, which was confirmed to work on biological targets, concerned in the type 2 diabetes mellitus for example α-glycosidase, aldose reductase or glucose cotransporter [167].

The *A. annua* having the anti-hypoinsulinemic activity and it is also prevent the hepatocytes damage by the inhibition of the lipopolysaccharide by the appearance of proinflammatory mediators TNF-α (tumor necrosis factor alpha), IL-1β (Interleukin 1 beta) by the appearance of COX-2 (cyclooxygenase 2) as well as iNOS (Inducible nitric oxide synthase) [17]

***Artemisia annua* derived product availabe in Market**

1- Nutricology Super Artemisinin,Vegicaps [171,172, 173].

2-Amalth *Artemisia annua* [174].

3- Deve Herbes Pure Sweet Wormwood Essential Oil (*Artemisia annua*) 100% Natural Therapeutic Grade Steam Distilled 300ml [175].

4- Tonga Herbs Artemisinin Extract Powder (200g) [176].
5- Artemisia Tea 100% natural [177].
6- Thorne Research, Artecin, 90 Capsules [178]
7- Nutricology, Artemisinin, 90 Vegetarian Capsules [179]

CONCLUSION

In all over the world, from the herbal plants, biological activity of *A. annua* is moderately less discovered against the plant pathogens and bugs pest. This genus is shown by greater than 40 species, specifically in the tropic area. This review study showed the active components of the essential oils which were obtained from various geographical areas, a marked difference was observed in the composition of various species which belong to the same genus. The main components were consisted from various terpenoids, terpenes and 1, 8-cineole, phenolic compounds, beta-pinene, thujone, camphor, caryophyllene, artemisia ketone, germacrene D and camphene were found as a primarily components in some species. a range of Artemisia oils and its active compounds have been explored as efficient insecticidal, antioxidant and antimicrobial agents. Several oils also showed the poor to moderate efficacy against the pathogens and pests. The oil contained the good antioxidant property only because of the availability of phenolic compounds. The information reviewed here is future to provide as a reference tool to populace in the field of plant protections and Chemistry of natural products.

In fact the present review emphasizes on the Artemisia essential oils's antimicrobial activity against phytopathogens, it has also showed the significant results against the some of human as well as animal pathogens. Lately this genus has magnetized the world's attention, when it grasped a Nobel Prize regarding its utility for the malaria treatment in traditional medicine system. Many preliminary investigations had been performed on the various species of Artemisia concerning its antioxidant, antimicrobial and insecticidal properties, but the more sophisticated bio-prospection required to explore its valuable bio-activities in opposite to the plant pathogens and bugs at the ground level. Present times are frantic times, in which attention of research has been shifted in the direction of, too exploration of the natural compounds, particularly for human wellbeing. More defined reporting and data investigation is still required. Another major problem such as residual toxicity, mammalian toxicity, phy-toxicity, legal obligation/regulations and its long-standing physiological and environmental outcomes of the efficient oils necessitate being replied.

REFERENCES

1. Pandey, N., Goswami, N., Tripathi, D., Rai, K. (2019). Epigenetic control of UV-B-induced flavonoid accumulation in Artemisia annua L. Planta, 249: 1-19.
2. Abad, M.J., Bedoya, L.M., Apaza, L.,Bermejo, P. (2012). The Artemisia L. genus: A review of bioactive essential oils. Molecules, 17:2542-2566.
3. Bora, K.S., Sharma, A. (2011). The genus Artemisia: A comprehensive review. Pharm. Biol, 49:101-109.
4. Allen, P.C., Lydon, J., Danforth, H.D. (1997). Effects of components of *Artemisia annua* on coccidia infections in chickens. Poultry science, 76: 1156-1163.
5. Mohamed, A.E.H., El-Sayed, M.A., Hegazy, M.E., Helaly, S.E., Esmail, AM., Mohamed, N.S. (2010). Chemical constituents and biological activities of Artemisia herba-alba, Rec. Nat. Prod. 4:1-25.
6. Pandey, A.V., Tekwani, B.L., Singh, R.L., Chauhan, V.S.(1999). Artemisinin, an endoperoxide antimalarial, disrupts the hemoglobin catabolism and heme detoxification systems in malarial parasite, J. Biol. Chem. 274:19383-19388.
7. Jarvis, C.E. (1993). A List of Linnaean Generic Names and Their Types; Koeltz Sciebtific Books; International Association for Plant Taxonomy: Bratislava, Slovakia ., 127, p. 100.
8. Ferreira, J.F.S., Luthria, D.L., Sasaki, T., Heyerick, A. (2010). Flavonoids from *Artemisia annua* L. as Antioxidants and Their Potential Synergism with Artemisinin against Malaria and Cancer, Molecules.15(5): 3135-3170.
9. Abad, M.J., Bedoya, L.M., Apaza, L., Bermejo, P. (2012). The Artemisia L. Genus: A Review of Bioactive Essential Oils. Molecules.17: 2542-2566.
10. Maham, M., Moslemzadeh, H., Jalilzadeh-Amin, G. (2014). Antinociceptive effect of the essential oil of tarragon (Artemisia dracunculus), Pharm. Biol. 52: 208-212.
11. David, J., Newman Gordon, M., Cragg David, G.I., Kingston. (2015). Natural Products as Pharmaceuticals and Sources for Lead Structures. The Practice of Medicinal Chemistry.,4; 101-139.
12. Ferreira., J.F.S., Vagner, A., Benedito, V. A., Sandhu, D., Jose, A., Liu, M.S.(2018). Seasonal and Differential Sesquiterpene Accumulation in Artemisia annua Suggest Selection Based on Both Artemisinin and Dihydroartemisinic Acid may Increase Artemisinin in planta, Front. Plant Sci., 9: 1-12.
13. Das, S. (2012). Artemisia annua (qinghao): a pharmacological review. Int. J. Pharm. Sci., 3(12): 4573-4577.

14. Penissi, A.B., Giordanob, O.S., Guzmánc, J.A., Rudolphd, M.I., Piezzia, R.S. (2006). Chemical and pharmacological properties of dehydroleucodine, a lactone isolated from Artemisia douglasiana. Molecular Medicinal Chemistry., 10:10-11.
15. McGready, R., Tan, S. O., Ashley, E. A., Pimanpanarak, M., Viladpainguen, J. (2008). A randomised controlled trial of artemether-lumefantrine versus artesunate for uncomplicated Plasmodium falciparum treatment in pregnancy. PLOS Med., 5(12): 1699-1715.
16. Goel, R., Kumari, R., Singh, V., Pandey, R., Kumari, R., Srivastava, S., Kumar, S. (2018). Perspectives of the Artemisia annua Dry Leaf Therapy (ALT) for Malaria and of its Re-Purposement as An Affordable Cure for ArtemisininTreatable Illnesses. Proc Indian Natn Sci Acad., 84: 731-780.
17. Septembre Malaterre, A., Rakoto , M.L., Marodon , C., Bedoui ,Y., Nakab, J., Simon E., Hoarau L., Savriama, S., Strasberg, D., Guiraud, P., Selambarom, J., Gasque, P. (2020). Artemisia annua, a Traditional Plant Brought to Light. Int. J. Mol. Sci, 21: 4986.
18. Brinda, P., Sasikala, B., Purushothaman, K. K. (1981). Pharmacognostic studies on Merugan kilzhangu, BMEBR. 3: 84-96.
19. Wilcox, M., Falquet, J., Ferreria, J.F.S., Gilbert, B.(2006). *Artemesia annua* a herbal tea for Malaria. Afr. J. Tradit. Complement, Altern. Med. 4: 121-123.
20. https://freakofnatural.com/artemisia-annua-the-most-efficient-malaria-cure-is-natural/
21. Meier, zu., Biesen C (2011). The rise to prominence of *Artemisia annua* L.–the transformation of Chinese plant to a global pharmaceutical. African Sociological Review. 14(2): 24-46.
22. MR, V. (2009). Chemical composition and antimicrobial activity of the essential oil of *Artemisia annua* L. from Iran, Pharmacognosy Res. 1: 21-24.
23. Ferreira, J.F.S., Luthria, D.L., Sasaki, T., Heyerick, A. (2010). Flavonoids from *Artemisia annua* L. as Antioxidants and Their Potential Synergism with Artemisinin against Malaria and Cancer, Molecules.15(5): 3135-3170.
24. Kazemi, M., Yasrebifar, Z. (2012). Essential oils composition from different parts of Artemisia kermanensis Podl, Asian J. Chem., 24(1): 200-202.
25. Durden, K., Sellars, S., Cowell, B., Brown, J.J., Pszczolkowski, M.A.(2011). Artemisia Annua Extracts, Artemisinin and 1,8-Cineole, Prevent Fruit Infestation by a Major, Cosmopolitan Pest of Apples. Pharm. Biol., 49, 563-568.
26. Santos, F.A., Rao, V.S.N. (2000). Antiinflammatory and Antinociceptive Effects of 1,8-Cineole a Terpenoid Oxide Present in Many Plant Essential Oils. Phytother. Res., 14, 240-244.
27. Vilela, G.R., de Almeida, G.S., D, Arce, M.A.B.R., Moraes, M.H.D., Brito, J.O., da Silva, M.F.d.G.F., Silva, S.C., de Stefano Piedade, S.M., Calori-Domingues, M.A., da Gloria, E.M.(2009). Activity of Essential Oil and Its Major Compound, 1,8-Cineole, from Eucalyptus Globulus Labill., against the Storage Fungi Aspergillus Flavus Link and Aspergillus Parasiticus Speare. J. Stored Prod. Res., 45, 108-111.
28. Murata, S., Shiragami, R., Kosugi, C., Tezuka, T., Yamazaki, M., Hirano, A., Yoshimura, Y., Suzuki, M., Shuto, K., Ohkohchi, N.(2013). Antitumor Effect of 1, 8-Cineole against Colon Cancer. Oncol. Rep., 30, 2647-2652.
29. De Figueiredo, F.R., Monteiro, A.B., de Menezes, I.R., dos Sales, V.S., do Nascimento, E., de Souz Rodrigues, C., Bitu Primo, A.J., da Cruz, L., do Amaro, É.N., de Araújo Delmondes, G.(2019). Effects of the Hyptis Martiusii Benth. Leaf Essential Oil and 1,8-Cineole (Eucalyptol) on the Central Nervous System of Mice. Food Chem. Toxicol.,133: 110802.
30. Sampath, S., Subramani, S., Janardhanam, S., Subramani, P., Yuvaraj, A., Chellan, R. (2018). Bioactive Compound 1,8-Cineole Selectively Induces G2/M Arrest in A431 Cells through the Upregulation of the P53 Signaling Pathway and Molecular Docking Studies. Phytomedicine., 46, 57-68.
31. Rodenak-Kladniew, B., Castro, A., Stärkel, P., Galle, M., Crespo, R. (2020). 1,8-Cineole Promotes G0/G1 Cell Cycle Arrest and Oxidative Stress-Induced Senescence in HepG2 Cells and Sensitizes Cells to Anti-Senescence Drugs. Life Sci.,243, 117271.
32. Yang, H., Woo, J., Pae, A.N., Um, M.Y., Cho, N.-C., Park, K.D., Yoon, M., Kim, J., Lee, C.J., Cho, S.(2016). α-Pinene, a Major Constituent of Pine Tree Oils, Enhances Non-Rapid Eye Movement Sleep in Mice through GABAA-Benzodiazepine Receptors. Mol. Pharm., 90, 530-539.
33. Albuquerque, M.R.J.R., Costa, S.M.O., Bandeira, P.N., Santiago, G.M.P., Andrade-Neto, M., Silveira, E.R., Pessoa, O.D.L. (2007). Nematicidal and Larvicidal Activities of the Essential Oils from Aerial Parts of Pectis Oligocephala and Pectis Apodocephala Baker. An. Da Acad. Bras. De Ciencias. 79(2), 209-213.
34. Rivas da Silva, A.C., Lopes, P.M., Barros de Azevedo, M.M., Costa, D.C.M., Alviano, C.S., Alviano, D.S.(2012). Biological Activities of α-Pinene and β-Pinene Enantiomers. Molecules. 17(6), 6305-6316.
35. Kim, M., Sowndhararajan, K., Park, S.J., Kim, S.(2018). Effect of Inhalation of Isomers, (+)-α-Pinene and (+)-β-Pinene on Human Electroencephalographic Activity According to Gender Difference. Eur. J. Integr. Med., 17, 33-39.
36. Benelli, G., Govindarajan, M., Rajeswary, M., Vaseeharan, B., Alyahya, S.A., Alharbi, N.S., Kadaikunnan, S., Khaled, J.M., Maggi, F.(2018). Insecticidal Activity of Camphene, Zerumbone and α-Humulene from Cheilocostus Speciosus Rhizome Essential Oil against the Old-World Bollworm, Helicoverpa Armigera. Ecotoxicol. Environ. Saf., 148: 781-786.
37. Okuniewski, M., Paduszynski, K., Domanska, U. (2016). Thermodynamic Study of Molecular Interactions in Eutectic Mixtures Containing Camphene. J. Phys. Chem. B., 120: 12928-12936.
38. Wang, S., Zhang, D., Hu, J., Jia, Q., Xu, W., Su, D., Song, H., Xu, Z., Cui, J., Zhou, M. (2017). A Clinical and Mechanistic Study of Topical Borneol-induced Analgesia. Embo Mol. Med., 9: 802-815.

39. Wang, Y-Y., Ryu, A.-R., Jin, S., Jeon, Y.-M., Lee, M-Y. (2017). Chlorin E6-Mediated Photodynamic Therapy Suppresses P. Acnes-Induced Inflammatory Response via NFκB and MAPKs Signaling Pathway. PLOS ONE., 12: e0170599.
40. Ji, J., Zhang, R., Li, H., Zhu, J., Pan, Y., Guo, Q. (2020). Analgesic and Anti-Inflammatory Effects and Mechanism of Action of Borneol on Photodynamic Therapy of Acne. Environ. Toxicol. Pharmacol.,75: 103329.
41. Ge, Y., Wang, Z., Xiong, Y., Huang, X., Mei, Z., Hong, Z.(2016). Anti-Inflammatory and Blood Stasis Activities of Essential Oil Extracted from Artemisia Argyi Leaf in Animals. J. Nat. Med., 70: 531-538.
42. Chen, X., Lin, Z., Liu, A., Ye, J., Luo, Y., Luo, Y., Mao, X., Liu, P., Pi, R. (2010). The Orally Combined Neuroprotective Effects of Sodium Ferulate and Borneol against Transient Global Ischaemia in C57 BL/6Mice. J. Pharm. Pharmacol., 62: 915-923.
43. Ho, D.D., Lau, C.P., Ng K.H., Kong Y.C., Cheng K.F., Chan, K.P.(1991). Anti-Implantation Activity of S(−)- and R(+)-Camphor-Yuehchukene in Rats. Eur. J. Pharmacol., 205:209-212.
44. Ng, P.C., Ho, D.D., Ng, K.H., Kong, Y.C., Cheng, K.F., Stone, G. (1994). Mixed Estrogenic and Anti-Estrogenic Activities of Yuehchukene–a Bis-Indole Alkaloid. Eur. J. Pharmacol., 264, 1-12.
45. Chatterjie, N., Alexander, G.J. (1986). Anticonvulsant Properties of Spirohydantoins Derived from Optical Isomers of Camphor. Neurochem. Res.11, 1669-1676.
46. Laude, E.A., Morice, A.H., Grattan, T.J. (1994). The Antitussive Effects of Menthol, Camphor and Cineole in Conscious Guinea-Pigs. Pulm. Pharmacol., 7: 179-184.
47. Tinwell, H., Lefevre Paul, A., Moffat Graeme, J., Burns, A., Odum, J., Spurway, T.D., Orphanides, G., Ashby, J.(2002). Confirmation of Uterotrophic Activity of 3-(4-Methylbenzylidine)Camphor in the Immature Rat. Environ. Health Perspect. 110: 533-536.
48. Park, T.J., Seo, H.K., Kang, B.J., Kim, K.T. (2001). Noncompetitive Inhibition by Camphor of Nicotinic Acetylcholine Receptors. Biochem. Pharmacol. 61:787-793.
49. Schlumpf, M., Cotton, B., Conscience, M., Haller, V., Steinmann, B., Lichtensteiger, W.(2001). In Vitro and in Vivo Estrogenicity of UV Screens. Environ. Health Perspect. 109: 239-244.
50. Holbech, H., Norum, U., Korsgaard, B., Poul, B.(2002). The Chemical UV-Filter 3-Benzylidene Camphor Causes an Oestrogenic Effect in an in Vivo Fish Assay. Pharmacol. Toxicol., 91: 204-208.
51. Mueller, S.O., Kling, M., Arifin Firzani, P., Mecky, A., Duranti, E., Shields-Botella, J., Delansorne, R., Broschard, T., Kramer, P.-J.(2003). Activation of Estrogen Receptor α and ERβ by 4-Methylbenzylidene-Camphor in Human and Rat Cells: Comparison with Phyto- and Xenoestrogens. Toxicol. Lett., 142: 89-101.
52. Arakaki, N., Shimoji, Y., Wakamura, S.(2009). Camphor: An Attractant for the Cupreous Polished Chafer, Protaetia Pryeri Pryeri (Janson) (Coleoptera: Scarabaeidae). Appl. Entomol. Zool. 44: 621-625.
53. Zhao, M., Du, J.(2020). Anti-Inflammatory and Protective Effects of D-Carvone on Lipopolysaccharide (LPS)-Induced Acute Lung Injury in Mice. J. King Saud Univ.-Sci., 32:1592-1596.
54. Vinothkumar, R., Sudha, M., Viswanathan, P., Kabalimoorthy, J., Balasubramanian, T., Nalini, N.(2013). Modulating Effect of D-Carvone on 1,2-Dimethylhydrazine-Induced Pre-Neoplastic Lesions, Oxidative Stress and Biotransforming Enzymes, in an Experimental Model of Rat Colon Carcinogenesis. Cell Prolif., 46, 705-720.
55. Moro, I.J., Gondo, G.D.G.A., Pierri, E.G., Pietro, R.C.L.R., Soares, C.P., de Sousa, D.P., Santos, A.G.(2017). Evaluation of Antimicrobial, Cytotoxic and Chemopreventive Activities of Carvone and Its Derivatives. Braz. J. Pharm. Sci., 53.
56. De Cassia da Silveira e Sa, R., Andrade, L.N., de Sousa, D.P. (2013). A Review on Anti-Inflammatory Activity of Monoterpenes. Molecules., 18, 1227-1254.
57. Bier, M.C.J., Medeiros, A.B.P., De Kimpe, N., Soccol, C.R.(2019). Evaluation of Antioxidant Activity of the Fermented Product from the Biotransformation of R-(+)-Limonene in Solid-State Fermentation of Orange Waste by Diaporthe Sp. Biotechnol. Res. Innov., 3, 168-176.
58. Bacanli, M., Ba saran, A.A.; Ba¸saran, N.(2015). The Antioxidant and Antigenotoxic Properties of Citrus Phenolics Limonene and Naringin. Food Chem. Toxicol., 81, 160-170.
59. Chidambara Murthy, K.N., Jayaprakasha, G.K., Patil, B.S. (2012). D-Limonene Rich Volatile Oil from Blood Oranges Inhibits Angiogenesis, Metastasis and Cell Death in Human Colon Cancer Cells. Life Sci., 91, 429-439.
60. Quiroga, P.R., Nepote, V., Baumgartner, M.T. (2019). Contribution of Organic Acids to α-Terpinene Antioxidant Activity. Food Chem. 277, 267-272.
61. Bejeshk, M.A., Samareh Fekri, M., Najafipour, H., Rostamzadeh, F., Jafari, E., Rajizadeh, M.A., Masoumi-Ardakani, Y.(2019). Anti-Inflammatory and Anti-Remodeling Effects of Myrtenol in the Lungs of Asthmatic Rats: Histopathological and Biochemical Findings. Allergol. Et Immunopathol. 47, 185-193.
62. Sepici, A, Gurbuz, I.,Cevik C., Yesilada, E.(2004). Hypoglycaemic Effects of Myrtle Oil in Normal and Alloxan-Diabetic Rabbits. J. Ethnopharmacol., 93: 311-318.
63. Aleksic, V., Knezevic, P.(2014). Antimicrobial and Antioxidative Activity of Extracts and Essential Oils of Myrtus Communis L. Microbiol. Res.,169, 240-254.
64. Clark, A.M. (1996). Natural Products as a Resource for New Drugs. Pharm. Res., 13, 1133-1144.
65. Wang, X., Zheng, B., Ashraf, U., Zhang, H., Cao, C., Li, Q., Chen, Z., Imran, M., Chen, H., Cao, S. (2020). Artemisinin Inhibits the Replication of Flaviviruses by Promoting the Type I Interferon Production. Antivir.
66. Wong, Y.K., Xu, C., Kalesh, K.A., He, Y., Lin, Q., Wong, W.S.F., Shen, H-M., Wang, J.(2017). Artemisinin as an Anticancer Drug: Recent Advances in Target Profiling and Mechanisms of Action. Med. Res. Rev.37, 1492-1517.

67. Idowu, A.O., Bhattacharyya, S., Gradus, S., Oyibo, W., George, Z. Black, C., Igietseme, J., Azenabor, A.A.(2018). Plasmodium Falciparum Treated with Artemisinin-Based Combined Therapy Exhibits Enhanced Mutation, Heightened Cortisol and TNF-α Induction. Int. J. Med. Sci., 15: 1449-1457.
68. Wang, Y., Wang, Y., You, F., Xue, J.(2020). Novel Use for Old Drugs: The Emerging Role of Artemisinin and Its Derivatives in Fibrosis. Pharmacol. Res.
69. Martino, E., Tarantino, M., Bergamini, M., Castelluccio, V., Coricello, A., Falcicchio, M., Lorusso, E., Collina, S.(2019).Artemisinin and Its Derivatives; Ancient Tradition Inspiring the Latest Therapeutic Approaches against Malaria. Future Med. Chem., 11, 1443-1459.
70. Suberu, J.O., Gorka, A.P., Jacobs, L., Roepe, P.D., Sullivan, N., Barker, G.C., Lapkin, A.A. (2013). Anti-Plasmodial Polyvalent Interactions in Artemisia Annua L. Aqueous Extract–Possible Synergistic and Resistance Mechanisms. PLoS ONE., 8, e80790.
71. Efferth, T., Herrmann, F., Tahrani, A., Wink, M. (2011). Cytotoxic Activity of Secondary Metabolites Derived from Artemisia Annua L. towards Cancer Cells in Comparison to Its Designated Active Constituent Artemisinin. Phytomedicine., 18, 959-969.
72. Zhu, X.X., Yang, L., Li, Y.J., Zhang, D., Chen, Y., Kostecka, P., Kmoniekova, E., Zídek, Z. (2013). Effects of Sesquiterpene, Flavonoid and Coumarin Types of Compounds from Artemisia Annua L. on Production of Mediators of Angiogenesis. Pharmacol. Rep., 65, 410-420.
73. Sharma, G., Kapoor, H., Chopra, M., Kumar, K., Agrawal, V.(2014). Strong Larvicidal Potential of Artemisia Annua.. Leaf Extract against Malaria (Anopheles Stephensi Liston) and Dengue (Aedes Aegypti L.) Vectors and Bioassay-Driven Isolation of the Marker Compounds. Parasitol. Res., 113, 197-209.
74. Flobinus, A., Taudon, N., Desbordes, M., Labrosse, B., Simon, F., Mazeron, M-C., Schnepf, N.(2014).. Stability and Antiviral Activity against Human Cytomegalovirus of Artemisinin Derivatives. J. Antimicrob. Chemother. 69, 34-40.
75. Lee, J., Kim, M-H., Lee, J-H., Jung, E., Yoo, E-S., Park, D.(2012). Artemisinic Acid Is a Regulator of Adipocyte Differentiation and C/EBP δ Expression. J. Cell Biochem. 113(7): 2488-2499.
76. Tsevegsuren, N., Edrada, R., Lin, W., Ebel, R., Torre, C., Ortlepp, S., Wray, V., Proksch, P.(2007). Biologically Active Natural Products from Mongolian Medicinal Plants Scorzonera Divaricata and Scorzonera Pseudodivaricata. J. Nat. Prod. 70, 962-967.
77. Zidorn, C., Petersen, B.O., Udovi ci c, V., Larsen, T.O.; Duus, J.O.; Rollinger, J.M., Ongania, K-H., Ellmerer, E.P., Stuppner, H.(2005). Podospermic Acid, 1,3,5-Tri-O-(7,8-Dihydrocaffeoyl) Quinic Acid from Podospermum Laciniatum (Asteraceae). Tetrahedron Lett. 46:1291-1294.
78. Yang, Y-J., Liu, X., Wu, H-R., He, X-F., Bi, Y-R., Zhu, Y., Liu Z-L.(2013). Radical Scavenging Activity and Cytotoxicity of Active Quinic Acid Derivatives from Scorzonera Divaricata Roots. Food Chem. 138: 2057-2063.
79. Yazdi, S.E., Prinsloo, G., Heyman, H.M., Oosthuizen, C.B., Klimkait, T., Meyer, J.J.M. (2019). Anti-HIV-1 Activity of Quinic Acid Isolated from Helichrysum Mimetes Using NMR-Based Metabolomics and Computational Analysis. S. Afr. J. Bot. 126: 328-339.
80. Zhang, J-L., Yan, R-J., Yu, N., Zhang, X., Chen, D-J., Wu, T., Xin, J-G. (2018). A New Caffeic Acid Tetramer from the Dracocephalum Moldavica L. Nat. Prod. Res. 32: 370-373.
81. Choi, H.G., Tran, P.T., Lee, J-H., Min, B.S., Kim, J.A.(2018). Anti-Inflammatory Activity of Caffeic Acid Derivatives Isolated from the Roots of Salvia Miltiorrhiza Bunge. Arch. Pharm. Res.41: 64-70.
82. Langland, J., Jacobs, B., Wagner, C.E., Ruiz, G., Cahill, T.M.(2018). Antiviral Activity of Metal Chelates of Caffeic Acid and Similar Compounds towards Herpes Simplex, VSV-Ebola Pseudotyped and Vaccinia Viruses. Antivir. Res. 160: 143-150.
83. Mishra, M., Panta, R., Miyares, M.(2016). Influence of Coffee and Its Components on Breast Cancer: A Review. Asian Pac. J. Trop. Dis., 6: 827-831.
84. Habtemariam, S.(2017). Protective Effects of Caffeic Acid and the Alzheimer's Brain: An update. Mini review Med Chem., 17(8):667-674.
85. Adisakwattana, S. (2017). Cinnamic Acid and Its Derivatives: Mechanisms for Prevention and Management of Diabetes and Its Complications. Nutrients., 9(2):163.
86. Murillo, A.G., Fernandez, M.L. (2017). The Relevance of Dietary Polyphenols in Cardiovascular Protection. Curr. Pharm. Des., 23(17): 2444-2452.
87. Silva, T., Oliveira, C., Borges, F. (2014). Caffeic Acid Derivatives, Analogs and Applications: A Patent Review (2009–2013). Expert Opin. Ther. Pat., 24(11):1257-1270.
88. Cao, Z., Zhang, H., Cai, X., Fang, W., Chai, D., Wen, Y., Chen, H., Chu, F., Zhang, Y.(2017). Luteolin Promotes Cell Apoptosis by Inducing Autophagy in Hepatocellular Carcinoma. Cell. Physiol. Biochem., 43(5): 1803-1812.
89. Lin, P., Tian, X-H., Yi, Y-S., Jiang,W-S., Zhou, Y-J., Cheng,W-J.(2015). Luteolin-Induced Protection of H_2O_2-Induced Apoptosis in PC12 Cells and the Associated Pathway. Mol. Med. Rep.,12(5):7699-7704.
90. Nunes, C., Almeida, L., Barbosa, R.M., Laranjinha, J. (2017). Luteolin Suppresses the JAK/STAT Pathway in a Cellular Model of Intestinal Inflammation. Food Funct. 8, 387-396.
91. Yao, Z-H., Yao, X-L., Zhang, Y., Zhang, S-F., Hu, J-C.(2018). Luteolin Could Improve Cognitive Dysfunction by Inhibiting Neuroinflammation. Neurochem. Res., 43(4), 806-820.
92. Wei, B., Lin, Q., Ji, Y-G., Zhao, Y-C., Ding, L-N., Zhou, W-J., Zhang, L-H., Gao, C-Y., Zhao, W.(2018). Luteolin Ameliorates Rat Myocardial Ischaemia-Reperfusion Injury through Activation of Peroxiredoxin II. Br. J. Pharmacol. 175(16): 3315-3332.

93. Jang, C.H., Moon, N., Oh, J., Kim, J-S. (2019). Luteolin Shifts Oxaliplatin-Induced Cell Cycle Arrest at G0/G1 to Apoptosis in HCT116 Human Colorectal Carcinoma Cells. Nutrient., 11(4),770.
94. Lesjak, M., Beara, I., Simin, N., Pintac, D., Majkic, T., Bekvalac, K., Orcic, D.; Mimica-Dukic, N.(2018). Antioxidant and Anti-Inflammatory Activities of Quercetin and Its Derivatives. J. Funct. Foods., 40: 68-75.
95. Duarte, J., Perez-Vizcaino, F., Zarzuelo, A., Jimenez, J., Tamargo, J. (1993). Vasodilator Effects of Quercetin in Isolated Rat Vascular Smooth Muscle. Eur. J. Pharmacol., 239(1-3): 1-7.
96. Luna-Vazquez, F.J., Ibarra-Alvarado, C., Rojas-Molina, A., Rojas-Molina, I., Zavala-Sánchez, M.Á.(2013). Vasodilator Compounds Derived from Plants and Their Mechanisms of Action. Molecules. 18(5): 5814-5857.
97. Li, Y., Yao, J., Han, C.,Yang, J., Chaudhry, M.T., Wang, S., Liu, H., Yin, Y.(2016). Quercetin, Inflammation and Immunity. Nutrients., 8(3): 167.
98. Kashyap, D., Mittal, S., Sak, K., Singhal, P., Tuli, H.S.(2016). Molecular Mechanisms of Action of Quercetin in Cancer:Recent Advances. Tumor Biol. 37(10), 12927-12939.
99. Ezzati, M., Yousefi, B., Velaei, K., Safa, A.(2020). A Review on Anti-Cancer Properties of Quercetin in Breast Cancer. Life Sci. 248:117463.
100. Patel, R.V., Mistry, B.M., Shinde, S.K., Syed, R., Singh, V., Shin, H-S. (2018). Therapeutic Potential of Quercetin as a Cardiovascular Agent. Eur. J. Med. Chem. 155: 889-904.
101. Ferreira, C.G.T., Campos, M.G., Felix, D.M., Santos, M.R., de Carvalho, O.V., Diaz, M.A.N., Fietto, J.L.R., Bressan, G.C., Silva-Junior, A., de Almeida, M.R.(2018). Evaluation of the Antiviral Activities of Bacharis Dracunculifolia and Quercetin on Equid Herpesvirus 1 in a Murine Model. Res. Vet. Sci.120: 70-77.
102. Ganeshpurkar, A., Saluja, A.K.(2017). The Pharmacological Potential of Rutin. Saudi Pharm. J. 25(2):149-164.
103. Suganya, S.N., Sumathi, T.(2017). Effect of Rutin against a Mitochondrial Toxin, 3-Nitropropionicacid Induced Biochemical, Behavioral and Histological Alterations-a Pilot Study on Huntington's Disease Model in Rats. Metab. Brain Dis., 32(2): 471-481.
104. Al-Dhabi, N.A., Arasu, M.V., Park, C.H., Park, S.U.(2015). An Up-to-Date Review of Rutin and Its Biological and Pharmacological Activities. Excli. J.14: 59-63.
105. Singh, M., Kaur, M., Silakari, O.(2014). Flavones: An Important Scaffold for Medicinal Chemistry. Eur. J. Med. Chem. 84: 206-239.
106. Kaur, P., Shukla, S., Gupta, S. (2008). Plant Flavonoid Apigenin Inactivates Akt to Trigger Apoptosis in Human Prostate Cancer: An in Vitro and in Vivo Study. Carcinogenesis., 29(11): 2210-2217.
107. Bao, Y-Y., Zhou, S-H., Fan, J., Wang, Q-Y. (2013). Anticancer Mechanism of Apigenin and the Implications of GLUT-1 Expression in Head and Neck Cancers. Future Oncol. 9(9): 1353-1364.
108. Banerjee, K., Mandal, M. (2015). Oxidative Stress Triggered by Naturally Occurring Flavone Apigenin Results in Senescence and Chemotherapeutic Effect in Human Colorectal Cancer Cells. Redox Biol.5: 153-162.
109. Bian, M., Zhang, Y., Du, X., Xu, J., Cui, J., Gu, J., Zhu, W., Zhang, T., Chen, Y.(2017). Apigenin-7-Diglucuronide Protects Retinas against Bright Light-Induced Photoreceptor Degeneration through the Inhibition of Retinal Oxidative Stress and Inflammation. Brain Res.1663:141-150.
110. Shukla, S., Gupta, S. (2010). Apigenin: A Promising Molecule for Cancer Prevention. Pharm Res. 27(6): 962-978.
111. Jamali-Raeufy,N., Baluchnejadmojarad, T., Roghani, M., Keimasi, S., Goudarzi, M.(2019). Isorhamnetin Exerts Neuroprotective Effects in STZ-Induced Diabetic Rats via Attenuation of Oxidative Stress, Inflammation and Apoptosis. J. Chem. Neuroanat. 102: 101709.
112. Yang, J.H., Kim, S.C., Shin, B.Y., Jin, S.H., Jo, M.J., Jegal, K.H., Kim, Y.W., Lee, J.R., Ku, S.K., Cho, I.J.(2013). O-Methylated Flavonol Isorhamnetin Prevents Acute Inflammation through Blocking of NF-KB Activation. Food Chem. Toxicol. 59: 362-372.
113. Wu, Q., Kroon, P.A., Shao, H., Needs, P.W., Yang, X.(2018). Differential Effects of Quercetin and Two of Its Derivatives, Isorhamnetin and Isorhamnetin-3-Glucuronide, in Inhibiting the Proliferation of Human Breast-Cancer MCF-7 Cells. J. Agric. Food Chem. 66(27): 7181-7189.
114. Yang, J.H., Shin, B.Y., Han, J.Y., Kim, M.G., Wi, J.E., Kim, Y.W., Cho, I.J., Kim, S.C., Shin, S.M., Ki, S.H.(2014). Isorhamnetin Protects against Oxidative Stress by Activating Nrf2 and Inducing the Expression of Its Target Genes. Toxicol. Appl. Pharmacol. 274(2): 293-301.
115. Lee, Y.S., Lee, S., Lee, H.S., Kim, B-K. Ohuchi, K., Shin, K.H.(2005). Inhibitory Effects of Isorhamnetin-3-O-Beta-D-Glucoside from Salicornia Herbacea on Rat Lens Aldose Reductase and Sorbitol Accumulation in Streptozotocin-Induced Diabetic Rat Tissues. Biol. Pharm. Bull. 28(5): 916-918.
116. Jamali-Raoufi, N., Keimasi, S., Baluchnejadmojarad, T. (2018). Isorhamnetin Mitigates Learning and Memory Disturbances in Streptozotocin-Induced Diabetic Rats. J. Basic Clin. Pathophysiol. 6: 37-42.
117. Yang, E-J., Kim, G-S., Jun, M., Song, K-S. (2014). Kaempferol Attenuates the Glutamate-Induced Oxidative Stress in Mouse-Derived Hippocampal Neuronal HT22 Cells. Food Funct. 5(7), 1395-1402.
118. Rajendran, P., Rengarajan, T., Nandakumar, N., Palaniswami, R., Nishigaki, Y., Nishigaki, I.(2014). Kaempferol, a Potential Cytostatic and Cure for Inflammatory Disorders. Eur. J. Med. Chem. 86: 103-112.
119. Dang, Q., Song, W., Xu, D., Ma, Y., Li, F., Zeng, J., Zhu, G., Wang, X., Chang, L.S., He, D. (2015). Kaempferol Suppresses Bladder Cancer Tumor Growth by Inhibiting Cell Proliferation and Inducing Apoptosis. Mol. Carcinog. 54: 831-840.
120. Sekiguchi, A., Motegi, S., Fujiwara, C., Yamazaki, S., Inoue, Y., Uchiyama, A., Akai, R., Iwawaki, T., Ishikawa, O. (2019). Inhibitory Effect of Kaempferol on Skin Fibrosis in Systemic Sclerosis by the Suppression of Oxidative Stress. J. Dermatol. Sci. 96: 8-17.

121. Sadasivam, K., Kumaresan, R. (2011). Antioxidant Behavior of Mearnsetin and Myricetin Flavonoid Compounds-A DFT Study. Spectrochim. Acta Part A .79(1): 282-293.
122. De Souza, P., Gasparotto, A., Crestani, S., Stefanello, M.E.A., Marques, M.C.A., da Silva-Santos, J.E., Kassuya, C.A.L.(2011). Hypotensive Mechanism of the Extracts and Artemetin Isolated from Achillea Millefolium L. (Asteraceae) in Rats. Phytomedicine. 18: 819-825.
123. Lee, D., Kim, C-E., Park, S-Y., Kim, K.O., Hiep, N.T., Lee, D., Jang, H-J., Lee, J.W., Kang, K.S. (2018). Protective Effect of Artemisia Argyi and Its Flavonoid Constituents against Contrast-Induced Cytotoxicity by Iodixano in LLC-PK1 Cells. Int. J. Mol. Sci. 19(5):1387.
124. Hu, J., Ma, W., Li, N., Wang, K-J., Hu, J., Ma, W., Li, N., Wang, K-J.(2017). Antioxidant and Anti-Inflammatory Flavonoids from the Flowers of Chuju, a Medical Cultivar of Chrysanthemum Morifolim Ramat. J. Mex. Chem. Soc. 61: 282-289.
125. Li, W-X., Cui, C-B., Cai, B., Wang, H-Y., Yao, X-S. (2005). Flavonoids from Vitex Trifolia L. Inhibit Cell Cycle Progression at G2/M Phase and Induce Apoptosis in Mammalian Cancer Cells. J. Asian Nat. Prod. Res. 7: 615-626.
126. Langa, E., Pardo, J.I., Giménez-Rota, C., Gonzalez-Coloma, A., Hernaiz, M.J.; Mainar, A.M.(2019). Supercritical Anti-Solvent Fractionation of Artemisia Absinthium L. Conventional Extracts: Tracking Artemetin and Casticin. J. Supercrit. Fluids, 151, 15-23.
127. Chan, E.W.C., Wong, S.K., Chan, H.T. (2018). Casticin from Vitex Species: A Short Review on Its Anticancer and Anti-Inflammatory Properties. J. Integr. Med. 16(3): 147-152.
128. Lee, H., Jung, K-H., Lee, H., Park, S., Choi, W., Bae, H. (2015). Casticin, an Active Compound Isolated from Vitex Fructus, Ameliorates the Cigarette Smoke-Induced Acute Lung Inflammatory Response in a Murine Model. Int. Immunopharmacol. 28(2): 1097-1101.
129. Liou, C-J., Len, W-B., Wu, S-J., Lin, C-F., Wu, X-L., Huang, W-C. (2014). Casticin Inhibits COX-2 and INOS Expression via Suppression of NF-KB and MAPK Signaling in Lipopoly-stimulated mouse macrophages. J Ethanopharmacol.158: 310-316.
130. Zhu, Q-C., Wang, Y., Liu, Y-P., Zhang, R-Q.; Li, X., Su, W-H., Long, F., Luo, X-D., Peng, T.(2011). Inhibition of Enterovirus 71 Replication by Chrysosplenetin and Penduletin. Eur. J. Pharm. Sci. 44(3), 392-398.
131. Messaili, S., Colas, C., Fougère, L., Destandau, E.(2020). Combination of Molecular Network and Centrifugal Partition Chromatography Fractionation for Targeting and Identifying Artemisia Annua L. Antioxidant Compounds. J. Chromatogr. 1615, 460785.
132. Yin, Y., Gong, F-Y., Wu, X-X., Sun, Y., Li, Y-H., Chen, T., Xu, Q. (2008). Anti-Inflammatory and Immunosuppressive Effect of Flavones Isolated from Artemisia Vestita. J. Ethnopharmacol. 120(1): 1-6.
133. Sheng, X., Sun, Y., Yin, Y., Chen, T., Xu, Q. (2008). Cirsilineol Inhibits Proliferation of Cancer Cells by Inducing Apoptosis via Mitochondrial Pathway. J. Pharm. Pharmacol. 60: 1523-1529.
134. Sun, Y., Wu, X-X., Yin, Y., Gong, F-Y., Shen, Y., Cai, T-T., Zhou, X-B., Wu, X-F., Xu, Q. (2009). Novel Immunomodulatory Properties of Cirsilineol through Selective Inhibition of IFN-γ Signaling in a Murine model of inflammatory bowel disease. Biochemical Pharmacology.79(2): 229-238.
135. Tezuka, Y., Stampoulis, P., Banskota, A.H., Awale, S., Tran, K.Q., Saiki, I., Kadota, S. (2000). Constituents of the Vietnamese Medicinal Plant Orthosiphon Stamineus. Chem. Pharm. Bull. 48(11): 1711-1719.
136. Nagao, T., Abe, F., Kinjo, J., Okabe, H. (2002). Antiproliferative Constituents in Plants 10. Flavones from the Leaves of Lantana Montevidensis Briq. and Consideration of Structure-Activity Relationship. Biol. Pharm. Bull. 25(7): 875-879.
137. Androutsopoulos, V., Arroo, R.R.J., Hall, J.F., Surichan, S., Potter, G.A. (2008). Antiproliferative and Cytostatic Effects of the Natural Product Eupatorin on MDA-MB-468 Human Breast Cancer Cells Due to CYP1-Mediated Metabolism. Breast Cancer Res. 10(3): R39.
138. Chen, Z., Liao, L., Zhang, Z., Wu, L., Wang, Z.(2013). Comparison of Active Constituents, Acute Toxicity, Anti-Nociceptive and Anti-Inflammatory Activities of Porana Sinensis Hemsl., Erycibe Obtusifolia Benth and Erycibe Schmidtii Craib. J. Ethnopharmacol. 150(2): 501-506.
139. Kim, H-J., Jang, S.I., Kim, Y-J., Chung, H-T., Yun, Y-G., Kang, T-H., Jeong, O-S., Kim, Y-C.(2004). Scopoletin Suppresses Pro-Inflammatory Cytokines and PGE2 from LPS-Stimulated Cell Line, RAW 264.7 Cells. Fitoterapia. 75(3-4): 261-266.
140. Pan, R., Dai, Y., Gao, X., Xia, Y. (2009). Scopolin Isolated from Erycibe Obtusifolia Benth Stems Suppresses Adjuvant-Induced Rat Arthritis by Inhibiting Inflammation and Angiogenesis. Int. Immunopharmacol. 9(7-8): 859-869.
141. Shaw, C-Y., Chen, C-H., Hsu, C-C., Chen, C-C., Tsai, Y-C.(2003). Antioxidant Properties of Scopoletin Isolated from Sinomonium Acutum. Phytother. Res. 17(7): 823-825.
142. Moon, P-D., Lee, B-H., Jeong, H-J., An, H-J., Park, S-J., Kim, H-R., Ko, S-G., Um, J-Y., Hong, S-H., Kim, H-M.(2007). Use of Scopoletin to Inhibit the Production of Inflammatory Cytokines through Inhibition of the IκB/NF-KB Signal Cascade in the Human Mast Cell Line HMC-1. Eur. J. Pharmacol. 555(2-3): 218-225.
143. Thabet, A.A., Youssef, F.S., Korinek, M., Chang, F-R., Wu, Y-C., Chen, B-H., El-Shazly, M., Singab, A.N., Hwang, T-L.(2018). Study of the Anti-Allergic and Anti-Inflammatory Activity of Brachychiton Rupestris and Brachychiton Discolor Leaves (Malvaceae) Using in Vitro Models. BMC Complement. Altern. Med. 18(1): 299.

144. Messaili, S., Colas, C., Fougère, L., Destandau, E.(2020). Combination of Molecular Network and Centrifugal Partition Chromatography Fractionation for Targeting and Identifying Artemisia Annua L. Antioxidant Compounds. J. Chromatogr. A. 1615: 460785.
145. Cavar, S., Maksimovic, M., Vidic, D., Paric, A.(2012). Chemical Composition and Antioxidant and Antimicrobial. Activity of Essential Oil of Artemisia Annua L. from Bosnia. Ind. Crop. Prod. 37: 479-485.
146. Iqbal, S., Younas, U., Chan, K. W. (2012). Chemical Compostion of Artemesia annua L. Leaves and Antioxidant potential of Extracts as a function of extraction solvents, Molecules.,17:6020-6032.
147. Abdin, M.Z., Israr, M., Rehman, R.U., Jain, S. K. (2003). Artemisinin, a novel antimalarial drug: biochemical and molecular approaches for enhanced production. Planta Med., 69(4): 289-299.
148. Wilcox, J.K., Ash, S., Catignani, G.L.(2004). Antioxidants and prevention of chronic disease. Crit Rev Food Sci Nutr., 44(4):275-295.
149. Rezelman, D., Goris, H. (2008). The role of herbal products containing Artemisia annua in malaria treatment.
150. Septembre Malaterre, A., Rakoto , M.L., Marodon , C., Bedoui ,Y., Nakab, J., Simon E., Hoarau L., Savriama, S., Strasberg, D., Guiraud, P., Selambarom, J., Gasque, P. (2020). Artemisia annua, a Traditional Plant Brought to Light. Int. J. Mol. Sci, 21: 4986.
151. Mesa L.E., Lutgen, P., Velez, I., Segura A.M., and Robledo, S.M. (2015).Artemisia annua L. (2015) Potential Source of Molecules with Pharmacological Activity in Human Diseases. American Journal of Phytomedicine and Clinical Therapeutics. 5(3); 436-450.
152. Shalaby, H.A., Abdel-Shafy, S., Abdel-Rahman, K.A., Derbala, A.A. (2009). Comparative in Vitro Effect of Artemether and Albendazole on Adult Toxocara Canis. Parasitol. Res. 105(4): 967-976.
153. Patocka, J., Plucarb, B. (2003). Pharmacology and toxicology of absinthe, J Appl Biomed., 1:199-205.
154. Nofal, S.M., Mahmoud, S.S., Ramadan, A., Soliman, G.A., Fawzy, R. (2009). Anti-diabetic effect of Artemisia judaica Extracts. Res J Med Med Sci., 4(1):42-48.
155. MR., V. (2009). Chemical composition and antimicrobial activity of the essential oil of *Artemisia annua* from Iran, Pharmacognosy Research., 1(1):21-24.
156. Ferreira., J.F.S. (2008). Seasonal and post-harvest accumulation of artemisinin, artemisinic acid, and dihydroartemisinic acid in three accessions of Artemisia annua cultivated in West Virginia, USA, Planta Med., 74: 310-311.
157. Ferreira., J.F.S., Vagner, A., Benedito, V. A., Sandhu, D., Jose, A., Liu, M.S.(2018). Seasonal and Differential Sesquiterpene Accumulation in Artemisia annua Suggest Selection Based on Both Artemisinin and Dihydroartemisinic Acid may Increase Artemisinin in planta, Front. Plant Sci., 9: 1-12.
158. Echeverrigaray, S., Zacaria, J., Beltrao, R. (2010). Nematicidal Activity of Monoterpenoids Against the Root-Knot Nematode Meloidogyne Incognita. Phytopathology 100(2): 199-203.
159. Efferth, T. (2018) Beyond Malaria: The Inhibition of Viruses by Artemisinin-Type Compounds. Biotechnol. Adv. 36(6): 1730-1737.
160. Chang, Y-S., Woo, E-R. (2003). Korean Medicinal Plants Inhibiting to Human Immunodeficiency Virus Type 1 (HIV-1) Fusion. Phytother. Res. 17(4): 426-429.
161. McGready, R., Tan, S. O., Ashley, E. A., Pimanpanarak, M., Viladpainguen, J. (2008). A randomised controlled trial of artemether-lumefantrine versus artesunate for uncomplicated Plasmodium falciparum treatment in pregnancy. PLOS Med., 5(12): 1699-1715.
162. Goel, R., Kumari, R., Singh, V., Pandey, R., Kumari, R., Srivastava, S., Kumar, S. (2018). Perspectives of the Artemisia annua Dry Leaf Therapy (ALT) for Malaria and of its Re-Purposement as An Affordable Cure for ArtemisininTreatable Illnesses. Proc Indian Natn Sci Acad., 84: 731-780.
163. Firestone, G.L., Sundar, S.N. (2009). Anticancer activities of artemisinin and its bioactive derivatives. Expert reviews in Molecular Medicine.11: e32.
164. Efferth, T. (2015). Artemisinin–Second Career as Anticancer Drug?.World J Tradit Chin Med., 1(4): 2-25.
165. Lang, S. J., Schmiech, M., Hafner, S., Paetz, C., Steinborn, C., Huber, R., El Gaafary, M., Werner, K ., Schmidt, C.Q., Syrovets, T , Simmet, T. (2019). Antitumor activity of an Artemisia annua herbal preparation and identification of active ingredients. Phytomedicine.,62: 152962.
166. Oguariri, R.M., Adelsberger, J.W., Baseler, M.W., Imamichi, T. (2010). Evaluation of the Effect of Pyrimethamine, an Anti-Malarial Drug, on HIV-1 Replication. Virus Res. 153(2): 269-276.
167. Helal, E.G.E., Abou-Aouf, N., Khattab, A.L.M., Zoair, M.A. (2014). Anti-Diabetic Effect of Artemisia Annua (Kaysom) in Alloxan-Induced Diabetic Rats. Egypt. J. Hosp. Med. 57, 422-430.
168. Woerdenbag, H.J., Pras, N., Bos, R., Visser, J.F., Hendriks, H., Malingre, T.M.(1991). Analysis of Artemisinin and Related Sesquiterpenoids from Artemisia Annua L. by Combined Gas Chromatography/Mass Spectrometry. Phytochem. Anal. 2: 215-219.
169. Efferth, T., Romero, M.R., Wolf,D.G., Stamminger, T, Marin, J.J.G., Marschall, M. (2008). The Antiviral Activities of Artemisinin and Artesunate. Clin. Infect. Dis., 47(6): 804-811.
170. Alessandro, S.D., Scaccabarozzi, D., Signorini, L., Perego, F., Ilboudo, D.P., Ferrante, P., Delbue, S. (2020). The Use of Antimalarial Drugs against Viral Infection. Microorganisms., 8(1):1-26.
171. Lubbea, A., Seibertb, I., Klimkaitb, T., Kooya, F.V.D. (2012). Ethnopharmacology in overdrive: The remarkable anti-HIV activity of Artemisia annua. J. Ethnopharmacol., 141(3): 854-859.

172. Alesaeidi, S., Miraj, S. (2016). A Systematic Review of Anti-malarial Properties, Immunosuppressive Properties, Anti-inflammatory Properties, and Anti-cancer Properties of Artemisia Annua. Electron Physician., 8(10): 3150-3155.
173. https://www.amazon.in/Nutricology-Super-Artemisinin-Vegicaps-60
174. https://amalth.com/product/artemisia-annua-extract-105mg-90-veggie-capsules.
175. https://paytmmall.com/deve-herbes-pure-sweet-wormwood-essential-oil.
176. https://www.healthmug.com/product/tonga-herbs-artemisinin-extract-powder-200g.
177. https://www.amazon.com/Artemisia-Annua-Artemisia-Organic-Organic-Wormwood-Sweet-Tea-Organic/dp/B07WSGXPM2.
178. https://in.iherb.com/pr/Thorne-Research-Artecin-90-Capsules.
179. https://in.iherb.com/pr/Nutricology-Artemisinin-90-Vegetarian-Capsules.