

Pharmaceutical Applications of Artemisia: An Overview

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INTRODUCTION

Artemisia indica is a perennial shrub of Asteraceae family growing wildly in India, Nepal, Pakistan and other cold temperate areas in Asia (1, 2, 3, 4). There are around 400 species of Genus *Artemisia* and most of them are medicinally important (4). *A. indica* is one of the important plant of this Genus. The plant is also commonly called mugwort, and Indian wormwood (3, 5). The vernacular name of the plant in Nepal and Darjeeling, India is “Titepati” (6). The height of the plant measures from 2-8 meters (3). It propagates vegetatively by stolons and by dispersion of seeds by wind (7). It grows in high altitudes, grasslands, forest edges and uncultivated lands (7). Here, the use of the plant in ethnomedicine and the pharmacological properties of the plant and its compounds are reviewed.



A.indica leaves



A.indica flowers



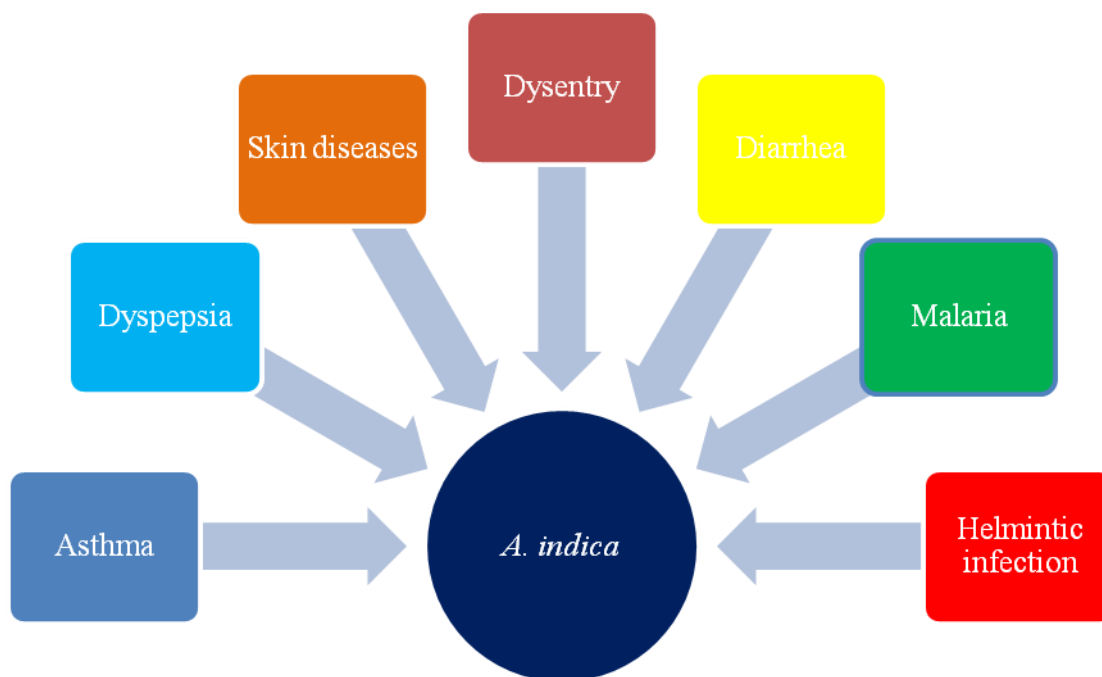
Artemisia indica plant

Classification of *Artemisia indica*:

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Asterales
Family	Asteraceae
Genus	<i>Artemisia</i>
Species	<i>Indica</i>

USE IN TRADITIONAL MEDICATION

A.indica is used traditionally in India for the treatment of hepatobiliary diseases, dyspepsia and fever (8). In Thai medicine the plant is used as an effective antimalarial agent. (5). In Nepal juice of *A. indica* is used for the treatment of diarrhea, abdominal pain, skin diseases and dysentery (2). The plant is consumed as food in by people in Okinawa, Japan and Garo people in Meghalaya, India (2). In Darjeeling, India the leaves and young shoots of the plant are used for the treatment of asthma, helminthic infections, skin diseases, amoebic dysentery and used as stomachic purgative (6).



Traditional Uses of *A. indica*

PHYTOCHEMICAL CONSTITUENTS

Oil obtained from the extract of *Artemisia indica* showed the presence of davanone, alpha pinene, beta pinene, myrtenal, piperitone, germacrene, cadinene, curcumene, muurolol, alpha humulene, sabinene, beta myrcene, beta elemene, trans-caryophyllene, and beta farnesene (4). Satyal et al reported the presence of ascaridole, isoascaridole, and transverbenol in *A. indica* oil (10). Exiguaflavanone-A, exiguaflavanone-B and maacklain which have antimalarial activity were also isolated from *A. indica* (11). Artemisia ketone, borneol, p-cymene, alpha thujone and chrysanthenyl acetate were reported in the oil of *A. indica* (2). Presence of artemisin has also been reported in *A. indica* (12). Khan et al reported the presence of carnosol, ursolic acid, and oleanolic acid in *A. indica* (13). Flavonoids like casticin, eupatin, chrysopenetin are also found in *A. indica* (5).

Phytochemicals in *A. indica* and their pharmacological effect

Compound	Pharmacological Activity	References
Artemisin	Antimalarial	5
Davanone	Insect deterrent, antifungal, antispasmodic	14, 15
Pinene	Antioxidant, anticancer	16, 17
Myrcene	Enhance immune response, treatment of ischemic stroke	Uyeda et al, 2016; 18
Elemene	Larvicidal, anticancer	18
Caryophyllene	Antiinflammatory, prevents alcoholic steatohepatitis, suppress osteoclastogenesis, treats hyperlipidemia, induce neuritogenesis, anticancer, analgesic	18, 19, 20, 21
Farnesene	Plant defense	22
Ascaridole	Anti-parasitic, Larvicidal	23, 24
Thujone	Antiangiogenic, red mite repellent in poultry industry	25; 26
Exiguaflavanone	Antimalarial	27
Maacklain	Antimalarial	27
Borneol	Analgesic, Antidepressant	28; 29
Carnosol	Antidaibetic, Anti-cancer, Neuroprotection, Anti-inflammatory, Anti-oxidant	30, 31, 32

Ursolic acid	Antiangiogenic, antitumor, antidepressant, prevent leishmaniasis	33, 34, 35
Casticin	Anticancer, Prevention of lung injury, Anti-inflammatory, Anti-hyperprolactinemia activity, Immunomodulatory activity	36, 37, 38, 39, 40
Chrysoplenetin	Anticancer, Anti-malarial, Inhibition of replication of Enterovirus 71	41, 42, 43
Oleanolic acid	Anticancer, Antifilarial, Inhibition of atherosclerosis, Treatment of malaria and anaemia, anti-tumor, hepatoprotection, anti-diabetic	44, 15, 45, 46, 47
Humulene	Anti-angiogenic, oviposition deterrent, larvicidal	48, 49

ANTIMICROBIAL ACTIVITY

Extract of *A. indica* inhibited the growth of *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi* and *Pseudomonas aeruginosa* (50). Essential oil from this plant inhibited the growth of *Bacillus subtilis*, *Staphylococcus epidermidis*, *Shigella dysenteriae* and *Klebsiella pneumonia* (Rashid et al, 2013). Extract and essential oil from this plant showed antifungal activity against *Aspergillus niger*, *Penicillium chrysogenum*, *Aspergillus flavus*, *Aspergillus fumigatus* and *Fusarium solani* (50, 2).

ANTICANCER ACTIVITY

Zeng et al showed the anticancer effects of *A. indica* on MCF-7, BHY, Colo 205 cell lines. It was also reported that luteolin and luteolin obtained from this plant had maximum anticancer activity where they reduced membrane potential of mitochondria and induced DNA damage (51). Rashid et al also reported the anticancer effects of essential oil from *A. indica* on cell lines of human leukemia, lung, colon and liver (Rashid et al, 2013). The essential oil showed maximum growth inhibition against leukemia. In another study by Tiwary et al, *A. indica* showed more than 50% inhibition of growth of human breast cancer, hepatocarcinoma and cervical adenocarcinoma cell lines (6).

ANTIMALARIAL ACTIVITY

Various compounds present in *A. indica* such as artemisin, Davanone, Exiguaflavanone-A, exiguafavanone-B and maacklain have shown antimalarial activity (9, 52). Artemisin has shown the potential to treat drug resistant malaria (Mannan et al, 2011). The pharmacological action of these compounds present in *A. indica* corroborates the use of the plant for the treatment of malaria in ethnomedicine.

EFFECT ON CENTRAL NERVOUS SYSTEM

Oleanic acid, carnosol and ursolic acid obtained from have shown the ability to modulate central nervous system. Khan et al showed that these compounds modulated GABA-A receptors positively without any toxicity in mice models (11). Thus, their report suggested that *A. indica* can be used a source for compounds for the treatment of epilepsy and relieve from depression and anxiety.

ANTIDIABETIC AND ANTIHYPERLIPIDEMIC

Ahmad et al showed the antidiabetic and antihyperlipidemic activity of *A. indica* on mice models of diabetes (3). Oral administration of extract of this plant to these mice showed lowering of blood glucose, cholesterol, low density lipoproteins, and serum creatinine. Their study also found that administration of *A. indica* extract to mice improves the function of liver and kidneys compared to mice treated with Streptozotocin. This study shows that *A.indica* can be useful in the treatment of diabetes and prevention of various cardiovascular diseases.

ANTIINFLAMMATORY AND ANALGESIC ACTIVITY

Sagar et al reported the analgesic and antiinflammatory activity of *A. indica* extract in mice and rats models. Administration of extract of *A. indica* provided protection against writhing and elevated pain threshold in the model organisms (Sagar et al, 2010). The extract also showed antiinflammatory activity by the reduction of paw edema in mice administered with carrageenan (8). This study corroborates the use of the plant extract in traditional medicine as an analgesic for the treatment of stomach pain and as an antiinflammatory drug in the treatment of asthma.

ANTIOXIDANT ACTIVITY

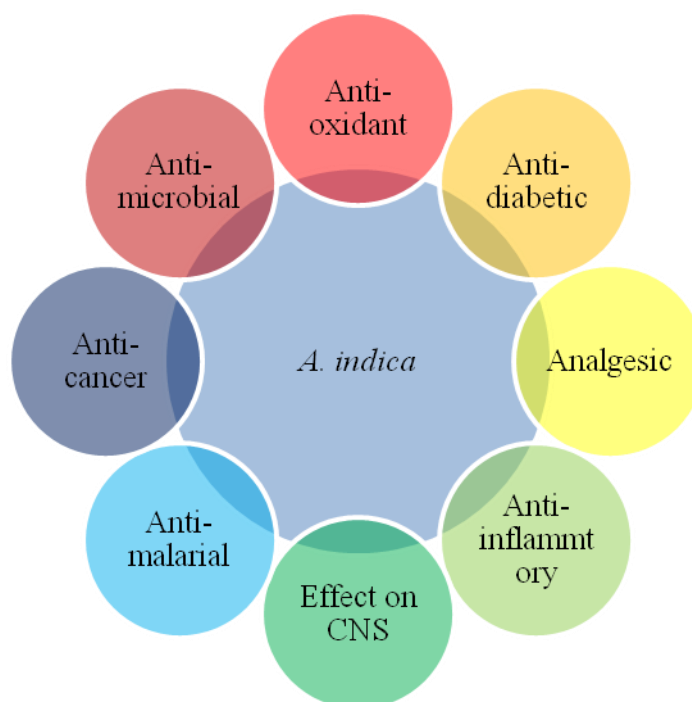
Essential oil obtained from *A.indica* has shown the ability to scavenge DPPH and hydroxyl radicals (2). This suggests that *A. indica* can be used as a potential source of antioxidant, used in antimicrobial packaging of food product and to prolong shelf life of foods.

ANTIHELMINTHIC ACTIVITY

A. indica has shown the antihelmintic activity against nematodes such as *Haemonchus contortus* and *Teladorsagia* species (Khan et al, 2015). Infections of these parasites in sheep and goats cause major economic loss to farmers and the evolution of resistance to the nematodes against currently available antihelmintic drugs is a serious problem. In this regard *A. indica* has successfully inhibited the egg hatching of the nematodes, showed larvicidal activity and killed adult worms (53).

PRODUCTION OF CAFFEIC ACID

Aspergillus awamori extract converted the polyphenols present in *A. indica* to caffeic acid (54). Caffeic acids are secondary metabolites which prevent from oxidative stress and have antimicrobial, anti-inflammatory and antitumor properties (54). This report implies that the total polyphenols present in *A. indica* can be used for the commercial production of caffeic acid.



Pharmacological importance of *A. indica*

CONCLUDING REMARKS AND FUTURE PROSPECTS

Artemisia indica has been used in traditional medicine for the treatment of various infections and diseases. Various studies on the extract of the plant have shown numerous pharmacological properties such as anticancer, antioxidant, antimalarial, anti-diabetic, anti-inflammatory, anti-helminthic and analgesic activity. Different phytochemicals have also been identified in the extract of the plant that has plethora of health benefits. Future studies should be focused on synthesizing nanoparticles based on the extract of *A. indica* that will lead to development of more effective, safe and cheap herbal drugs. Further, it is imperative to determine which part of the plant has more bioactive compounds with health benefits. The claims made in different studies about various pharmacological activities need to be substantiated. Studies on various animal models to assess the pharmacodynamic and pharmacokinetic property of the plant extract are also required. Toxicity of the plant extract needs to be studied before going for the clinical application.

This study summarizes the information on various traditional use and pharmacological property of *Artemisia indica*. Generally, the plant is neglected as a weed but this plant can have various medicinal uses which need to be studied and substantiated. We hope that the information summarized here will help to make this plant more valuable and help in future research for finding novel herbal therapy for various ailments.

References

1. P. Satyal, P. Paudel, A. Kafle, S. K. Pokharel, B. Lamichhane, N. S. Dosoky, D. M. Moriarity, W. N. Setzer, Bioactivities of volatile components from Nepalese *Artemisia* species, *Nat Prod Commun*, Vol. 7(12), pp. 1651-8, Dec, 2012.
2. Rashid, M. A. Rather, W. A. Shah, B. A. Bhat, Chemical composition, antimicrobial, cytotoxic and antioxidant activities of the essential oil of *Artemisia indica* Willd, *Food Chem*, Vol. 138(1), pp. 693-700, May, 2013.
3. W. Ahmad, I. Khan, MA Khan, M Ahmad, F Subhan, N Karim, Evaluation of antidiabetic and antihyperlipidemic activity of *Artemisia indica* linn (aerial parts) in Streptozotocin induced diabetic rats, *J Ethnopharmacol*, Vol.151 (1) pp. 618-23, Jan, 2014.

4. S. Z. Haider, M. Mohan, H. C. Andola, Constituents of *Artemisia indica* Willd. from Uttarakhand Himalaya: A source of davanone, *Pharmacognosy Res*, Vol. 6(3), pp. 257-9, Jul, 2016.
5. D. Tasdemi, M. Tierney, R. Sen, M. C. Bergonzi, B. Demirci, A. R. Bilia, K. H. Baser, R. Brun, M. Chatterjee, Antiprotozoal Effect of *Artemisia indica* Extracts and Essential Oil, *Planta Med*, Vol. 81(12-13), pp. 1029-37, Aug, 2015.
6. K. Tiwary, S. Bihani, Kumar, R. Chakraborty, R. Ghosh, The in vitro cytotoxic activity of ethno-pharmacological important plants of Darjeeling district of West Bengal against different human cancer cell lines, *BMC Complement Altern Me*, Vol. 7, pp. 15:22, Feb, 2015.
7. Y. Shimono, Hayakawa, S. Kurokawa, T. Nishida, H. Ikeda, N. Futagami, Phylogeography of mugwort (*Artemisia indica*), a native pioneer herb in Japan, *J Hered*, Vol. 104(6), pp. 830-41, Nov-Dec, 2013.
8. M. K. Sagar, P. K. Ashok, H. Chopra, K. Upadhyaya, Phytochemical and pharmacological potential of *Artemisia indica* in experimental Animal Models, *Pharmacologyonline*, Vol. 2, pp. 1-4, 2010.
9. R. Chanphen, Y. Thebtaranonth, S. Wanauppathamkul, Y. Yuthavong, Antimalarial principles from *Artemisia indica*, *J Nat Prod*, Vol. 61 (9), pp. 1146-7, July, 1998.
10. A. Mannan, I. Ahmed, W. Arshad, I. Hussain, B. Mirza, Effects of vegetative and flowering stages on the biosynthesis of artemisinin in *Artemisia* species, *Arch Pharm Res*, Vol. 34(10), pp. 1657-61, Oct, 2011.
11. I. Khan, N. Karim, W. Ahmad, A. Abdelhalim, M. Chebib, GABA-A Receptor Modulation and Anticonvulsant, Anxiolytic, and Antidepressant Activities of Constituents from *Artemisia indica* Linn. *Evid Based Complement Alternat Med*, Vol. 2016, Article ID 1215393, pp. 12, 2016.
12. G. V. Bhagavathy, G. M. V. Nieves, M. Z. Webb, K. R. Chauhan, Arthropod Deterrents from *Artemisia pallens* (Davana Oil) Components, *Nat Prod Commun*, Vol. 10 (8), pp. 1335-6, Aug, 2015.
13. K. C. Morrison, J. P. Litz, K. P. Scherpelz, P. D. Dossa, D. A. Vosburg, A concise, biomimetic total synthesis of (+)-davanone, *Org Lett*, Vol. 11(10), pp. 2217-8, May, 2009.

14. Z. Djerrad, A. Djouahri, L. Kadik, Variability of *Pinus halepensis* Mill, essential oils and their antioxidant activities depending on the stage of growth during vegetative cycle, *Chem Biodivers*, Dec, 2016.
15. K. S. Senathilake, E. H. Karunanayake, S. R. Samarakoon, K. H. Tennekoon, E. D. de Silva, A. Adhikari, Oleanolic acid from antifilarial triterpene saponins of *Dipterocarpus zeylanicus* induces oxidative stress and apoptosis in filarial parasite *Setaria digitata* in vitro, *Exp Parasitol*, Vol. 177, pp. 13-21, Mar, 2017.
16. G. B. Burcu, C. Osman, C. Aslı, O. M. Namik, B. T. Neşe, The protective cardiac effects of B-myrcene after global cerebral ischemia/reperfusion in C57BL/J6 mouse, *Acta Cir Bras*, Vol. 31 (7), pp. 456-62, July, 2016.
17. M. Govindarajan, M. Rajeswary, S. Senthilmurugan, P. Vijayan, N. S. Alharbi, S. Kadaikunnan, J. M. Khaled, G. Benelli, Curzerene, trans- β -elemenone, and γ -elemene as effective larvicides against *Anopheles subpictus*, *Aedes albopictus*, and *Culex tritaeniorhynchus*: toxicity on non-target aquatic predators, *Environ Sci Pollut Res Int*, Mar, 2017.
18. Z. V. Varga, C. Matyas, K. Erdelyi, R. Cinar, D. Nieri, A. Chicca, B. T. Nemeth, J. Paloczi, T. Lajtos, L. Corey, G. Hasko, B. Gao, G. Kunos, J. Gertsch, P. Pacher, Beta-caryophyllene protects against alcoholic steatohepatitis by attenuating inflammation and metabolic dysregulation in mice, *Br J Pharmacol*, Jan, 2017.
19. M. D. Baldissera, C. F. Souza, T. H. Grando, P. H. Doleski, A. A. Boligon, L. M. Stefani, S. G. Monteiro, Hypolipidemic effect of β -caryophyllene to treat hyperlipidemic rats. *Naunyn Schmiedebergs Arch Pharmacol*, Vol. 390 (2), pp. 215-223, Feb, 2017.
20. N. A. Santos, N. M. Martins, F. M. Sisti, L. S. Fernandes, R. S. Ferreira, O. de Freitas, A. C. Santos, The cannabinoid beta-caryophyllene (BCP) induces neuritogenesis in PC12 cells by a cannabinoid-receptor-independent mechanism, *Chem Biol Interac*, Vol. 61, pp. 86-95, Jan, 2017.
21. K. Fidy, A. Fiedorowicz, L. Strzdała, A. Szumny, β -caryophyllene and β -caryophyllene oxide-natural compounds of anticancer and analgesic properties, *Cancer Med.*, Vol. 5 (10), pp. 3007-3017, Oct, 2016.
22. X. Yang, K. Nambou, L. Wei, Q. Hua, Heterologous production of α -farnesene in metabolically engineered strains of *Yarrowia lipolytica*, *Bioresour Technol*, Vol. 216, pp. 1040-8, Sept, 2016.

23. G. Geroldinger, M. Tonner, H. Hettegger, M. Bacher, L. Monzote, M. Walter, K. Staniek, T. Rosenau, L. Gille, Mechanism of ascaridole activation in Leishmania, *Biochem Pharmacol*, Vol. 2, pp. 132, pp. 48-6, May, 2017.
24. S. de Castro, D. B. da Silva, J. D. Tibúrcio, M. E. Sobral, V. Ferraz, A. G. Taranto, J. E. Serrão, J. M. de Siqueira, S. N. Alves, Larvicidal activity of essential oil of *Peumus boldus* Molina and its ascaridole-enriched fraction against *Culex quinquefasciatus*, *Exp Parasitol*, Vol. 71, pp. 84-90, Dec, 2016.
25. Torres, Y. Vargas, D. Uribe, C. Carrasco, C. Torres, R. Rocha, C. Oyarzún, R. S. Martín, C. Quezada, Pro-apoptotic and anti-angiogenic properties of the α / β -thujone fraction from *Thuja occidentalis* on glioblastoma cells, *J Neurooncol*, Vol. 128(1), pp. 9-19, May, 2016.
26. M. A. Tabari, M. R. Youssefi, G. Benelli, Eco-friendly control of the poultry red mite, *Dermanyssus gallinae* (Dermanyssidae), using the α -thujone-rich essential oil of *Artemisia sieberi* (Asteraceae): toxic and repellent potential, *Parasitol Res*, Vol. 116 (5), Apr, 2017.
27. K. Scharffetter-Kochanek, M. Wlaschek, P. Brenneisen, M. Schaeue, R. Blaudschun, J. Wenk, UV-induced reactive oxygen species in photocarcinogenesis and photoaging. *Biol Chem*, Vol. 378(11), pp. 1247-57, Nov, 1997.
28. T. Hou, X. Li, C. Peng, Borneol enhances the antidepressant effects of asiaticoside by promoting its distribution into the brain, *Neurosci Lett*, Vol. 646, pp. 56-61, Apr, 2017.
29. T. Hou, X. Li, C. Peng, Borneol enhances the antidepressant effects of asiaticoside by promoting its distribution into the brain, *Neurosci Lett*, Vol. 646, pp. 56-61, Apr, 2017.
30. M. R. de Oliveira, The Dietary Components Carnosic Acid and Carnosol as Neuroprotective Agents: a Mechanistic View, *Mol Neurobiol*, Vol 53 (9), pp. 6155-6168, Nov, 2016.
31. T. Farkhondeh, S. Samarghandian, A. Borji, Evaluation of antidiabetic activity of carnosol (phenolic diterpene in rosemary) in streptozotocin-induced diabetic rats, *Cardiovasc Hematol Disord Drug Targets*, Vol. 17, pp. 11-17, Dec, 2016.
32. D. Sánchez-Camargo, V. García-Cañas, M. Herrero, A. Cifuentes, E. Ibáñez, Comparative Study of Green Sub- and Supercritical Processes to Obtain Carnosic Acid and Carnosol-Enriched Rosemary Extracts with in Vitro Anti-Proliferative Activity on Colon Cancer Cells, *Int J Mol Sci*, Vol. 17(12), Dec, 2016.

33. W. Cheng, F. Z. Dahmani, J. Zhang, H. Xiong, Y. Wu, L. Yin, J. Zhou, J. Yao, Anti-angiogenic activity and antitumor efficacy of amphiphilic twin drug from ursolic acid and low molecular weight heparin, *Nanotechnology*, Vol. 28 (7), pp. 075102, Feb, 2017.
34. R. K. Singla, L. Scotti, A. K. Dubey, In silico studies revealed multiple neurological targets for the antidepressant molecule ursolic acid, *Curr Neuropharmacol*, Vol. 15 (8), pp. 1100-1106, Dec, 2017.
35. J. A. Jesus, T. N. Fragoso, E. S. Yamamoto, M. D. Laurenti, M. S. Silva, A. F. Ferreira, J. H. Lago, G. S. Gomes, L. F. Passero, Therapeutic effect of ursolic acid in experimental visceral leishmaniasis, *Int J Parasitol Drugs Drug Resist*, Vol. 7 (1), pp. 1-11, Dec, 2016.
36. X. L. Song, Y. J. Zhan, X. F. Wang, W. J. Zhang, Z. Wang, F. Zhang, Y. J. Zhang, J. H. Lu, J. W. Me, Y. P. Hu, L. Chen, H. F. Li, Y. Y. Ye, Y. B. Liu, J. Gu, Casticin induces apoptosis and G0/G1 cell cycle arrest in gallbladder cancer cells, *Cancer Cell Int*, Vol. 5, pp. 17:9, Jan, 2017.
37. Wang, L. Zeng, T. Zhang, J. Liu, W. Wang, Casticin inhibits lipopolysaccharide-induced acute lung injury in mice, *Eur J Pharmacol*, Vol. 15, pp. 172-8, Oct, 2016.
38. Y. J. Li, Y. Guo, Q. Yang, X. G. Weng, L. Yang, Y. J. Wang, Y. Chen, D. Zhang, Q. Li, X. C. Liu, X. X. Kan, X. Chen, X. X. Zhu, E. Kmoníčková, Z. Zídek, Flavonoids casticin and chrysosplenol D from *Artemisia annua* L. inhibit inflammation in vitro and in vivo, *Toxicol Appl Pharmacol*. Vol. 286(3), pp. 151-8, Aug, 2015.
39. Q. Ye, Q. Y. Zhang, C. J. Zheng, Y. Wang, L. P. Qin, Casticin, a flavonoid isolated from *Vitex rotundifolia*, inhibits prolactin release in vivo and in vitro, *Acta Pharmacol Sin*, Vol. 31(12), pp. 1564-8, Dec, 2010.
40. A. Mesaik; Azizuddin, S. Murad, K. M. Khan, R. B. Tareen, A. Ahmed, A. Rahman, M. I. Choudhary, Isolation and immunomodulatory properties of a flavonoid, casticin from *Vitex agnus-castus*, *Phytother Res*, 23(11), pp. 1516-20, Nov, 2007.
41. S. Awale, T. Z. Linn, F. Li, Y. Tezuka, A. Myint, A. Tomida, T. Yamori, H. Esumi, S. Kadota, Identification of chrysosplenetin from *Vitex negundo* as a potential cytotoxic agent against PANC-1 and a panel of 39 human cancer cell lines (JFCR-39), *Phytother Res.*, Vol. 25 (12), pp. 1770-5, Dec, 2011.
42. S. Wei, H. Ji, B. Yang, L. Ma, Z. Bei, X. Li, H. Dang, X. Yang, C. Liu, X. Wu, J. Chen, Impact of chrysosplenetin on the pharmacokinetics and anti-malarial efficacy of artemisinin against *Plasmodium berghei* as well as in vitro CYP450 enzymatic activities in rat liver microsome, *Malar J*, Vol. 4, pp. 14:432, Nov, 2015.

43. Q. C. Zhu, Y. Wang, Y. P. Liu, R. Q. Zhang, X. Li, W. H. Su, F. Long, X. D. Luo, T. Peng, Inhibition of enterovirus 71 replication by chrysosplenetin and penduletin, *Eur J Pharm Sci*, Vol. 44 (3), 392-8, Oct, 2011.
44. Y. Wang, Y. Luo, C. Li, X. Zhang, C. Pi, L. Yu, Wang S, Zhong Z. Optimized formulation of multivesicular liposomes loaded with oleanolic acid enhanced anticancer effect in vitro, *Drug Des Devel Ther*, Vol. 11, pp. 955-968, Mar, 2017.
45. Q. Zhang, R. An, X. Tian, M. Yang, M. Li, J. Lou, L. Xu, Dong Z. β -Caryophyllene Pretreatment Alleviates Focal Cerebral Ischemia-Reperfusion Injury by Activating PI3K/Akt Signaling Pathway, *Neurochem Res*, Vol. 42 (5), Feb, 2017.
46. H. Sibiya, C. T. Musabayane, M. V. Mabandla, Transdermal delivery of oleanolic acid attenuates pro-inflammatory cytokine release and ameliorates anaemia in P. berghei malaria, *Acta Trop*, Vol. 171, pp. 24-29, Mar, 2017.
47. S. Wang, D. Zhang, J. Hu, Q. Jia Q, W. Xu, D. Su D, H. Song, Z. Xu, J. Cui, M. Zhou, J. Yang, J. Xiao, A clinical and mechanistic study of topical borneol-induced analgesia, *EMBO Mol Med*, Apr 10, 2017.
48. G. Benelli, M. Rajeswary, M. Govindarajan, Towards green oviposition deterrents? Effectiveness of *Syzygium lanceolatum* (Myrtaceae) essential oil against six mosquito vectors and impact on four aquatic biological control agents, *Environ Sci Pollut Res Int*, Vol. 25 (11), pp. 10218-10227, April, 2018.
49. G. K. Gilcy, G. Kuttan, Evaluation of Antiangiogenic Efficacy of *Emilia sonchifolia* (L.) DC on Tumor-Specific Neovessel Formation by Regulating MMPs, VEGF, and Proinflammatory Cytokines. *Integr Cancer Ther*, Vol. 15(4), pp. NP1-NP12, Dec, 2016.
50. T. Javid, M. Adnan, A. Tariq, B. Akhtar, R. Ullah and N. M. AbdElsalam, Antimicrobial activity of three medicinal plants (*Artemisia indica*, *Medicago falcate* and *Tecoma stans*), *Afr J Tradit Complement Altern Med*, Vol. 12 (3), pp. 91-96, 2015.
51. X. Y. You, Q. Xue, Y. Fang, Q. Liu, C. F. Zhang, C. Zhao, M. Zhang, X. H. Xu, Preventive effects of *Ecliptae Herba* extract and its component, ecliptasaponin A, on bleomycin-induced pulmonary fibrosis in mice, *J Ethnopharmacol*, Vol. 175, pp. 172-80, Dec, 2015.
52. S. Ganguly, S. Bandyopadhyay, A. Bera, M. Chatterjee, Antipromastigote activity of an ethanolic extract of leaves of *Artemisia indica*, *Indian Journal of Pharmacology*, Vol. 38(1), Apr, 2017.

53. S. Khan, K. Afshan, B. Mirza, J. E. Miller, A. Manan, S. Irum, S. S. Rizvi, M. Qayyum, Anthelmintic properties of extracts from Artemisia plants against nematodes, Trop Biomed, Vol. 2(2), pp. 257-68, Jun, 2015.
54. M. Yoshimoto, R. Kurata-Azuma, M. Fujii, D. X. Hou, K. Ikeda, T. Yoshidome, M. Osako, Enzymatic production of caffeic acid by koji from plant resources containing caffeoylquinic acid derivatives, Biosci Biotechnol Biochem, Vol. 69(9), pp. 1777-81, Sept, 2005.