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Review Article

A Comprehensive Review on Traditional Knowledge, Phytochemistry and Pharmacological Properties of *Acalypha indica* L.

Sahukari Ravi, Punabaka Jyothi, Bhasha Shanmugam, Ganjikunta Venkata Subbaiah, Singamala Hari Prasad, Kesireddy Sathyavelu Reddy

ABSTRACT

Acalypha indica is a significant medicinal plant. The purpose of this review is to bring traditional usage, phytochemistry, and scientific applications of *A. indica* up to date. Microbial infections, fertility, stomach ulcers, snake bites, pains, wounds, liver/kidney problems, and rheumatism have all been traditionally treated with *A. indica* paste, decoction, sap, and synergy with other plants/plant products, which have all been scientifically proven through *in vitro* and *in vivo* experiments. Regardless of traditional knowledge, this plant extracts have been scientifically proven to help against cancer, inflammation, cardiac damage, diabetes, TB, and malaria. Phytochemical investigation revealed that *A. indica* has phenols, flavonoids, tannins, coumarins, alkaloids and their glycosides, saponins, volatiles and fatty acids. In summary, the presence of phytoconstituents is responsible for the *A. indica* traditional and pharmacological qualities. Further, conformational clinical trails in humans are necessary to ascertain the extracts efficacy. Extensive future studies are to be conducted to reveal the mechanism of action, pharmacokinetic properties and active phythochemicals of *A. indica* extracts.

Key words: *Acalypha indica*, Phytochemicals, Pharmacological properties, Traditional uses, Medicinal plants.

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INTRODUCTION

Among the 270,000 higher plants many are known to be of medicinally importance in India.[1] Due to plants diversity in India and their usage in traditional medicine to treat many diseases, India is hub for medicinal plants / natural medicine. The primary health care of Indian people greatly met through the consumption of traditional medicine (Ayurveda, Sidha and Unani) in different formulations due to lack of modern health facilities and very expensive of medical treatment. Despite the fact that there are 456 *Acalypha* species,[2] only a few were used traditionally and examined scientifically. *A. indica* is one among them, and it is frequently used to cure a variety of diseases. Besides of India, it also occupied around Asia and African countries etc, to treat diverse health issues. More importantly, available information on this plant has not been reviewed completely in previously published reviews. Hence, medicinal importance of this plant was made an attraction to review the available information for the asset to scientific community.

Data collection

Information on traditional uses of *A. indica* and scientific evidence as gathered from local books published on *A. indica* and internet sources. In addition, scientific literature databases such as Pubmed, Medline, Google scholar, Science direct, Springer, Wiley online library, The plant database,[2] Kew-Royal botanical garden[3] and other online resources have also been utilized. Doctoral theses available on *A. indica* have been obtained from Shodhganga,[4] a reservoir of Indian theses and also from local universities of Andharapradesh. The phytochemical structures have drawn in Marvin Sketch. To obtain information from above sources, initial search was started with *A. indica*. Further, some other scientific key words have used which include 'biological activity', 'phytochemicals', 'phytoconstituents', 'isolation of compounds', 'nanoparticles' and 'micro particles' where *A. indica* has been kept as a common prefix for all key words. By gathering all the available information, we comphressively reviewed about A. *indica*.

Acalypha indica L.

Synonyms

The plant *A. indica* belongs to *Euphorbiaceae*. It grows in India, Indian Ocean islands, South-East Asia, Oceania, East Africa to southern Africa including South Africa and introduced into warmer parts of the world (Figure 1).[5,6] The accepted binomial is *Acalypha indica* L. but there are other scientific

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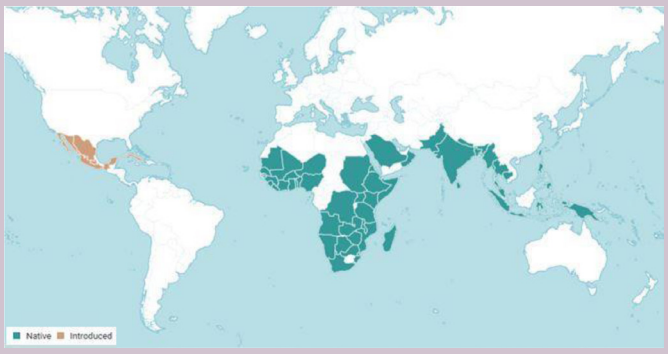


Figure 1: Geographical distribution of *A. indica*.[11]

synonyms including *Acalypha bailloniana* Müll.Arg.; *Acalypha canescens* Benth.; *Acalypha caroliniana* Blanco; *Acalypha chinensis* Benth.; *Acalypha ciliata* Benth.; *Acalypha cupamenii* Dragend.; *Acalypha decidua* Forssk.; *Acalypha fimbriata* Baill.; *Acalypha indica* K.Schum. and Hollr.; *Acalypha indica* var. *australis* F.M.Bailey; *Acalypha indica* var. *bailloniana* (Müll.Arg.) Hutch.; *Acalypha indica* var. *minima* (H.Keng) S.F.Huang and T.C.Huang.; *Acalypha indica* Vell.; *Acalypha somalensis* Pax.; *Acalypha somalium* Müll.Arg.; *Acalypha spicata* Forssk.; *Cupamenis indica* (L.) Raf.; *Ricinocarpus baillonianus* (Müll.Arg.) Kuntze.; *Acalypha indica* var. *mexicana* (Müll.Arg.) Pax and K.Hoffm. *Ricinocarpus deciduus* (Forssk.) Kuntze. and *Ricinocarpus indicus* (L.) Kuntze; *Acalypha tenuis* Klotzsch ex Pax and K.Hoffm.[2,3]

Vernacular names

Though, this plant has scientific name and synonyms, the local people have given a specific name to it for their convenience as follows: Chikka Emas and Galak Kuching (Malay); Tie xian (Chinese); rumput bolong-bolong, Rumput kokosongan, Kucing-kucingan and Lelatang (Indonesian); Ricinelle des Indes, Oreille de chatte, Horrisa and Herba chatte (French); Indian acalypha, Indian nettle and three-seeded mercury (English); Brennkraut (German); Ricinela (Spanish); Alcalifa (Brazil). Besides, Indians have given special prirority in the naming of this plant. Kuppichettu, Kuppinta, Gaayapaku and Muripinda (Telugu); Kuppaimeni and Kuppaveni (Tamil); Kuppigada (Kannada); Kuppameni (Malayalam); Sveta-basanta (Gujaratis); Kuppikhokli (Hindi); and Haritamanjari (Sanskrit).[7,8]

It is a common weed, annual herb; grows up to 30-70 cm height, sometimes little more. This plant has few ascending branches, which are angled and pubescent; the leaves are broadly ovate, longer than 3-5 cm with serrate edges and arranged pinnately; stipules are very minute; flowers are sessile, present on erect axillary spikes and grow longer than the leaf; male flowers are minute, crowded and distally arranged; the stamens of female flowers are scattered along with inflorescence axis, where each one is subtended by a conspicuous semicircular foliaceous toothed green bract; the capsules are hispid and about 1 mm wide with 3-locular.[9]

Effect of season (summer and monsoon) and altitudes (275, 350 and 550 m above mean sea level) on *A. indica* growth have been studied by Krishnan *et al.* (2000).[10] They considered six parameters including leaf (length, breadth and number), branches, and tap root (height and length). Finally, they confirmed that the monsoon and top hill 550 m were suitable growth conditions for *A.indica.*

Local and traditional uses of *A.indica*.

A common weed *A.indica* is used traditionally to alleviate spectrum of diseases of human. Though geographical occupancy of *A.indica* is large but its traditional information is less abundant (Table 1). Traditional uses from India, Western Nepal, Bangladesh, Mozambique, North Djibouti, Seychelles, Réunion, East Africa, Namibia, Mauritius, Mozambique, Indonesia, Ethiopia, Northern Transvaal, Sri Lanka and Southern Thailand are available today. Among these, Indians used this plant very abundantly; next to Africans followed by other people. Indians are well aware of this plant because of its usage in their traditional medicine Ayurveda including in almost all states (Table 1).

People have used this plant leaves as a juice to treat cough,[12-14] ear ache, head ache, syphilitic ulcer, anti-parasiticide,[15,16] constipation,[14,17] rheumatoid arthritis, pneumonia, emetic,[18,20] and scabies.[21] The juice from the whole plant is used to treat bronchitis, [22] snake bites,[23], pneumonia[24] and flatulence.[25] Besides, this plant leaves were made into paste alone and used to treat many ailments which include dermatological problems, wounds, chest pain, burns, snake bite and itching whereas the root paste applied to alleviate fungal infections while total plant paste used against diuretic, constipation, skin problems, severe cough.[26-36] Also, leaves were used to prepare a decoction for the treatment of asthma[37], intestinal lavage,[38] cough, dysentery,[39] cold,[14] and joint pains[21] whereas decoction from the roots was used for asthma, liver and kidney cleaning, as laxative, against intestinal worms and for stomach-ache.[21,38] Other parts of this plant like the stem prepared as a decoction against hemorrhoids.[38] A decoction from the entire plant ingested to treat earache, toothache, burns and wheezing.[18,40] Along with juice, paste and decoction, the other sources also practiced which include infusion, sap and powder.[40,21]

This plant/ parts were combined with other plant/parts to treat many diseases in India including: leaves mixed with calcium hydroxide for cough relaxation;[12] external application of leaves grind in lime juice or common salt was used against parasites, dog bites, dermatitis and wounds of animals, whereas small balls prepared in lime juice taken orally to cure asthma.[15,17,21,27,37,41] Vomiting of animals was prevented by feeding the leaves combined with seeds of *Acorus calamus* L.; Black quarter disease using a combination of leaves with seeds of *Piper nigrum* L., leaves of *Leucas aspera* (Willd.) Link and the bulb of *Allium cepa* L.; leaf juice with *Ferula assa-foetida* L. plant used for constipation of animals [17] leaves and block pepper grains each nine crushed in cow ghee and taken twice a day with butter milk during jaundice;[35] leaves paste with lime juice applied on ring worms;[42] A paste of this plant's leaves with clove and black pepper was applied to cure the maggot wounds;[17] leaf powder or decoction combined with garlic is used against intestinal worms;[43] epilepsy was treated by orally using the leaves combined with pepper, garlic and *Leucas aspera* (Willd) Link leaves; on other way oral ingestion of leaves mixed with *Cardiospermum halicacabum* L. boiled in *Azadirachta indica* A.Juss. oil; leaves with onions were ground, then rubbed on the chest, neck and hips.[44] Paste of *A.indica, Azadirachta indica, Mimosa pudica* leaves with flowers of *Albizzia lebbeck* taken orally for itching.[45] Bronchitis was treated by combining *A.indica* leaves and *Jumellea fragrans* (Thouars) Schltr. tuber infusions with honey. Oral intake of leaves combined with roots of *Tylophora indica* (Burm.f.) Merr vomit the stomach poison.[21] *A.indica* roots with pepper, ginger and honey get rid of the hook and tape worms in children.[46]

The following benefcial effects of the plant without extraction method are : leaves and roots used against diarrhea;[47] seeds used against cholesterol and rheumatism;[48] total plant used to treat animal diseases such as anthrax and black quarter,[17] human diseases include severe cough,[43] antifertility,[49,50] eye infections,[51] piles, pistula,[52] expectorant,[29] arthritis, haemoptysi, mania, bed sores, syphilis,[50] wound healing,[53] flatulence,[25] rheumatism[54] and antiseptic.[31] This incomplete traditional information about *A.indica* extraction is an important one for further utilization in global community.

Table 1: Local and traditional uses of *A.indica*.

S.No	Plant source	Practiced on	By whom/where	Refs.
		Leaves		
1	Uniform mixture of leaf juice and garlic	Anthelmentic	North Maharashtra, India	[55]
2	Decoction (50 mL/day) of leaves taken for one week orally/ small balls (50 mg each) prepared in lemon juice and taken twice a day orally; About 10-15 leaves boiled in one glass of water, then cooled extract about 3 glasses given to the asthma patients upto cure.	Asthma	Andhra Pradesh, India; Boro tribal people of Goalpara district, Assam, India	[37, 56,57]
3	Dry leaves powder	Bedsores	North Maharashtra, India	[55]
4	Leaves of this plant combined with seeds of *Piper nigrum* L., leaves of *Leucas aspera* (Willd.) Link and bulb of *Allium cepa* L. are fed to animals	Black quarter disease of animals	Tamil Nadu, India	[17]
5	Combined leaf infusion with tuber infusion of *Jumellea fragrans* (Thouars) Schltr. were sweetened with honey; leaf juice.	Bronchitis	Seychelles, East Africa; Southern Bankura of West Bengal, India; Boro tribal people of Goalpara district, Assam, India;	[19, 21, 57]
6	Leaf paste applied on burns	Burns	Terai forest, Western Nepal	[18]
7	Oral ingestion of leaves paste	Chest pain	Malayali tribes in Jawadhu hills of Eastern ghats, Tamil Nadu, India; Silent valley of Kerala, India.	[35]
8	Leaf decoction taken internally; leaf juice prescribed for children	Cold	Malayali tribes in Jawadhu hills of Eastern ghats, Tamil Nadu, India; People of Kalahandi District, Odisha, India.	[14]
9	Leaf juice mixed with 5 grams of *Ferula assa-foetida* L. plant and then used against constipation; Leaf juice taken at night; A leaf petiole dipped in castor oil was inserted into anus of a child for 2 min to relief.	Constipation of animals and humans	Andhra Pradesh, India; Gulbarga district, Karnataka, India; People of Kalahandi District, Odisha, India	[14, 17, 58]
10	Juice of fresh leaves mixed with small amount of calcium hydroxide and applied externally on the throat twice a day for five days; Leaves decoction taken internally; A tea spoon of leaf juice taken orally three times a day for 5-6 days; leaf juice prescribed for children	Cough relaxation	Palliyars of Saduragiri Hills, Western Ghats, Tamil Nadu, India; Malayali tribes in Jawadhu hills of Eastern ghats, Tamil Nadu, India; Satpuda forest east, Maharashtra, India; People of Kalahandi District, Odisha, India.	[12, 13, 14]
11	Leaves	Diabetes	Vidarbha region, Maharashtra, India	[59]
12	Leaves	Diarrhea	Bangladesh	[47]
13	Leaf paste with lime applied on bitten area two times a day for 3-4 days	Dog bite	Village people of Shimoga District, Karnataka, India	[27]
14	Decoction of leaves	Dysentery	Philippines	[39]
15	Juice of leaves	Ear ache	Western Kachchh, Gujarat, India; Tharu tribe of Uttarakhand, India	[15, 60, 61]
16	Leaf juice	Emetic	Southern Bankura of West Bengal, India.	[19]
17	Leaves ground with pepper, garlic and leaves of *Leucas aspera* (Willd.)Link then given orally; Leaves mixed with *Cardiospermum halicacabum* L. then subjected to boiling in *Azadirachtaindica* A.Juss. oil and resulted extract given; Leaves ground with onion resulted mixture rubbed on chest, neck and hips or poured into ears and nose of children below 12 years old and the same	Epilepsy	Yanadis of Cuddapah district, Andhra Pradesh, India. Palliyans of Southern WesternGhats, Tamil Nadu, India.	[44]
18	Leaf sap used as eye drops	Eye infection	East Africa, Namibia	[21]
19	Topical application of leaf paste on head	Fungal infection	Palamalairegion of Eastern Ghats, India; Silent valley of Kerala, India.	[26, 35]
20	Leaf paste applied topically	Ganglion	Tadjourah District of Randa, in north Djibouti.	[62]

Continued....

Table 1: Continued....

21	Crushed leaves applied topically and decoction taken orally.	Haemorrhoid	Canhane village, Massingir district, Mozambique	[38]
22	Juice of leaves used as nasal drop.	Head ache	Dhenkanal district, Odisha, India.	[15, 16]
23	Leaves and roots (2:1) crushed then supplied with food once a day for five days/ Leaf powder and decoction with small amount of garlic were given to children to expell worms; Ground leaves, decoction and macerated solution subjected to Enema procedure; the leaves ground in water then taken along with sap of Allium sativum	Intestinal worns of cattle / humans	Andhra Pradesh, India; Canhane village, Massingir district, Mozambique; Shaiji Community in Southwestern Bangladesh	[17, 43, 38, 34]
24	Leaf paste prepared and then taken orally	Itching	Kani tribals in Tirunelveli hills, India	[28]
25	Leaves and black pepper grains each nine crushed in cow ghee taken twice a day with butter milk; leaves paste ingested as orally	Jaundice	East Godavari district, Andhra Pradesh, India; Silent valley of Kerala, India.	[63, 35]
26	Leaf decoction used as massage cream/ Poultice of leaves and stem	Joint pains	Comoros; Tribals of Western Ghats, Kerala.	[21, 46]
27	Crushed leaves applied topically and infusion of leaves taken orally	Laxative	Canhane village, Massingir district, Mozambique; Southern Bankura of West Bengal, India; Western Kachchh, Gujarat, India.	[38, 19, 60]
28	Leaf of this plant mixed with lime juice or quicklime or common salt then applied externally	Parasiticide	India	[15]
29	Leaf juice	Pnemonia	Southern Bankura of West Bengal, India; Boro tribal people of Goalpara district, Assam, India	[19, 57]
30	Infusions of leaves and *Tylophora indica* (Burm.f.) Merr. roots drunk orally	Poisoning of stomach	Réunion	[21]
31	Leaf infusion; Oral administration of tender leaves aqueous extract	Purgative	Réunion and Madagascar; Nicobarese Tribals of Car Nicohar Island, India	[21, 64]
32	Freshly prepared leaf juice is applied on rheumatoid arthritis	Rheumatoid arthritis	Terai forest, Western Nepal; Southern Bankura of West Bengal, India.	[18, 19]
33	Leaf paste with lime juice applied on infected area; Leaf juice applied externally on ringworms.	Ringworm	Rewa district, Madhya Pradesh, India; Terai region of Uttar Pradesh, India	[42, 65]
34	Leaf paste mixed with lemon juice and applied on Scabies of animals; Juice of crushed leaves mixed with salt/ decoction of leaves	Scabies of animals and humans	Kalahandi district, Odisha, India; Mauritius; Terai region of Uttar Pradesh, India	[17, 21, 65]
35	Leaf paste alone/mixed with pepper and applied; paste prepared in water and externally applied on skin two times a day for period of one week; Crushed leaves; Leaf paste mixed with a pinch of lime and was applied;	Skin diseases of animals and humans	Andhra Pradesh, India; Valaiyans of Madurai District, Western Ghats, Tamil Nadu, India; Medagascar; Kodagu district, Karnataka, India; Kancheepuram District, Tamil Nadu, India; Bhadrak District of Odisha, India.	[17, 66, 21,41,32, 33]
36	Leaf paste applied on bitten area; leaves boiled with salt for half an hour and given to the affected animal usually cattle.	Snake bites	Village people of Shimoga District, Karnataka, India; Shaiji Community in Southwestern Bangladesh.	[27, 34]
37	Juice of leaves applied locally	Syphilitic ulcers	Southern Bankura of West Bengal, India.	[15, 19]
38	Combination of leaves of this plant with seeds of *Acorus calamus* L. were ground then fed to animals; Leaf juice prevents the vomiting in humans	Vomiting of animals/ humans	Tamil Nadu, India; Satpuda forest east, Maharashtra, India.	[17, 13]

Continued....

Table 1: Continued...

39	Crushed leaves use to applied on wounds till cure; Leaf paste mixed with kitchen salt and applied on wounded area; This plant leaves, 3 cloves and 4 block peppers were made into paste then applied on maggot wounds;Leaves of *Acalypha indica*, *Mimosa pudica*, *Azadirachta indica* and flowers of *Albizzia lebbeck* made into paste and then taken orally once a day for 3 days; Leaf paste prepared and then taken orally; Leaf ground to make paste and applied on the wound	Wound healing of animals and humans	Nizamabad district, Telangana, India; Tamil Nadu, India; Tribal people of Western Ghats of Tamil Nadu, India; Kani tribals in Tirunelveli hills, India; Shaiji Community in Southwestern Bangladesh.	[17, 45, 28, 34]
		Roots		
1	Root decoction or infusion	Asthma	Seychelles and Réunion, Africa; Satpuda forest east, Maharashtra, India.	[13]
2	Roots boiled in water and then eat	Constipation	Shaiji Community in Southwestern Bangladesh.	[34]
3	Topical application of root paste	Fungal infection	Palamalairegion of Eastern Ghats, India	[26]
4	Decoction of root mixed with ginger, pepper and honey	Hook worms and tape worms in children	Tribals of Western Ghats, Kerala, India	[46]
5	Roots and leaves (1:2) crushed and then supplied with food once a day for five days; Root decoction	Intestinal worms of cattle and humans	Andhra Pradesh, India; Seychelles	[17, 21]
6	One table spoon per day of root decoction given orally for month	Lactation	Gondu tribes of Seethagondi Grampanchayath, Adilabad District, Andhra Pradesh, India;	[67]
7	Infusion and decoction of roots administrated orally	Laxative	Bangladesh; Canhane village, Massingir district, Mozambique.	[47, 38]
8	Root decoction or infusion	Liver and kidney cleaning	Seychelles and Réunion, Africa	[21]
9	Root	Rheumatism	Satpuda forest east, Maharashtra, India.	[13]
10	Root decoction	Stomach-ache.	Seychelles	[21]
		Stem		
1	Decoction of stem administrated orally	Hemorrhoid	Canhane village, Massingir district, Mozambique	[38]
	Seeds			
1	Seeds	Cholesterol	The Kabanjahe traditional market, North Sumatra, Indonesia	[48]
2	Seeds	Rheumatism	The Kabanjahe traditional market, North Sumatra, Indonesia	[48]
		Total plant		
1	Whole plant	Anthrax in cattle and camel	Ethiopia	[17]
2	Whole plant	Antifertility (Emmenagogue)	India	[49, 50]
3	Whole plant	Antiseptic	Siddha healers in Virudhunagar district of Tamil Nadu, India	[31]
4	Whole plant	Arthritis	India	[50]
5	15 to 20 mL of whole plant extract was used for one week ; Extract taken at morning expels the sputum and cures; Whole plant juice taken thrice a day	Asthma.	East Godavari and Krishna Districts, Andhra Pradesh, India; Gulbarga district, Karnataka. India; Jhalawar district, Rajasthan, India	[40,50, 68, 58, 24]
6	Whole plant	Bed sores and sores on lips	India	[50]
7	Whole plant	Black quarter disease in animals	Ethiopia	[17]
8	Whole palnt extract given orally	Brain weakness	Jhalawar district, Rajasthan, India	[24]

Continued....

Table 1: Continued....

9	Crushed whole plant juice given to children/ Paste of whole plant used externally	Bronchitis	Irular, the tribal people of Marudhamalai hills, Coimbatore and Village people of Thoppampatti, Dindigul district, Tamil Nadu, India; East Godavari District, Andhra Pradesh, India;	[22, 40, 50, 30]
10	Whole plant decoction or powder	Burns	India	[40]
11	Whole plant paste used externally	Constipation	Village people of Thoppampatti, Dindigul district, Tamilnadu, India	[50, 30]
12	Whole plant paste used externally	Dermatological ailments	Siddha healers in Virudhunagar district and Village people of Thoppampatti, Dindigul district of Tamil Nadu, India; Araku Valley, Andhra Pradesh, India.	[31, 30, 69]
13	Whole plant	Digestive disorders	Ratanpur region of Bilaspur district , Chhattisgarh, India	[70]
14	Whole plant paste used externally	Diuretic	East Godavari District, Andhra Pradesh, India; Village people of Thoppampatti, Dindigul district, Tamilnadu, India; Malaysia	[40, 30, 52]
15	Plant decoction is given orally	Earache	Terai forest, Western Nepal	[18]
16	Whole plant in the form of fresh or dry eaten as raw material.	Emetic	East Godavari District, Andhra Pradesh, India; Krabi and Songkhla provinces of southern Thailand; South America; Buxar district, Bihar, India.	[40, 50, 25, 71]
17	Whole plant	Expectorant	East Godavari District, Andhra Pradesh, India; Malaysia	[40, 50, 52]
18	Whole plant	Eye diseases	Northern Transvaal	[51]
19	Boiled juice of whole plant given orally	Flatulence	Krabi and Songkhla provinces of southern Thailand	[25]
20	Poultice of whole plant	Headache	India; Mauritius.	[50, 21]
21	Mixing this plant with equal amount of castor oil	Laxative	Malaysia	[52]
22	Whole plant	Mania	India	[50]
23	One table spoon of plant extract given twice a day for three days	Mouth ulcers of babies	Theoraon tribe of Jashpur District, Chhattisgarh, India	[72]
24	Whole plant	Piles	Malaysia	[52]
25	Whole plant	Pistula	Malaysia	[52]
26	Whole plant juice given orally thrice a day	Pneumonia	Jhalawar district, Rajasthan, India;	[24]
27	Tea made from boiled plant taken	Purgative	Malaysia	[52]
28	Whole plant	Rheumatism	Odisha, India.	[54]
29	Plant paste with little salt applied externally	Scabies	Gulbarga district, Karnataka. India	[58]
30	Whole plant paste applied on throat once a day for two days	Severe cough	Rural people of Sivagangai District, Tamil Nadu, Southern India	[36]
31	Whole plant	Severe cough associated with bleeding.	Siddha healers in Virudhunagar district of Tamil Nadu, India.	[43, 50, 31]
32	Juice of whole plant given orally	Snake bites	Western and Sabaragamuwa provinces of Sri Lanka	[23]
33	Whole plant	Syphilis	India	[50]
34	Plant decoction is given orally	Toothache	Terai forest, Western Nepal; India	[18, 40]
35	Plant extract with buttermilk taken	Urinary infections	Gulbarga district, Karnataka. India	[58]
36	Whole plant decoction or powder	Wheezing	India	[40]
37	Whole plant	Wound healing	Sugali tribes of Yerramalais of Kurnool district, Andhra, Pradesh, India; Washim District,Maharashtra, India.	[53,73]

Phytochemicals

Qualitatively estimated phytochemicals

Total plant

Methanolic extract has phenolic, flavonoid, alkaloid, tannin, steroid, terpenoids and saponin compounds; whereas alkaloid, flavonoid, phenolic and saponins found in diethyl ether, ethyl acetate and ethanolic extracts.[74,75] In an experiment, Pragada *et al.* (2011)[76] have found steroids, amino acids and oils in hexane fraction of aqueous alcoholic extract; tannins, amino acids, steroids and oils in ethyl acetate fraction; saponins, flavonoids, aminoacids and oils in methanolic fraction.

Leaves

leaves have alkaloid, tannin, steroid, saponin, flavonoid, glycoside and phenolic compounds (ethanolic extract); sterols (petroleum ether and chloroform extracts); reducing sugar, coumarin, antho cyanin, anthra quinone, saponin, cardiac glycoside, terpenoid, tannin, alkaloid, flavonoid and phenolic compounds (methanolic extract).[43,77,78] Balakrishnan *et al.* (2009)[79] were screened to identify the saponin, alkaloid, terpernoid, phenolic and flavonoids in methanol and water extracts of roots.

Quantified phytochemicals

Subsequent to qualitative analysis of plant extracts, quantification gives an idea for further fractionation and isolation of compounds. Quantified phytochemicals of *A. indica* is shown in Table 2. Flavanones were quantified in methanolic extract, hydroalcoholic extract and its fractions of chloroform and butanol of leaves. Among these, a rich amount (2.56 mg/g) found in butanol insoluble fraction. Flavonoid (29.896 mg/g) and total phenolic (111.321 mg/g) content in lyophilized methanolic extract of leaves were higher than other extracts and fractions. About 16.1 mg/g of saponins were found in methanolic extract of leaves.[76,78,80-82]

Isolated and identified phytochemicals

Traditional attempts on *A.indica* stated the possibilities for pharmacological investigation/research and to established potentiality by isolation of phyto chemicals. To explore phytochemistry of *A.indica,* researchers performed chromatography and spectroscopy techniques. Table 3 presents the phyto constituents of *A.indica* and their biological properties.

A.indica has major phytochemical classes such as alkaloids, polyphenols (flavonoids, tannins, coumarins, hydroxy benzoic acids and hydroxy cinnamic acids), volatile compounds, fatty acid derivatives and others.

Alkaloids and their glycosides

Alkaloids are very essential secondary metabolites of plants and being exhibited potential activity on deadly diseases. In this concern, Hungeling *et al.* (2009)[87] and Nahrstedt *et al.* (1982)[93] have been isolated alkaloids from leaves-inflorescences powder, whereas Ravi *et al.* (2017)[78] identified in leaves of *A.indica* (Tables 3, 4). Among, 8 compounds have been noticed as toxic due to the presence of cyanide hence they called as cynogenic glycosides. These cynogenic compounds are important to the plants to overcome environmental stress and protection from predators but its consumption is very fatal to the humans, which will be discussed in the discussion section of this review. *A.indica* alkaloid rescinnamine used as antihypertensive drug, Pergolide sulfone acts as dopamine receptor inhibitor, Lupinine as anti-coagulant and ambelline has antiproliferative property[88, 89, 92,220] but other alkaloids are not tested in biological systems yet. The chemical structure of alkaloids is presented in Table 4.

Polyphenols

Polyphenols are most significant and definitely abundant among the groups of phytochemicals of plant kingdom, classified into sub classes and sub divisions based on their origin, structural features and biological function. The flavonoids occupied large portion in polyphenols than coumarins, tannins, hydroxy benzoates, hydroxy cinnamic acid and others. The followings are polyphenolic classes and their respective compounds of *A.indica*.

Flavonoids

Ten flavonoid structures of this plant are shown in Table 5. Catechin, dehydrovariabilin, rutin and naringenin were identified in the leaves;[78, 84] quercetin 3-0-β-D-glucoside, rutin and kaempfeorl have been isolated from total plant; whereas, nicotiflorin, biorobin, clitorin and mauritianin were isolated from extracts of leaves and flowers.[147] Production of these compounds in this plant is to overcome the oxidative stress caused by biotic and abiotic factors. Apart from this, these compounds also have other beneficial biological properties as mentioned in Table 3.

Tannins

Eleven tannins were isolated from total plant of *A.indica* using chromatography techniques (Table 6).[137,210] These are poly hydroxyl compounds being played crucial role in the scavenging of free radicals and its associated diseases. Except few (Potassium brevifolincarboxylate, acaindinin, acetonylgeraniin A, euphormism M2 and repandusinic acid), rest of tannins have been tested experimentally for biological activities as presented in Table 3, hence further isolation and experimental validation of tannins of *A.indica* needs to be reported.

Coumarins

Coumarins are one of sub classes of the polyphenols, having potential antioxidant, anti-inflammatory and anti-cancer activities.[106,108-110] Three coumarins have ben found in *A.indica* by the application of RP-HPLC and HR-LC-MS as mentioned in Table 3.[78, 84] The 2D structures have drawn and illustrated in Table 7.

Other polyphenols

Apart from the earlier mentioned polyphenols, hydroxy benzoic acid (Gallic acid and Syringic acid) and hydroxy cinnamic acid (Caffeic acid) are present in *A.indica* (Table 8).

Volatile compounds and fatty acids

The compounds come under volatile category are aldehydes, alcohols, alkanes, alkenes, aromatics, esters, ethers, ketones, steroids and terpenoids. To some extent, fatty acids also come under volatile category based on their chain length. If chain length increases eventually volatilablity decreases. Table 9 shows volatile compounds of *A.indica* and their biological properties are mentioned in Table 3.

Other Phytochemicals

Along with major phytochemical classes of *A.indica* as mentioned above, it has other classes including acetyl, acyclic alkane, alkylated phenol, aluminium glycinate, amine, amino acid, aminoglycoside, anthraquinone, benzene derivative, benzimidazole, benzoate glycoside, benzofurans, benzoxazole, carbazole, carboxy aldehyde, cardenolide, carotenoid, ceramide, cyclic imide, cyclitol, cyclohexanes, dicarboxylic acids, enkephaline peptide, ethanolamine. glucosides, glyceride, glycol, heterocycle, heterocyclic amine, imidazoles, imidazole derivative, imide, imino acid, indene, indoles, indole glycoside, lactones, leukotriene, limnoid, malate, modified dipeptide, n-substituted glycine, nucleosides, organosiloxine, peptides, phenols, phenyl ether, phenyl propionate, phthalic acids, piperidine, porphyrin, prostaglandins, purine, pyrazine derivative, pyridine, pyridine derivatives, pyrone, pyrrole, pyrroles, pyrrolidine, quinolines, salicylate, siloxane, sugar alcohol, sulfanilamide, tocopherol,

Table 2: Quantitative estimation of different phytochemicals from various solvent extracts.

S.No	Plant part-Extract	Phytochemicals quantified	Equivalent standard	Quantity/dry weight	Reference
1	Leaves- Methanol	Flavanones	Naringenin	6.55% w/w	[81]
2	Hydroalcoholic extract	Flavanones	Hesperidin	0.80 mg/g	[80]
3	Leaves -Chloroform soluble fraction from hydroalcoholic extract	Flavanones	Hesperidin	0.097 mg/g	[80]
4	Leaves -Butanol soluble fraction of hydroalcoholic extract	Flavanones	Hesperidin	0.61 mg/g	[80]
5	Leaves -Butanol insoluble fraction of hydroalcoholic extract	Flavanones	Hesperidin	2.56 mg/g	[80]
6	Leaves- Petroleum ether	Flavonoids	Catechin	8.38 mg/g	[83]
7	Leaves- Chloroform	Flavonoids	Catechin	11.04 mg/g	[83]
8	Leaves- Ethyl acetate	Flavonoids	Catechin	14.48 mg/g	[83]
9	Leaves- Acetone	Flavonoids	Catechin	19.57 mg/g	[83]
10	Stem- Petroleum ether	Flavonoids	Catechin	6.83 mg/g	[83]
11	Stem- Chloroform	Flavonoids	Catechin	8.50 mg/g	[83]
12	Stem- Ethyl acetate	Flavonoids	Catechin	11.27 mg/g	[83]
13	Stem- Acetone	Flavonoids	Catechin	15.05 mg/g	[83]
14	Stem- Methanol	Flavonoids	Catechin	13.78 mg/g	[83]
15	Root - Petroleum ether	Flavonoids	Catechin	7.68 mg/g	[83]
16	Root - Chloroform	Flavonoids	Catechin	9.08 mg/g	[83]
17	Root - Ethyl acetate	Flavonoids	Catechin	13.52 mg/g	[83]
18	Root - Acetone	Flavonoids	Catechin	16.55 mg/g	[83]
19	Root - Methanol	Flavonoids	Catechin	14.08 mg/g	[83]
20	Hydroalcoholic extract	Flavonoids	Quercetin	2.02 mg/g	[80]
21	Leaves -Chloroform soluble fraction from hydroalcoholic extract	Flavonoids	Quercetin	0.0156 mg/g	[80]
22	Leaves -Butanol soluble fraction of hydroalcoholic extract	Flavonoids	Quercetin	3.21 mg/g	[80]
23	Leaves -Butanol insoluble fraction of hydroalcoholic extract	Flavonoids	Quercetin	0.96 mg/g	[80]
24	Total plant -Ethanolic extract	Flavonoids	Rutin	8.75 mg/g	[82]
25	Leaves-Methanol	Flavonoids	Epicatechin Quercetin catechin	29.896 mg/g; 1.76% w/w; 67.87 mg/g 17.85 mg/g	[78, 81, 83, 84]
26	Leaves-Petroleum ether (Sequential extraction)	Flavonoids	Quercetin	81.00 mg/g	[83]
27	Leaves- Chloroform (Sequential extraction)	Flavonoids	Quercetin	30.00 mg/g	[83]
28	Leaves- Methanol (Sequential extraction)	Flavonoids	Quercetin	70.67 mg/g	[83]
29	Aqueous Methanol-70% ((Sequential extraction))	Flavonoids	Quercetin	6.67 mg/g	[83]
30	Leaves-Methanol	Phenols	Gallic acid	111.321 mg/g 10.89% w/w 373.54 mg/g	[78, 81, 84]
31	Leaves -Hydroalcoholic extract	Phenols	Gallic acid	7.9 mg/g	[80]
32	Leaves -Chloroform soluble fraction from hydroalcoholic extract	Phenols	Gallic acid	1.14 mg/g	[80]
33	Leaves -Butanol soluble fraction of hydroalcoholic extract	Phenols	Gallic acid	6.7 mg/g	[80]
34	Leaves -Butanol insoluble fraction of hydroalcoholic extract	Phenols	Gallic acid	0.58 mg/g	[80]
35	Total plant -Hydro alcoholic	Phenols	Gallic acid	1.63 mg/g	[76]
36	Total plant -Ethyl acetate fraction	Phenols	Gallic acid	7.21 mg/g	[76]
37	Total plant -Methanolic fraction	Phenols	Gallic acid	2.11 mg/g	[76]
38	Total plant -Hexane fraction	Phenols	Gallic acid	1.45 mg/g	[76]
39	Total plant -Ethanolic extract	Phenols	Tannic acid	9.27 mg/g	[76]
40	Leaves-Petroleum ether (Sequential extraction)	Phenols	Gallic acid	20.00 mg/g	[84]

Continued....

Tabl 2: Continued....

41	Leaves-Chloroform (Sequential extraction)	Phenols	Gallic acid	10.00 mg/g	[84]
42	Leaves-Methanol (Sequential extraction)	Phenols	Gallic acid	306.67 mg/g	[84]
43	Leaves-Aqueous Methanol (70%) (Sequential extraction)	Phenols	Gallic acid	60.00 mg/g	[84]
44	Leaves- Petroleum ether	Phenols	Gallic acid	10.56 mg/g	[83]
45	Leaves- Chloroform	Phenols	Gallic acid	13.85 mg/g	[83]
46	Leaves- Ethyl acetate	Phenols	Gallic acid	16.15 mg/g	[83]
47	Leaves- Acetone	Phenols	Gallic acid	20.03 mg/g	[83]
48	Leaves- Methanol	Phenols	Gallic acid	18.68 mg/g	[83]
49	Stem- Petroleum ether	Phenols	Gallic acid	7.98 mg/g	[83]
50	Stem- Chloroform	Phenols	Gallic acid	11.36 mg/g	[83]
51	Stem- Ethyl acetate	Phenols	Gallic acid	13.57 mg/g	[83]
52	Stem- Acetone	Phenols	Gallic acid	15.66 mg/g	[83]
53	Stem- Methanol	Phenols	Gallic acid	14.58 mg/g	[83]
54	Root - Petroleum ether	Phenols	Gallic acid	8.03 mg/g	[83]
55	Root - Chloroform	Phenols	Gallic acid	12.05 mg/g	[83]
56	Root -- Ethyl acetate	Phenols	Gallic acid	14.71 mg/g	[83]
57	Root - Acetone	Phenols	Gallic acid	17.34 mg/g	[83]
58	Root - Methanol	Phenols	Gallic acid	15.03 mg/g	[83]
59	Leaves- Methanol	Saponins	-	16.1 mg/g	[78]

toluidines and tyronine. The respective compound names of each class are available in Table 3. Miscellaneous compounds are mentioned at the end of Table 3 (Serial number starting from 218 to 250).

Pharmacological Properties

Safety

Safety is a measurement of toxic levels of plant extracts during the toxicity studies. In case of reports available on safety aspect of this plant extracts, aqueous ethanolic extract of 2000 mg/kg and 3000 mg/kg didn't show any abnormalities in mice and rats respectively.[221] The chloroform and n-butanol soluble/insoluble fractions of hydroalcoholic extract of leaves didn't show any behavioral changes and mortality in rats up to 4000 mg/kg.[80] Dosage studies ranging from 100-2000 mg/kg for 14 days with methanolic extract/fraction of leaves not exhibited any changes in biochemical parameters (SGOT, SGPT, ACP, ALP, LDH, creatinine, glucose, protein and uric acid,), haematological issues (hemoglobin, packed cell volume, white blood cell and erythrocyte sedimentation rate), organs weight (heart, brain, spleen, liver and kidney) and mortality.[81,222] Godipurge *et al.* (2015)[82] have reported that polyphenolic extract (5000 mg/kg) didn't show any adverse effcts such as mild diarrhea, depression and weight loss. Similarly, toxicity study in rats with different doses of methanolic extract (Phase I: 10-1000 mg/kg and phase II: 1000-5000 mg/kg) for 12 hrs have not shown any mortality and toxic symptoms. [84] Shirwaikar *et al.* (2004)[223] have reported that intra peritoneal administration of ethanolic extract (5000 mg/kg) didn't produce any toxic effects in rats even after 72 hrs.

Antioxidant activity

Several *in vitro* studies indicated that *A.indica* has antioxidant/radical scavenging potentiality. In final concentration of 0.640 mg/mL of hydro ethanolic extract (70%), fractions of methanol, ethyl acetate and hexane of total plant on DPPH radical showed scavenging of 51.09 % (IC_{50}: 0.61632 mg/mL), 66.5 % (IC_{50}: 0.5542 mg/mL), 52.09% (IC_{50}: 0.19125 mg/mL) and 63.19 % (IC_{50}: 0.24914 mg/mL) respectively, whereas the same concentration of ascorbic acid shown 94.74% (IC_{50}: 0.022 mg/mL).[76] The same DPPH mitigation property of methanolic extract of leaves has been tested by Badami and Channabasavaraj, (2007),[224] Shanmugapriya *et al.* (2011),[225] Sanseera *et al.* (2012),[99] Selvamani (2015)[83] and Ravi *et al.* (2017).[78] Among their results, the good scavenging property was noticed by Ravi *et al.* (2017) [78] (62.948 % at 0.050 mg/mL, IC_{50}: 0.028 mg/mL) whereas, the standard ascorbic acid had IC_{50}: 0.004 mg/mL. All the effective doses/IC_{50} values of leaves and other plant parts on DPPH is summarized in Table 12. An insight into ABTS radical assay for methanol, chloroform and hexane extracts of leaves showed the IC_{50} values of 6.370, 6.310 and 6.130 mg/mL respectively, whereas the standard trolax has 1.320 mg/mL.[99] The other study also revealed potential ABTS scavenging property of methanolic extract of leaves, root and stem with the IC_{50}: 0.005, 0.024 and 0.014 mg/mL respectively, whereas the standard ascorbic acid and rutin showed 0.011 mg/mL and 0.52 µg/mL respectively.[224] In a subsequent study, Selvamani, (2015)[83] found IC_{50} concentrations of acetone extract of leaves (0.252 mg/mL), root (0.288 mg/mL), stem (0.323 mg/mL) and compared with standard BHT (0.225 mg/mL). Similarly, *A.indica* leaf, root and stem extracts/fractions scavenge the hydrogen peroxide, superoxide radicals, nitric oxide,and metal ions (iron and molybdenum); protect the hydroxyl radicals induced sugar damage and lipid peroxidation.[78, 79, 83, 99, 126, 224, 226]

Anticancer activity

Anticancer property of *A.indica* for methanolic extract of leaves on NCI-H187-small cell lung cancer cell lines using Resazurin cell viability fluorescent assay revealed good activity with IC_{50} concentration of 25.00 µg/mL, but it has no potent activity on KB-oral cavity and MCF7-

Table 3: List of phytochemical compounds isolated and identified by different chromatographic tenchniques in *A.indica*.

S.No	Compound Name	Type	Method	Plant source	Pubchem ID	Biological Property	References
1	3,8-Nanodiene-2-one,(E)-	Acetyl	GC-MS	TP	-	-	[75, 43]
2	2-methyl tricosane	Acyclic Alkane	GC-MS	TP	-	-	[85]
3	Hexanal	Aldehyde	GC-MS	TP	CID: 6184	Incresed the anxiety	[85, 86]
4	Acalyphin amide	Alkaloid	MLCCC	L-Inf	CID: 102286669	-	[87]
5	Epiacalyphin amide cycloside	Alkaloid	MLCCC	L-Inf	-	-	[87]
6	Ar-Acalyphidone	Alkaloid	MLCCC	L-Inf	CID: 102286671	-	[87]
7	Rescinnamine	Alkaloid	HR-LC-MS	L	CID: 5280954	Antihypertensive action	[78, 88]
8	Pergolide sulfone	Alkaloid	HR-LC-MS	L	CID: 155750	Acted as dopamine receptor inhibitor	[78, 89, 90]
9	Lupinine	Alkaloid	HR-LC-MS	L	CID:91461	Anti coagulant in the form of artificial polymer. Binds to the nicotinic and muscarine acetylcholine receptors	[78, 91, 92]
10	Ambelline	Alkaloid	HR-LC-MS	L	CID:25092366	Antiproliferative	[78]
11	2-acetyl-4-methoxy-1,2-dimethyl-6-oxo-3-{[3,4,5-triacetyl-6-(2-oxopropyl)oxan-2-yl]oxy}-1,2,3,6-tetrahydropyridine-3-carbonitrile	Alkaloid	C.Chromat	L-Flw	-	-	[93]
12	2-acetyl-5-methoxy-1-methyl-6-oxo-3-{[3,4,5-triacetyl-6-(2-oxopropyl)oxan-2-yl]oxy}-1,2,3,6-tetrahydropyridine-3-carbonitrile	Alkaloid	C.Chromat	L-Flw	-	-	[93]
13	2-hydroxy-5-methoxy-1-methyl-6-oxo-3-{[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl] oxy}-1,2,3,6-tetrahydropyridine-3-carbonitrile	Alkaloid	C.Chromat	L-Flw	-	-	[93]
14	Acalyphin	Alkaloid	MLCCC/ C.Chromat	L-Flw	CID: 49787014	-	[87, 93]
15	Epiacalyphin	Alkaloid	MLCCC	L-Inf	CID: 102286666	-	[87]
16	Noracalyphin	Alkaloid	MLCCC	L-Inf	CID: 102286667	-	[87]
17	Epinoracalyphin	Alkaloid	MLCCC	L-Inf	CID: 102286668	-	[87]
18	Seco-Acalyphin	Alkaloid	MLCCC	L-Inf	CID: 102286670	-	[87]
19	Ethyl tetradecane	Alkane	GC-MS	TP	CID: 41311	-	[85]
20	2-methyl pentadecane	Alkane	GC-MS	TP	CID:15267	-	[85]
21	7-butyl docosane	Alkane	GC-MS	TP	-	-	[85]
22	7-hexyl eicosane	Alkane	GC-MS	TP	-	-	[85]
23	2,2-dimethyl dodecane	Alkane	GC-MS	TP	-	-	[85]
24	Decane	Alkane	GC-MS	TP	CID: 15600	-	[85]
25	Tricosane	Alkane	GC-MS	TP	CID: 12534	-	[94]
26	Hexatriacontane	Alkane	GC-MS	TP	CID: 12412	-	[85]
27	Octacosane	Alkane	GC-MS	L	CID: 12408	-	[95]
28	Tridecane	Alkane	GC-MS	TP	CID: 12388	-	[85]
29	Heptacosane	Alkane	GC-MS	L	CID: 11636	-	[49]
30	Octadecane	Alkane	GC-MS	TP	CID:11635	-	[85]

Continued....

Table 3: Continued....

31	2,4-bis(1,1-dimethylethyl) phenol	Alkylated phenol	GC-MS	L	CID:528937	-	[95]
32	Dihydroxyaluminumaminoacetate	Aluminium glycinate	HR-LC-MS	L	CID: 18502861	Used in the treatment of stomach ulcers and gastritis	[78, 96]
33	3-Methylglutarylcarnitine	Amine	HR-LC-MS	L	CID: 128145	-	[78]
34	Cysteine	Amino acid	GC-MS	TP	CID: 5862	-	[75]
35	Amikacin	Aminoglycoside	HR-LC-MS	L	CID: 37768	Antibacterial agent used to treat urinary tract infections, Intra abdominal infections, Meningitis, Pneumonia, Sepsis, Multi drug resistant TB. Inactivates aminoglycoside-inactivating enzyme.	[78, 97]
36	2-Methylanthraquinone	Anthraquinone	NM	NM	CID: 6773	-	[98-100]
37	Benzene, 1,2,3-trimethyl	Benzene derivative	GC-MS	L	CID: 10686	-	[49]
38	O-Toluenesulfamide	Benzene derivative	HR-LC-MS	L	CID: 10334	-	[78]
39	Emedastine	Benzimidazole	HR-LC-MS	L	CID: 3219	Anti-histamine and H1 receptor inhibitor.	[78, 101]
40	Mebeverine metabolite (Veratric acid glucuronide)	Benzoate glycoside	HR-LC-MS	L	-	-	[78]
41	2-methyl-3-phenyl-1H-Indole	Benzofuran	GC-MS	TP	CID: 282402	-	[102]
42	Loliolide	Benzofuran	GC-MS	TP	CID: 100332	-	[94]
43	Coumaran	Benzofuran	GC-MS	TP	CID: 10329	Acetylcholine esterase inhibitor	[85, 103]
44	Dihydroactinidiolide	Benzoxazole	GC-MS	TP	CID: 6432173	-	[94]
45	Desmethylondansetron	Carbazole	HR-LC-MS	L	CID: 10891224	-	-
46	Isocyclocitral	Carboxy aldehyde	GC-MS	L		-	[95]
47	Peruvoside	Cardenolide	HR-LC-MS	L	CID: 12314120	Cardioprotective	[78, 104]
48	β-ionone	Carotenoid	GC-MS	TP	CID: 638014	Anti-carcinogenic agent	[85, 105]
49	C16 Sphinganine	Ceramide	HR-LC-MS	L	CID: 5283572	-	[78]
50	Ferulic acid	Coumaric acid	RP-HPLC	L	CID: 445858	Antioxidant; Anticancer; Anticardiovascular disease; Skin diseases treatment and Antidiabetic.	[84,106]
51	4-Methyldaphnetin	Coumarin	HR-LC-MS	L	CID: 5355836	Free radical scavenger, 5-lipoxygenase inhibitor, Anticancer, ERK/MAPK signalling inhibitor. Apoptosis inducer.	[78, 107-109]
52	3,3' Methylene bis (4-hydroxyl coumarin)	Coumarin	RP-HPLC	L	CID:54676038	Anticancer	[84, 110]
53	Succinimide	cyclic imide	NM	NM	CID: 11439	-	[111]
54	Quebrachitol	cyclitol	C.Chromat	L	CID: 151108	-	[98, 100]
55	Picrotin	Cyclohexane	HR-LC-MS	L	CID: 442291	Activates human bitter receptors (hTAS2Rs); Blocks the Homomeric Glycine Receptors	[78, 112]

Continued....

Table 3: Continued....

56	Dicyclomine	Cyclohexane	HR-LC-MS	L	CID: 3042	M1 muscarinic antagonist. Used to treat irritable bowel syndrome, Ulcerative colitis; Antispasmodic and Anticholinergic	[78]
57	Traumatic acid	Dicarboxylic acid	HR-LC-MS	L	CID: 5283028	Antioxidant; Enhances collagen biosynthesis; Growth factor for algae	[78, 113-114]
58	L-2-Aminoadipic acid	Dicarboxylic acid	HR-LC-MS	L	CID: 92136	Increases the protein synthesis and inhibits the autophagy in myotubes	[115]
59	Enkephaline, (D-Ala)2-Leu	Enkephaline peptide	HR-LC-MS	L	-	-	[78]
60	2-propenoic acid, 3-[5-acetyl-2,2-dimethylcyclopentyl], methyl ester,[1a(E),5a]-	Ester	GC-MS	L	-	-	[78]
61	Pentadecanoic acid, 14-methyl-, methyl ester	Ester	GC-MS	L	CID:21205	-	[78]
62	10-octadecenoic acid, methyl ester	Ester	GC-MS	L	CID:5364425	-	[78]
63	Heptadecanoic acid, 16-methyl-methyl ester	Ester	GC-MS	L	-	-	[78]
64	Hexadecanoic acid, 14-methyl, methyl ester	Ester	GC-MS	L	-	-	[78]
65	Nonadecanoic acid, 18-oxo, methyl ester	Ester	GC-MS	L	-	-	[78]
66	14-methylhexadecanoic acid, picolinyl ester	Ester	GC-MS	L	-	-	[78]
67	9-octadecenoic acid [Z], 2-hydroxy-1-(hydroxymethyl) ethyl ester	Ester	GC-MS	L	CID:5319879	-	[78]
68	Hexanedioic acid, bis(2-ethylhexyl) ester	Ester	GC-MS	TP	-	-	[94]
69	Eicosatrienoic acid methyl ester	Ester	GC-MS	TP	CID:6421258	-	[85]
70	Methyl arachidate	Ester	GC-MS	TP	CID:14259	-	[85]
71	Trifluoro acetic acid, n-heptadecyl ester	Ester	GC-MS	TP	-	-	[85]
72	Trifluoro acetic acid, n-octadecyl ester	Ester	GC-MS	TP	CID:522719	-	[85]
73	Propionylglycine methyl ester	Ester	HR-LC-MS	L	-	-	[78]
74	GPEtn(18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	Ester	HR-LC-MS	L	-	-	[78]
75	GPCho(16:0/3:1(2E))	Ester	HR-LC-MS	L	-	-	[78]
76	Ethyl ester of hexadecanoic acid	Ester	GC-MS	L	CID:12366	-	[95]
77	Hexadecanoic acid methyl ester	Ester	GC-MS	TP	CID: 8181	-	[85]
78	1,2-Benzenedicarboxylic acid, diisooctyl ester	Ester	GC-MS	L	CID: 33934	-	[116]
79	Choline	Ethanolamine	HR-LC-MS	L	CID:6209	A precursor for acetylcholine; maternal immune stimulator at lactation period; Used in PET imaging for cancer tracing.	[117, 118]
80	1,1-Diethoxy butane	Ether	GC-MS	L	CID:77225	-	[119]
81	1,1-Diethoxy pentane	Ether	GC-MS	L	CID:77223	-	[119]

Continued....

Table 3: Continued....

82	1,1-Diethoxy hexane	Ether	GC-MS	L	CID: 77224	-	[119]
83	1,1,3-Triethoxy propane	Ether	GC-MS	L	CID: 24624	-	[119]
84	1-Monolinoleoylglycerol trimethylsilyl ether	Ether	GC-MS	L	CID: 5366692	-	[119]
85	Ethyl pentanate	Fatty acid	GC-MS	L	CID:10882	-	[119]
86	Ethyl decanoate	Fatty acid	GC-MS	L	CID:8048	-	[119]
87	9,12-Octadecadienoic acid(Z,Z)-	Fatty acid	GC-MS	L/ TP	CID: 5280450		[49, 94]
88	Oleic acid	Fatty acid	GC-MS	L	CID: 445639	-	[116]
89	Tetradecanoic acid	Fatty acid	GC-MS	L	CID: 11005	-	[20, 116,120, 121]
90	Octadecanoic acid	Fatty acid	GC-MS	L	CID: 5281	-	[49]
91	n-Hexadecanoic acid	Fatty acid	GC-MS	L/ TP	CID: 985	-	[49, 78, 102, 116, 119]
92	13-Oxo-ODE	Fatty acid	HR-LC-MS	L	CID: 6446027	PPARα agonist, Ameliorates dyslipidemia and hepatic steatosis; Reduce mucosal damage; Down regulates the inflammation and inhibitor of LOX isozymes.	[78, 122, 123]
93	N-(2hydroxyethyl)palmitamide (Propylene glycol)	Fatty acid	HR-LC-MS	L	CID: 4671	Antiinflammatory; Antitoxic; Anti-traumatic shock; Antianaphylactic; AntiSerotonine; Antiviral; Induce DNA and RNA synthesis.	[78, 124, 125]
94	Lactone of PGF-MUM	Fatty acid	HR-LC-MS	L	-	-	[78]
95	9,12,15-Octadecatrienoic acid	Fatty acid	GC-MS	TP	CID: 5282822	-	[102]
96	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	Fatty acid	GC-MS	L	CID: 5280934	-	[49, 116, 126]
97	Isodecane	Fatty acyl	GC-MS	TP	CID: 13379	-	[85]
98	9-Nanodecene	Fatty acyl	GC-MS	TP	CID: 5364436	-	[102]
99	8,9-Dihydroxy-5,11,14eicosatrienoic acid	Fatty acyl	HR-LC-MS	L	CID:5312971	-	[78]
100	2R-hydroperoxy-9Z,12Z,15Zoctadecatrienoic acid	Fatty acyl	HR-LC-MS	L	CID:16061057	-	[78]
101	2,10-Dihydroxy-4,6,8decatriynoic acid	Fatty acyl	HR-LC-MS	L	CID: 5312795	-	[78]
102	9-Tricosene	Fatty acyl	GC-MS	TP	CID: 6385060	Stimulates female mating in Aphrodisiac of spider	[94, 127]
103	9,12,15 octadecatrienal	Fatty acyl	GC-MS	TP	CID: 5283384	-	[85]
104	9Z,12Z,15E-Octadecatrienoic acid	Fatty acyl	HR-LC-MS	L	CID:5312504	-	[78]
105	6,11-Octadecadiynoic acid	Fatty acyl	HR-LC-MS	L	CID:5312660	-	[78]
106	5,6-DiHETrE-EA	Fatty acyl	HR-LC-MS	L	CID:16061178	-	[78]
107	3,4-Tetradecadienoic acid	Fatty acyl	HR-LC-MS	L	CID: 5312405	-	[78]

Continued....

Table 3: Continued....

108	13-Tetradecen-2,4-diyn-1-ol	Fatty acyl	HR-LC-MS	L	CID: 5283270	-	[78]
109	13-Keto-9Z,11E,15Z octadecatrienoic acid	Fatty acyl	HR-LC-MS	L	CID: 11426350	-	[78]
110	12-Hydroxy-10-octadecynoic acid	Fatty acyl	HR-LC-MS	L	CID: 5312859	-	[78]
111	N-octacosonal	Fatty alcohol	NM	NM	CID:68406	Antinociceptive; Anti-Inflammation; Antiparkinson; Improve reproductive performance.	[78]
112	Tetradecen-1-ol	Fatty alcohol	GC-MS	TP	CID: 120110	-	[85]
113	Hexenol	Fatty alcohol	GC-MS	TP	CID: 5281167	-	[85]
114	Docosanol	Fatty alcohol	GC-MS	TP	CID: 12620	-	[127]
115	1-Eicosanol	Fatty alcohol	GC-MS	TP	CID: 12404	-	[127]
116	1-Hexadecanol	Fatty alcohol	GC-MS	L	CID: 2682	-	[95]
117	1-Triacontanol	Fatty alcohol	GC-MS	TP	CID: 68972	Anti-cancer	[127,128]
118	Octacosanol	Fatty alcohol	GC-MS	TP	CID: 68406	-	[127]
119	Palmitaldehyde	Fattyaldehyde	GC-MS	TP	CID: 984	-	[85]
120	Catechin	Flavanoids	HR-LC-MS	L	CID: 73160	Antioxidant; Neuroprotective; Neurodegenerative disorders; Anticancer; Reduce mitochondrial dysfunction; Anti-diabetic; Inhibitor of polyphenoloxidase and melanosis; Anti-inflammation; Used to treat dry eye disease; Activate brown adipose tissue and Ameliorates graft-versus-host disease.	[78, 129-135]
121	Dehydrovariabilin	Flavonoid	HR-LC-MS	L	CID: 624785	Antiprion	[78,136]
122	Quercetin 3-0-β-D-glucoside	Flavonoid	C.Chromat	TP	CID:44259136	Antiproliferative; Anti-cancer; Wound healing; Antimicriobial; Acute myocardial ischemia protection; Antioxidant; Melanin inhibition; β_2-adrenergic signaling; Anti-aging and Anti-inflammatory.	[137-145]

Continued....

Table 3: Continued....

123	Rutin	Flavonoid	C.Chromat/ RP-HPLC	TP/L	CID: 5280805	Antioxidant; Anti-Neuroinflammation; Sedative; Anticonvulsant; Antialzheimer; Treatment for hyperkinetic movement disorder; Antidepressant; Antiischemic; Analgesic; Antinociceptive; Antifungal; Anti-arthritic; Antidiabetic; Anti hypercholesterolemic; Antiplatelet aggregatory; Antiulcer; Antiasthmatic; Antiosteoporotic; Antiosteopenic; Anticataract; Antifertility; Anticancer; Antibacterial; Antifungal; Larvicidal; Antimalarial; Antiretroviral; Antiviral;Atopic dermatitis; Immune effects; Anti fatigue; Cardioprotective; Nephroprotective; Hepatoprotective and Wound healing.	[137,146]
124	Nicotiflorin	flavonoid	MLCC	L-F	CID: 5318767	-	[147]
125	Biorobin	flavonoid	MLCC	L-F	CID: 15944778	-	[147]
126	Clitorin	flavonoid	MLCC	L-F	CID: 11592917	-	[147]
127	Mauritianin	flavonoid	MLCC	L-F	-	-	[147]
128	Kaempferol	Flavonoid	GC-MS	TP	CID:5280863	Antioxidant activity; Apoptosis inducer; Anticancer; Anti-angiogenesis; Antiinflammation; Anticarcinogenic; Antimicrobial; Neuroprotective	[75, 148-151]
129	Naringenin	Flavonoid	RP-HPLC	L	CID:932	Antioxidant; Antimicrobial; Antiinflammatory; Antidiabetic; Anticancer; Neuroprotective and Cardioprotective	[84, 152]
130	β-D-glucoside	Glucoside	NM	NM	-	Antitumor and Antinecrosis	[153]
131	3-O-methyl-D-glucose	Glucoside	GC-MS	L	CID: 8973	-	[116, 154-156]
132	1-Hexadecanoyl-sn-glycerol	Glyceride	HR-LC-MS	L	CID:3084463	Food additive	[78,157]

Continued....

Table 3: Continued....

133	N-Tris[hydroxymethyl]methyl2-aminoethanesulfonic acid	Glycol	HR-LC-MS	L	CID: 81831	Antiinflammation; Effect on delayed hypersensitivity.	[78,124,158]
134	Triacetonamine	heterocycle	NM	NM	CID:13220	-	[98]
135	Piperidine-2,5-dione	Heterocyclic amine	GC-MS	L	CID: 533930	-	[49]
136	Gallic acid	Hydroxybenzoate	RP-HPLC	L	CID: 370	Antioxidant; Anticancer; Antimelanogenic; Antiinflamatory; Antimicrobial; Antiviral; Antiallergic; Neuroprotective; Anti diabetic; Anti diabetic; Cardioprotective; Anti Alzheimer; Nephroprotective and Hepatoprotective.	[84, 159-162]
137	Syringic acid	Hydroxybenzoate	RP-HPLC	L	CID:10742	Antidiabetic; Antioxidant; Anti acute pancreatitis.	[84,163,164]
138	Caffeic acid	hydroxycinnamic acid	RP-HPLC	L	CID:689043	Anticancer; Antioxidant; Radical scavenger; AntiInflammatory; AntiHuman Immunodeficiency Virus (HIV) and Antimicrobial.	[84, 165, 166]
139	Imidazole, 4-fluoro-5-hydroxyazomethyl--	Imidazole	GC-MS	L	CID: 574814	-	[78]
140	Ondansetron	Imidazole	HR-LC-MS	L	CID: 4595	Prevents vomiting and nausea during chemo therapy and radio therapy of cancer; Used in gastroenteritis.	[167, 168]
141	Clotrimazole	imidazole derivative	TLC	L	CID: 2812	Malaria chemotherapy; Antimicrobial and Antimycotic	[169- 171]
142	Ethosuximide M5	Imide	HR-LC-MS	L	-	-	[78]
143	Proline, 3,4-didehydro-	Imino acid	GC-MS	L/TP	CID:25202244	-	[43, 75]
144	Sulindac sulfide	Indene	HR-LC-MS	L	CID: 5352624	Non-steroidal anti-inflammatory drug targets the COX-2; Potential anticancer drug works on various upregulated (EGR-1, ATF3, NF-*k* B, E-cadherin, NAG-1, p21 and CHOP) and down regulated (β-Catenin, NF-*k* B, EGFR, PDE5, Nesprin-2, Cyclin D1) targets of lung, brest, colon, head/neck, ovarian, gastric, prostate and pancreatic cancers	[172]

Continued....

Table 3: Continued....

145	2-formyl-5,7dimethyl-1,2,3,4-tetrahydropyrimido(3,4-a) indole.	Indole	GC-MS	L		-	[78]
146	2-(4-methylphenyl) indolizine	Indole	GC-MS	L	CID:346948	-	[95]
147	Trandolapril glucuronide	Indole glycoside	HR-LC-MS	L	CID:92023960	-	[78]
148	13-hexyloxacyclotridec10-en-2-one	Lactone	GC-MS	L		-	[78]
149	2-Methyl-7-phenylindole	Lactone	GC-MS	L	CID: 610181	-	[95]
150	5-Methyl-2-phenylindolizine	Lactone	GC-MS	L	CID: 610180	-	[95]
151	Deoxykhivorin	Lactone	HR-LC-MS	L	CID: 6708722	Neuroprotective agent.	[173]
152	Leukotriene F4	Leukotriene	HR-LC-MS	L	CID: 5280938	Causes brochoconstriction.	[174]
153	Heudelottin C	Limnoid	HR-LC-MS	L	CID: 4270081	Filovirus inhibitor	[175]
154	Dimethyl citraconate	Malate	GC-MS	L	CID:5355715	-	[126]
155	Aurantiamide	Modified dipeptide	NM	NM	CID: 185904	-	[111]
156	Dimethylglycine	N-substituted glycine	HR-LC-MS	L	CID: 673	N-methyl-d-aspartate receptor (NMDAR) inhibitor; Antipsychotic activity. Effectively work on Autism , Pervasive developmental disorder, Allergies, Respiratory disorders, Inflammation, Cancer, Epilepsy, Alcoholism and Mitochondrial diseases.	[176-178]
157	Cytidine	Nucleoside	GC-MS	L	CID:6175	Antidepressant-like effects	[126, 179]
158	3-Deoxyguanosine	Nucleoside	HR-LC-MS	L	CID: 165138	Antitumor	[180]
159	Hexadecamethyl-heptasiloxane	organosiloxine	GC-MS	TP	CID:10912	-	[85]
160	Val TrpThr	Peptide	HR-LC-MS	L	-	-	[78]
161	Tyr Phe Tyr	Peptide	HR-LC-MS	L	-	-	[78]
162	Lys His Cys	Peptide	HR-LC-MS	L	-	-	[78]
163	His Ala Ala	Peptides	HR-LC-MS	L	-	-	[78]
164	Phenol,24 BIS(1,1-Dimethylethyl)	Phenol	GC-MS	L	CID: 7311	-	[181]
165	3- Methylphenol	Phenol	GC-MS	L	CID:342	-	[95]
166	Benzenemethanol, 2-(2aminopropoxy)-3-methyl	Phenyl ether	HR-LC-MS	L	CID: 93285	-	[78]
167	Ibuprofen	Phenyl propionate	HR-LC-MS	L	CID: 3672	Relaxes the Menstrual cramps, Arthritis, Fever, Inflammation, Cold, Toothaches; Lowers the blood pressure; Anticancer; Antialzheimers and Antiparkinsons	[182]
168	Fenoprofen glucuronide	Phenyl propionate glycoside	HR-LC-MS	L	-	Urinary metabolite of Fenoprofen, a pain killer and Antiarthritic agent	[183]
169	Di-(2-ethylhexyl)phthalate	Phthalic acid	GC-MS	L	-	-	[126]
170	Didodecyl phthalate	Phthalic acid	GC-MS	L	CID: 17082	-	[119]

Continued....

Table 3: Continued....

171	Terephthalic acid	Phthalic acid	HR-LC-MS	L	CID: 7489	Used in manufacture of polyester fibers, clothing and industrial filaments. Its co polymers used in packing of foods, water, edible oils, bevereges.	[184]
172	2,6-Piperidinedicarboxylic acid	Piperidine	HR-LC-MS	L	CID:557515	-	[78]
173	Harderoporphyrin	Porphyrin	HR-LC-MS	L	CID: 3081462	An intermediate of heme biosynthesis, elevated levels observed in harderoporphyria.	[185]
174	PGG2	prostaglandins	HR-LC-MS	L	CID: 5280883	Unstable prostaglandin G2, acts as vasodepressor agent, involved in platelet aggregation and release.	[186, 187]
175	4-Amino-3-methoxypyrazolo[3,4-d]pyrimidine, -	Purine	GC-MS	TP	CID:596791	-	[43, 75]
176	5,10-Diethoxy-2,3,7, 8-tetrahydro-1H, 6H-dipyrrolo[1,2-a;1',2'-d] pyrazine	Pyrazine derivative	GC-MS	TP	CID: 551125	-	[94]
177	Tropicamide	Pyridine	HR-LC-MS	L	CID:5593	Anticholinergic drug used as Pupillary dilation of eye.	[188]
178	2-Dimethylaminopyridine	Pyridine derivative	GC-MS	L	CID: 21885	-	[95]
179	4-(3-Pyridyl)-3-butenoic acid	Pyridine derivative	HR-LC-MS	L	CID:5478892	-	[78]
180	2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran4-one	Pyrone	GC-MS	L	CID:119838	-	[119]
181	Bilirubin	Pyrrole	HR-LC-MS	L	CID: 5280352	Antibacterial	[189]
182	1H-Pyrrole-2,5-dione,1- ethenyl-	Pyrroles	GC-MS	L/TP	CID: 24358	-	[43,75]
183	2,5-Pyrrolidinedione, 1-methyl-	Pyrrolidine	GC-MS	L	CID:21232168	-	[116]
184	Peucenin	Quinolines	HR-LC-MS	L	CID: 68477	-	[78]
185	Orthothymotinic Acid	Salicylate	HR-LC-MS	L	CID: 11052	-	[78]
186	Clotrisiloxane, Hexamathyl-	Siloxane	GC-MS	L	CID: 10914	-	[181]
187	27-Nor-5b-cholestane3a,7a,12a,24,25-pentol	Steroid	HR-LC-MS	L	CID:21252278	-	[78]
188	Beta-sitosterol	Steroid	GC-MS	TP	CID: 222284	Uterotrophic agent; Antifertility; Antiinflammatory and Anti-microbial	[102, 190,191]
189	Campesterol	Steroid	GC-MS	TP	CID: 173183	-	[102]
190	Stigmasterol	Steroid	GC-MS	TP	CID: 5280794	Antiosteoarthritic; Antihyper-cholestrolemic; Antitumor; Hypoglycemic; Antioxidant; Antiinflammatory ; Antimutagenic	[102, 192]
191	3beta,6alpha,7alphaTrihydroxy-5beta-cholan-24oic Acid	Steroid	HR-LC-MS	L	CID:5283822	-	[78]
192	4-C-methyl-myo-inositol	Sugar alcohol	GC-MS	L	CID: 244581		[119]

Continued....

Table 3: Continued....

193	Sulfamerazine	Sulfanilamide	HR-LC-MS	L	CID: 5325	-	[78]
194	Potassium brevifolincarboxylate	Tannin	C.Chromat	TP	CID: 101933031	-	[137]
195	Acaindinin	Tannin	C.Chromat	TP	CID: 101933032	-	[137]
196	l-O-galloyl-β-D-glucose	Tannin	C.Chromat	TP	-	Anti-inflammatory; MyD88/NF-κ B and MyD88/MAPK signalling pathways inhibitor and Antidiabetic.	[137, 193,194]
197	1,2,3,6-tetra-O-galloyl·β-D-glucose	Tannin	C.Chromat	TP	-	Antiviral and Anticancer	[137, 195-197]
198	Corilagin	Tannin	C.Chromat	TP	CID:73568	Anti-inflammatory; Antioxidant;. Anti-hyperalgesic; Antiulcer; Hepatoprotective; Anti-proliferation; Anti-tumour ;	[137, 198-203]
199	Geraniin	Tannin	C.Chromat	TP	CID:3001497	Antioxidant; Anti-tumour; Anti-infective; Antihyperglycemic and Anticancer activity	[137, 204-208]
200	Acetonylgeraniin A	Tannin	C.Chromat	TP	-	-	[137]
201	Euphormism M2	Tannin	C.Chromat	TP	-	-	[137]
202	Repandusinic acid A	Tannin	C.Chromat	TP	CID: 14483070	-	[137]
203	Chebulagic acid	Tannin	C.Chromat	TP	CID: 442674	Antibiabetic	[137, 209]
204	Tri-O-methylellagic acid	Tannin	NM	NM	-	Antimicrobial	[210]
205	Larixol Acetate	Terpene	HR-LC-MS	L	CID: 4615087	Transient receptor potential cation channel 6 (TRPC6) inhibitor	[78, 211]
206	Phytol	Terpene	GC-MS	L/ TP	CID: 5280435	Antischistosomal; Anxiolytic-like effects	[49,85,94, 116, 119, 212, 213]
207	Squalene	Terpene	GC-MS	L	CID: 638072	Protection of cyclophosphamide-induced toxicity	[49,119, 214]
208	Isophytol	Terpene	GC-MS	TP	CID: 10453	-	[102]
209	Pinane	Terpene	GC-MS	L	CID: 10129	-	[95]
210	Linalool	Terpene	GC-MS	TP	CID: 6549	-	[85]
211	Tunaxanthin J/ Chiriquixanthin B	Terpene	HR-LC-MS	L	CID: 16061201	-	[78]
212	Methoprene (S)	Terpene	HR-LC-MS	L	CID: 1711973	Accelerates sexual maturation in male and female	[78, 215]
213	Elephantopin	Terpene	HR-LC-MS	L	CID: 442206	Anticancer	[78, 216]
214	Flavoxanthin	Terpenoid	HR-LC-MS	L	CID:5281238	Food additive and food colouring agent	[217]
215	Vitamin E	Tocopherol	GC-MS	L/TP	CID: 14985	**Neuroprotection; Antioxidant;**	[102,119, 218]
216	Pararosaniline	Toluidines	HR-LC-MS	L	CID: 11292	Cells staining	[78, 219]
217	Thyroacetic acid	Tyronine	HR-LC-MS	L	-	-	[78]
218	Propanenitrile,3-(5-diethylamino-1-methoxy-3-pentynyloxy)-	-	GC-MS	TP	-	-	[75]
219	1-oxaspiro [2,5] octane, 5,5-dimethyl-4-(3-methyl-1,3-butadienyl)-	-	GC-MS	L	-	-	[78]

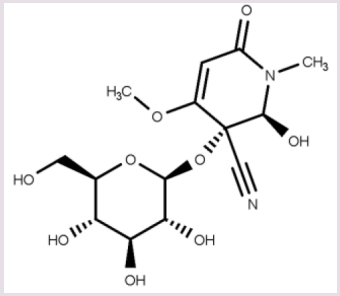
Continued....

Table 3: Continued....

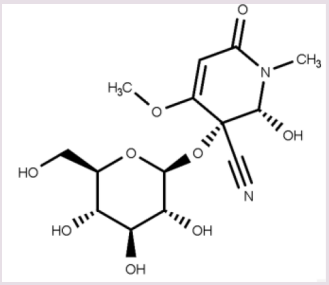
220	MOME inositol	-	GC-MS	L/TP	-	-	[94, 126]
221	Propanenitrile, 3-(5-diethylamino-l-methyl-3-pentynyloxy)-	-	GC-MS	L	-	-	[43]
222	Trifluoromethyl t-butyl disulfide	-	GC-MS	L	-	-	[119]
223	2,6,10 trimethyl undecatriene	-	GC-MS	TP	-	-	[85]
224	α-tulenol	-	GC-MS	TP	-	-	[85]
225	α-toaldehyde	-	GC-MS	TP	-	-	[85]
226	Benzopyran	-	GC-MS	TP	-	-	[85]
227	2-Methyl-3(3-Methyl-But-2 Enyl)-2(4-Methul-Pent-3-Enyl)-Oxetane	-	GC-MS	L	CID: 550119	-	[181]
228	Trimethyl[4-(1,1,3,3, Tetramethylbutyl) phenox] Silane	-	GC-MS	L	CID: 528938	-	[181]
229	1,3-Dioxolane, 4- Ethyl-5-Octyl-2,2Bis (Trifluoromethyl)-, Trans-	-	GC-MS	L		-	[181]
230	Bicyclo (3.1.1) heptane	-	GC-MS	TP	CID: 638057	-	[102]
231	hexamathyl and 1,3-dioxolane,4-ethyl-5-octyl-2,2-bis(Trifluoromethyl), Trans	-	GC-MS	L	-	-	[181]
232	Phenyl Methylhydrazino N-sulfamoylisosemicarbazide	-	GC-MS	L	-	-	[126]
233	3-Phenyl-1,2-pyrazole	-	GC-MS	L	-	-	[126]
234	(E)-1-(tert-butyldimethylsilyl)-4,4-dimethyl-2-penten-1-one	-	GC-MS	L	-	-	[126]
235	Thiophene, 2-propyl-	-	GC-MS	L	CID:73771	-	[126]
236	3-Oxo-20-methyl-11-à-hydroxyconanine-1,4-diene	-	GC-MS	L	-	-	[126]
237	Hexadecanoic acid, 2,3-dihydroxypropyl ester	-	GC-MS	L	-	-	[126]
238	4-cyanomethylquinoline	-	GC-MS	L	CID: 257387	-	[126]
239	Ramipril glucuronide	-	HR-LC-MS	L	CID: 71751964	-	[78]
240	Methyl N-(amethylbutyryl)glycine	-	HR-LC-MS	L	-	-	[78]
241	6-Hydroxydesmethylondansetron	-	HR-LC-MS	L	-	-	[78]
242	5-MethyltetrahydropteroyltriL-glutamate	-	HR-LC-MS	L	-	-	[78]
243	3-Deoxo-3betaacetoxydeoxydihydroge Dunin	-	HR-LC-MS	L	-	-	[78]
244	24-Nor-5beta-chol-22-ene3alpha,7alpha,12alpha-triol	-	HR-LC-MS	L	-	-	[78]
245	1-Octadecanoyl-2(5Z,8Z,11Z,14Zeicosatetraenoyl)-sn-glycero3-phosphate	-	HR-LC-MS	L	-	-	[78]
246	1-[[2-(2,3-dihydro-2-oxo-1Hindol-4yl)ethyl]propylcarbamate] glucuronide	-	HR-LC-MS	L	-	-	[78]
247	1,2 Di-(9Z,12Z,15Zoctadecatrienoyl)-3-O-Beta-Dgalactosyl-sn-glycerol	-	HR-LC-MS	L	-	-	[78]
248	1-(9Z-hexadecenoyl)-2(5Z,8Z, 11Z,14Z,17Zeicosapentaenoyl)-snglycerol	-	HR-LC-MS	L	-	-	[78]
249	(3S,7R)-epi-jasmonic acid (Fatty acyl)	-	HR-LC-MS	L	CID: 7251177	-	[78]
250	(22R)-1alpha,22,25trihydroxy-26,27-dimethyl23,24-tetradehydro-24ahomo-20-epivitamin D3 / (22R)-1a	-	HR-LC-MS	L	-	-	[78]

MLCC: Multilayer coutercurrent chroamatography; MLCCC: Multilayer coil coutercurrent chroamatography L-F:Combination of leaves and flowers; L:leaves; TP: Totalplant; HPLC:High performance liquid chromatography;GC-MS:Gas chromatograpy-mass spectroscopy; HR-LC-MS: High resolution- liquid chromatography-mass spectroscopy; L-Inf: combination of leaves-inflorescences; L-Flw: Leaves-flowers; TLC: Thin layer chromatography; NM: Not mentioned.

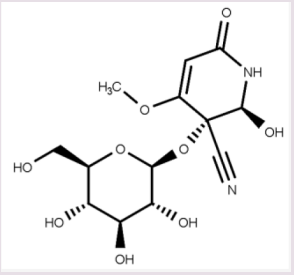
Table 4: Alkaloids of *A.indica*.



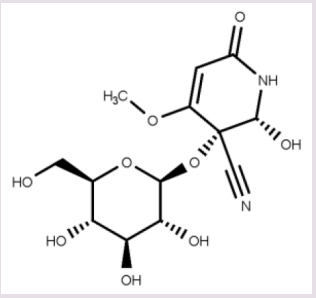
1.Acalyphin



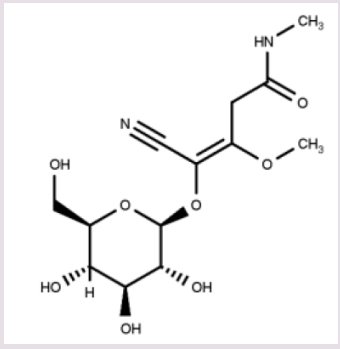
2.Epiacalyphin



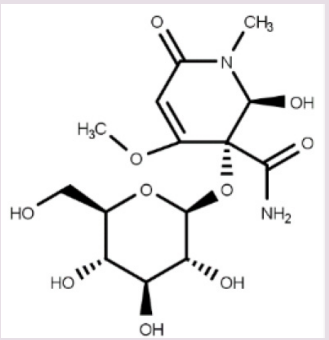
3.Noracalyphin



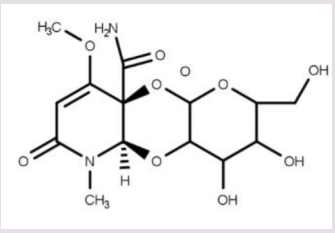
4. Epinoracalyphin



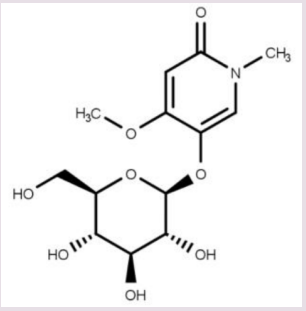
5.Seco-Acalyphin



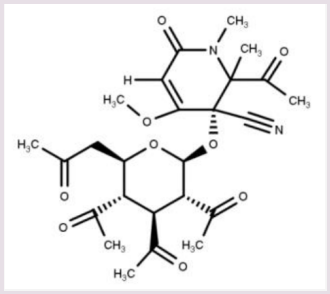
6.Acalyphin amide



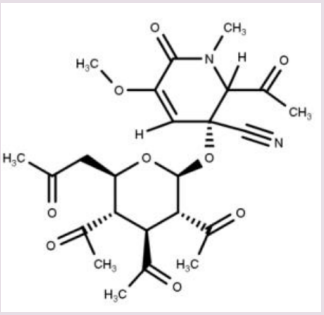
7.Epiacalyphin amide cycloside



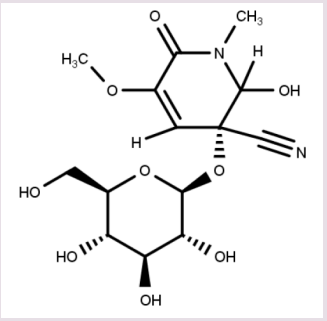
8.Ar-Acalyphidone



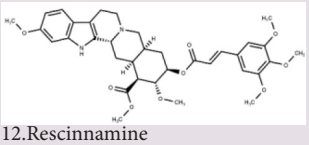
9. 2-acetyl-4-methoxy-1,2-dimethyl-6-oxo-
3-{[3,4,5-triacetyl-6-(2-oxopropyl) oxan-
2-yl]oxy}-1,2,3,6-tetrahydropyridine-3-carbonitrile



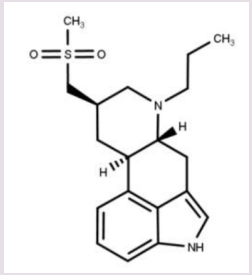
10. 2-acetyl-5-methoxy-1-methyl-6-oxo-
3-{[3,4,5-triacetyl-6-(2-oxopropyl)oxan-
2-yl]oxy}-1,2,3,6-tetrahydropyridine-3-carbonitrile



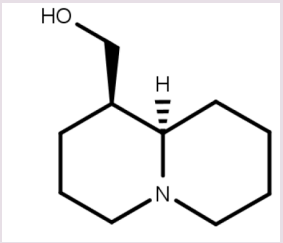
11. 2-hydroxy-5-methoxy-1-methyl-6-oxo-3-
{[3,4,5-trihydroxy-6-(hydroxymethyl) oxan-
2-yl]oxy}-1,2,3,6-tetrahydropyridine-3-carbonitrile



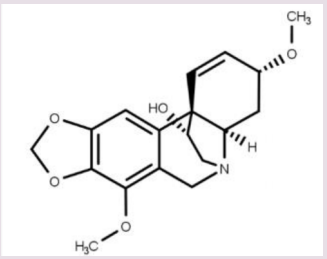
12.Rescinnamine



13.Pergolide sulfone

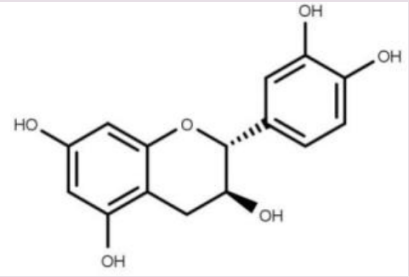


14.Lupinine

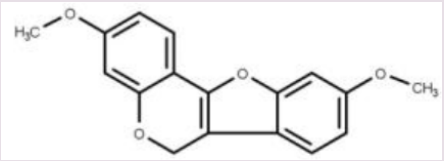


15.Ambelline

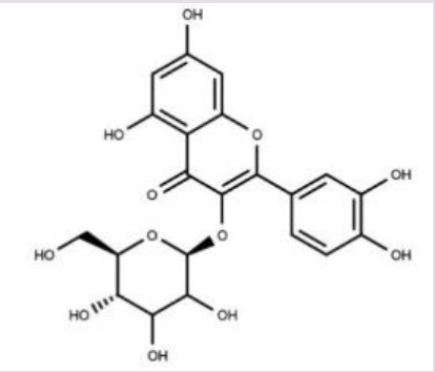
Table 5: Flavonoids of *A.indica*.



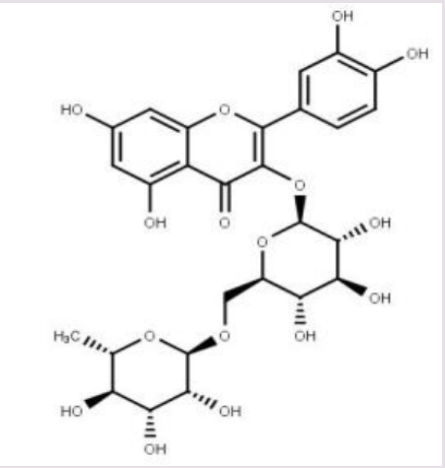
1.Catechin



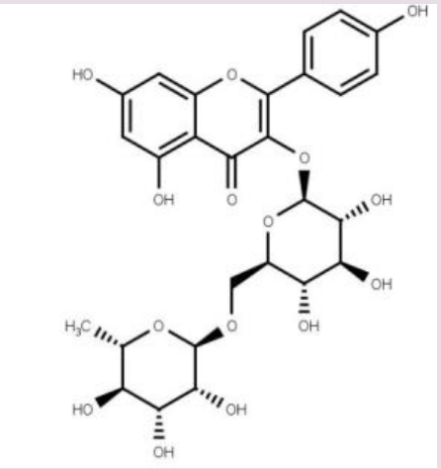
2.Dehydrovariabilin



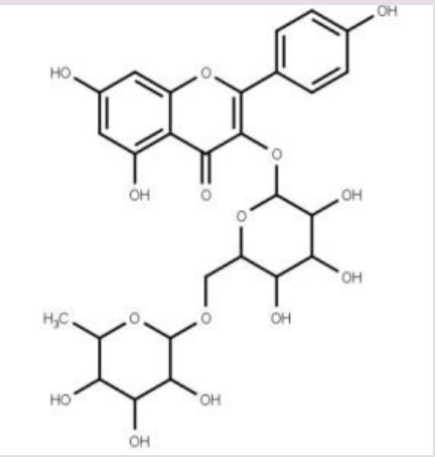
3.Quercetin 3-0-β-D-glucoside



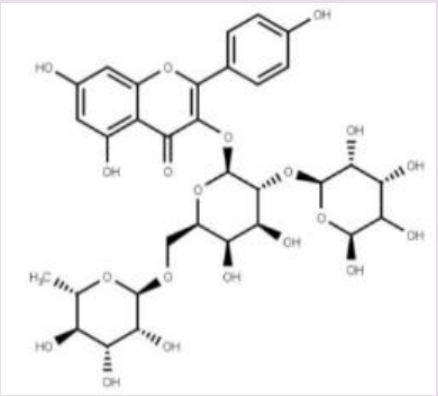
4.Rutin



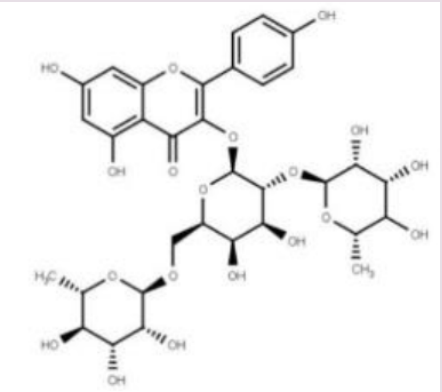
5.Nicotiflorin



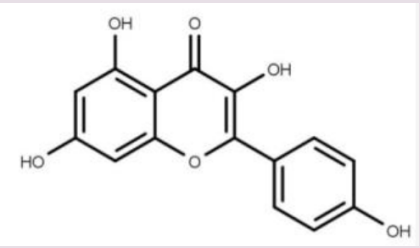
6.Biorobin



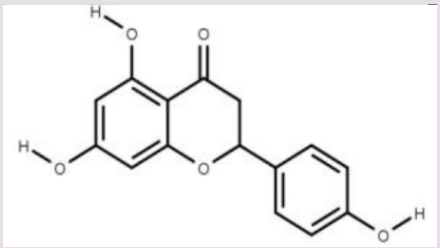
7.Clitorin



8.Mauritianin

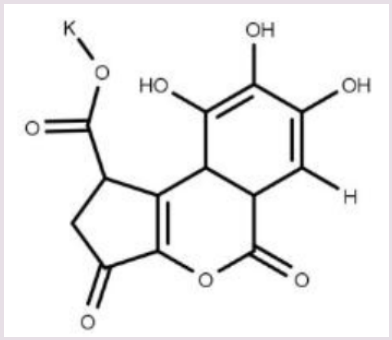


9.Kaempferol

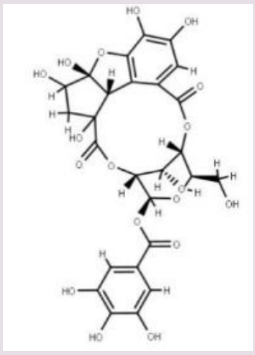


10.Naringenin

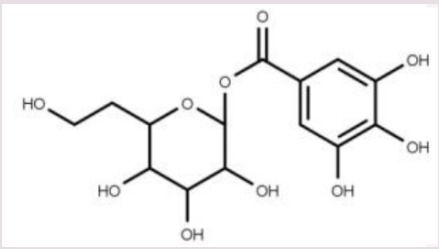
Table 6: **Tannins of *A.indica*.**



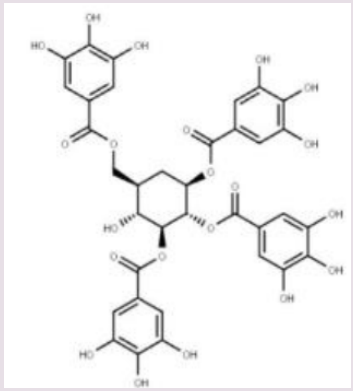
1.Potassium brevifolincarboxylate



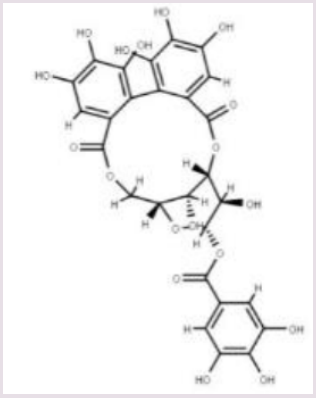
2.Acaindinin



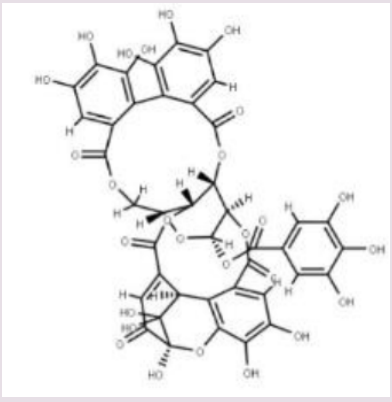
3. l-O-galloyl-β-D-glucose



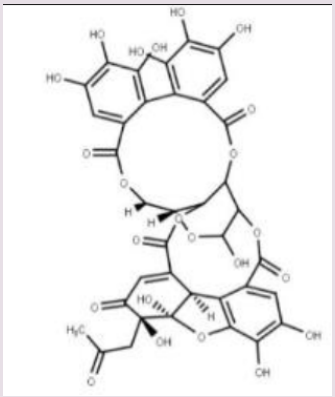
4. 1,2,3,6-tetra-O-galloyl·β-D-glucose



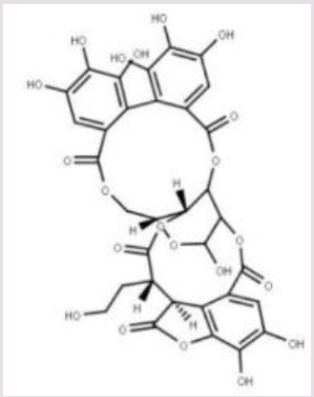
5.Corilagin



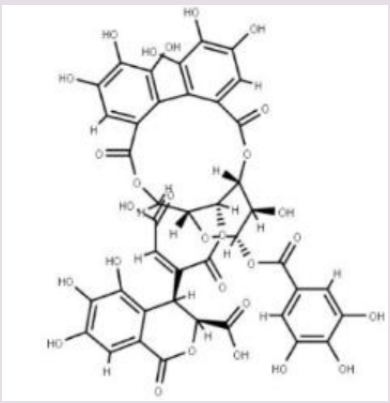
6.Geraniin



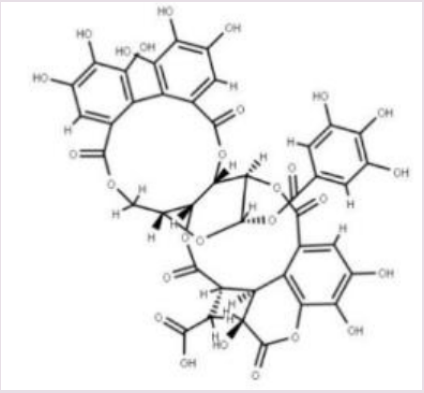
7. Acetonylgeraniin A



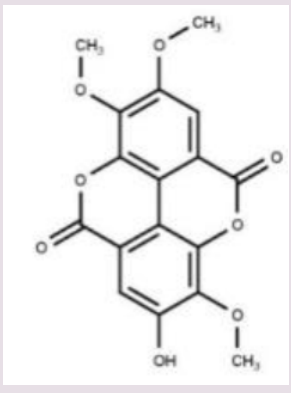
8.Euphormism M2



9.Repandusinic acid A

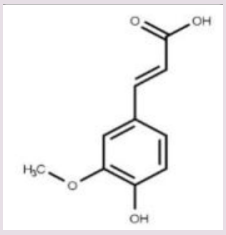


10.Chebulagic acid



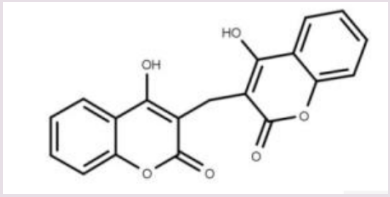
11.Tri-O-methylellagic acid

Table 7: Courmarins of *A.indica*.



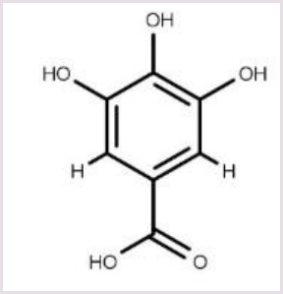
1. Ferulic acid

2. 4-Methyldaphnetin

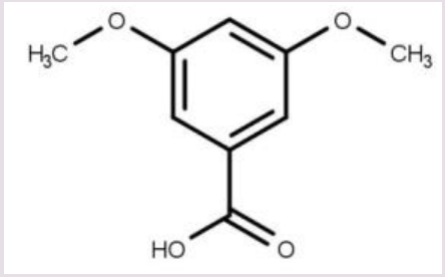


3. 3,3' Methylene bis (4-hydroxyl coumarin)

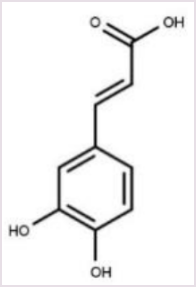
Table 8: Hydroxy benzoic acid and hydroxy cinnamic acids of *A.indica*



1.Gallic acid



2. Syringic acid



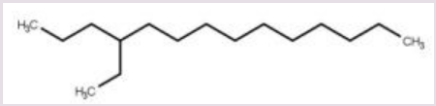
3. Caffeic acid

Table 9: Volatile compounds and fatty acids of *A.indica*.

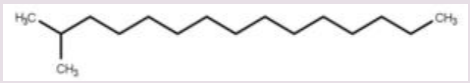
Aldehyde

1.Hexanal

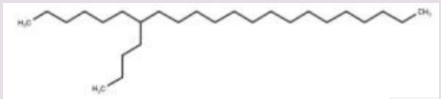
Alkanes



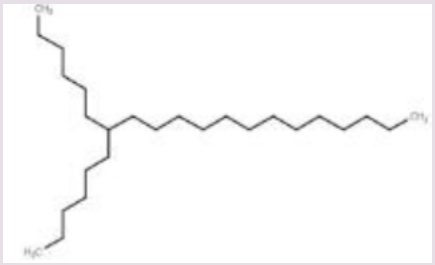
1.Ethyl tetradecane



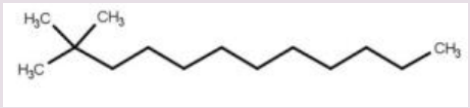
2. 2-methyl pentadecane



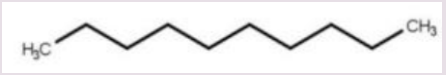
3. 7-butyl docosane



4. 7-hexyl eicosane



5. 2,2-dimethyl dodecane



6. Decane

7. Tricosane

8. Hexatriacontane

9. Octacosane

10. Tridecane

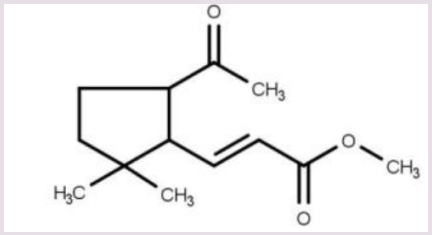
11. Heptacosane

12. Octadecane

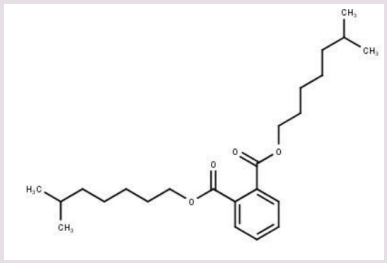
Continued....

Table 9: Continued...

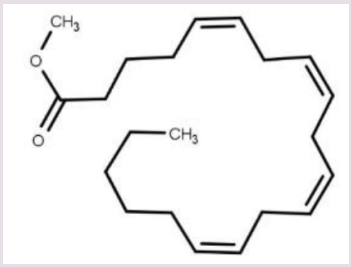
Esters



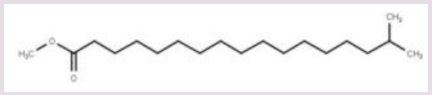
1. 2-propenoic acid, 3-[5-acetyl-2,2-dimethylcyclopentyl], methyl ester,[1a(E),5a]-



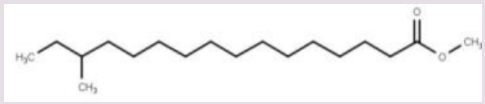
2. 1,2-Benzenedicarboxylic acid, di-isooctyl ester



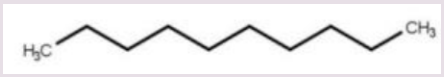
3. Eicosatrienoic acid methyl ester



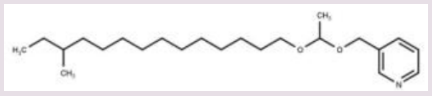
4. Heptadecanoic acid, 16-methyl- methyl ester



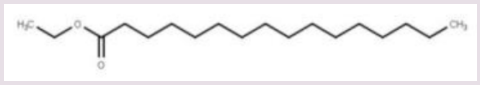
5. Hexadecanoic acid, 14-methyl, methyl ester



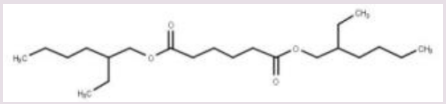
6. Nonadecanoic acid, 18-oxo, methyl ester



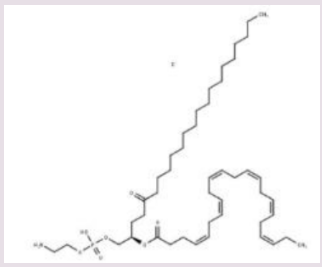
7. 14-methylhexadecanoic acid, picolinyl ester



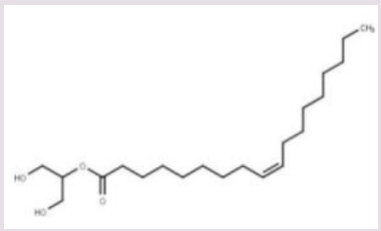
8. Ethyl ester of hexadecanoic acid



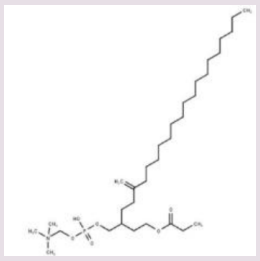
9. Hexanedioic acid, bis(2-ethylhexyl) ester



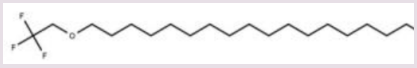
10. GPEtn(18:0/22:6(4Z,7Z,10Z,1 3Z,16Z,19Z))



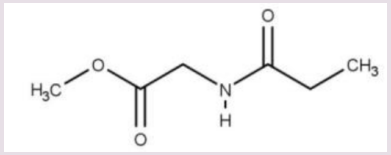
11. 9-octadecenoic acid [Z], 2-hydroxy-1-(hydroxymethyl) ethyl ester



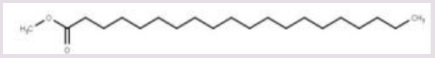
12. GPCho(16:0/3:1(2E))



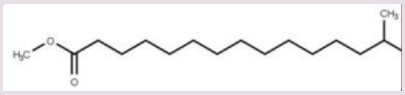
13. Trifluoro acetic acid, n-octadecyl ester



14. Propionylglycine methyl ester

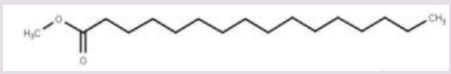


15. Methyl arachidate



16. Pentadecanoic acid, 14-methyl-, methyl ester

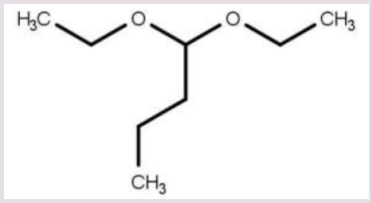
17. 10-octadecenoic acid, methyl ester



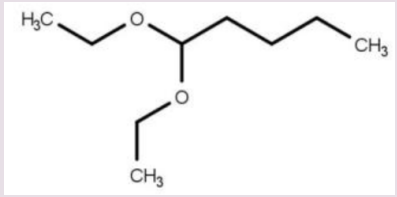
18. Hexadecanoic acid methyl ester

19. Trifluoro acetic acid, n-heptadecyl ester

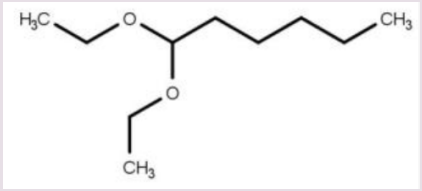
Ethers



1.1,1-Diethoxy butane



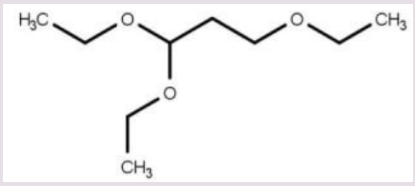
2. 1,1-Diethoxy pentane



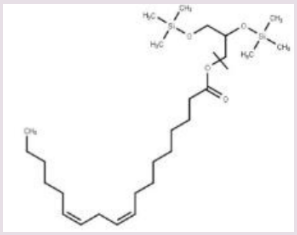
3. 1,1-Diethoxy hexane

Continued....

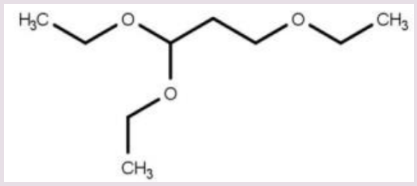
Table 9: Continued....



4. 1,1,3-Triethoxy propane

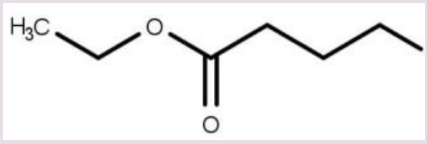


5. 1-Monolinoleoylglycerol trimethylsilyl ether

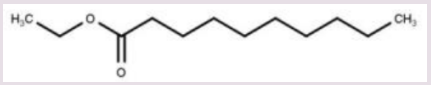


4. 1,1,3-Triethoxy propane

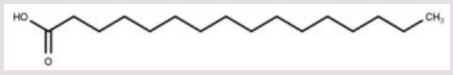
Fatty Acids (number 1-12), fatty acyls (13-26) and fatty alcohols (27-35)



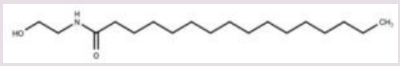
1. Ethyl pentanate



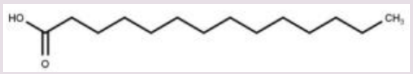
2. Ethyl decanoate



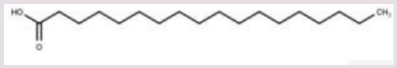
3. n-Hexadecanoic acid



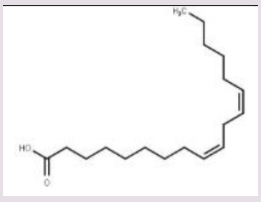
4. N-(2hydroxyethyl)palmitamide (Propylene glycol)



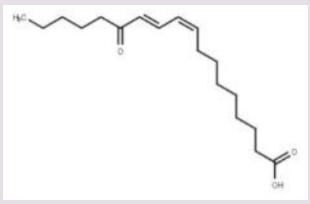
5. Tetradecanoic acid



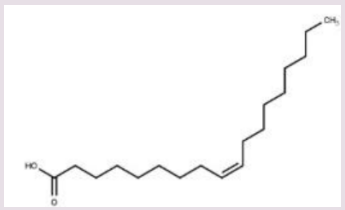
6. Octadecanoic acid



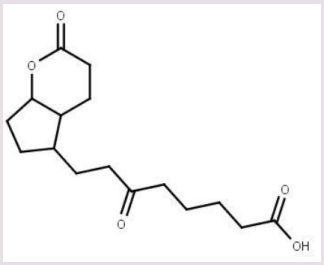
7. 9,12-Octadecadienoic acid(Z,Z)-



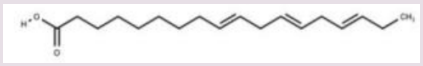
8. 13-Oxo-ODE



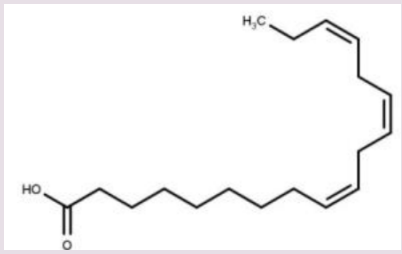
9. Oleic acid



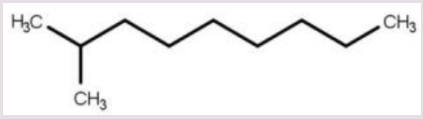
10. Lactone of PGF-MUM



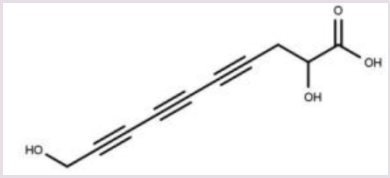
11.9,12,15-Octadecatrienoic acid



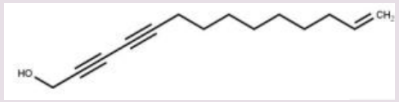
12.9,12,15-Octadecatrienoic acid, (Z,Z,Z)-



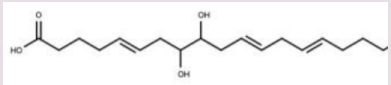
13. Isodecane



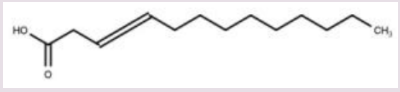
14. 2,10-Dihydroxy-4,6,8decatriynoic acid



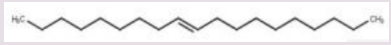
15. 13-Tetradecen-2,4-diyn-1-ol



16. 8,9-Dihydroxy-5,11,14eicosatrienoic acid

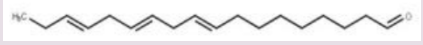


17. 3,4-Tetradecadienoic acid

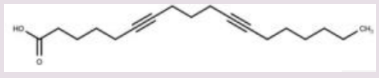


18. 9-Nanodecene

19. 9-Tricosene



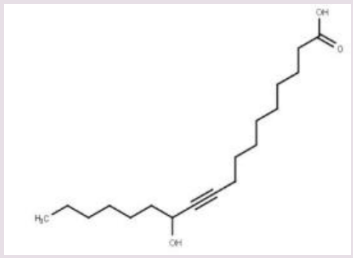
20. 9,12,15 octadecatrienal



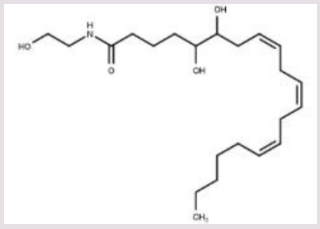
21. 6,11-Octadecadiynoic acid

Continued....

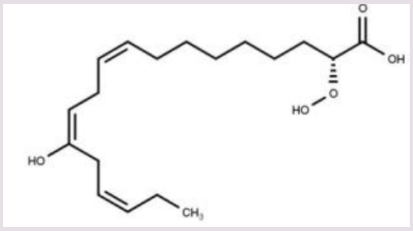
Table 9: Continued....



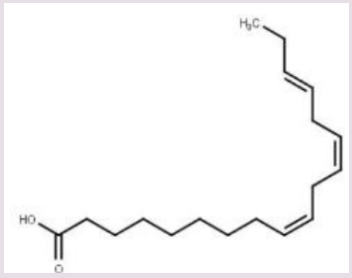
22. 12-Hydroxy-10-octadecynoic acid



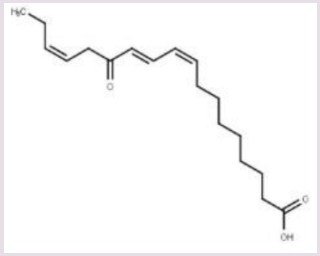
23. 5,6-DiHETrE-EA



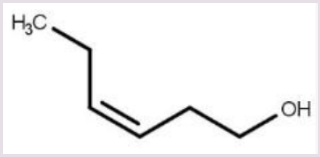
24. 2R-hydroperoxy-9Z,12Z,15Zoctadecatrienoic acid



25. 9Z,12Z,15E-Octadecatrienoic acid



26. 13-Keto-9Z,11E,15Z octadecatrienoic acid



27. Hexenol

28. 1-Triacontanol

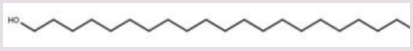
29. Octacosanol

30. N octacosonal

31. 1-Hexadecanol

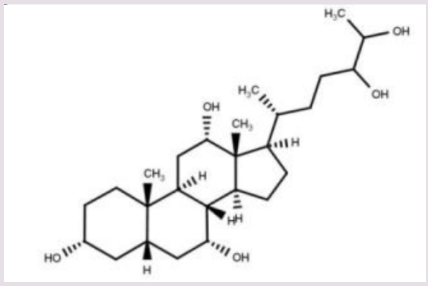
32. Tetradecen-1-ol

33. 1-Eicosanol

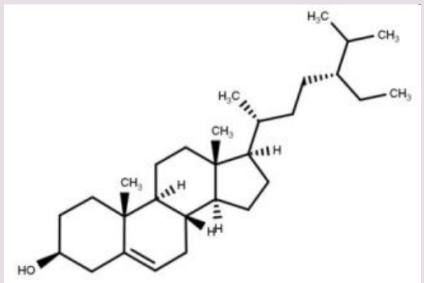


35. Docosanol

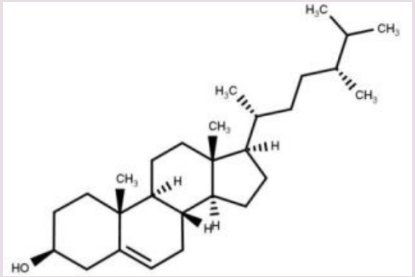
Steroids



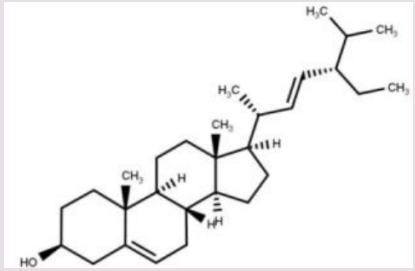
1. 27-Nor-5b-cholestane3a,7a,12a,24,25-pentol



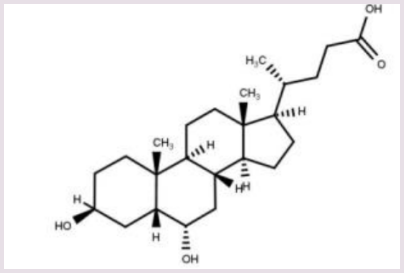
2. Beta-sitosterol



3. Campesterol



4. Stigmasterol

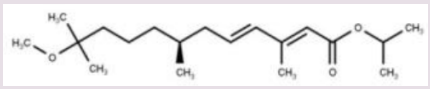


5. 3beta,6alpha,7alphaTrihydroxy-5beta-cholan-24oic Acid

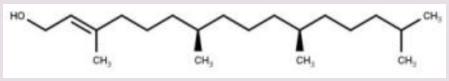
Continued....

Table 9: Continued....

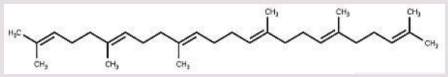
Terpenes/Terpenoid



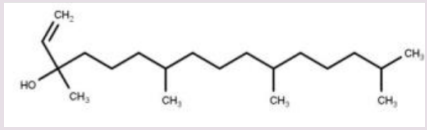
1. Methoprene (S)



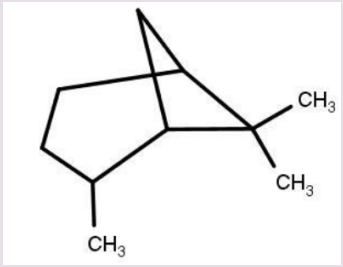
2. Phytol



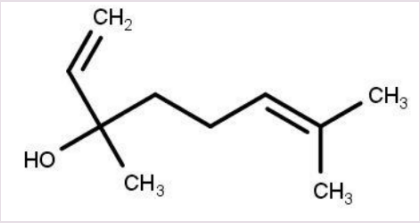
3. Squalene



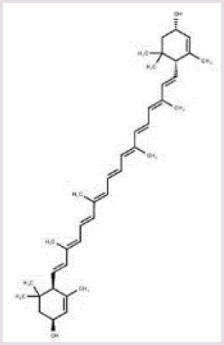
4. Isophytol



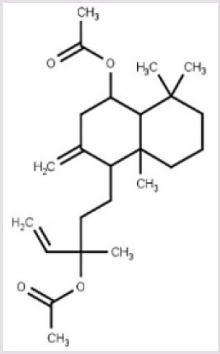
5. Pinane



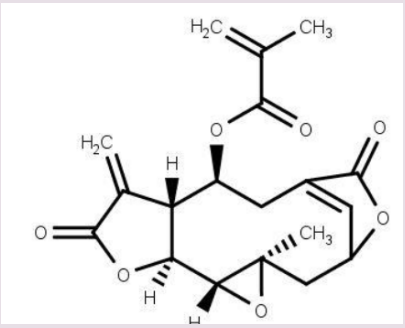
6. Linalool



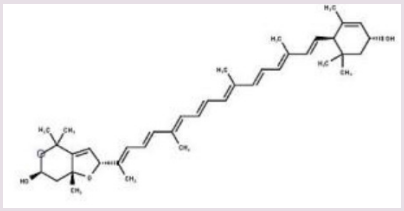
7. Tunaxanthin J/ Chiriquixanthin B



8. Larixol Acetate



9. Elephantopin



10. Flavoxanthin

breast cancer cell lines. Whereas, the positive controls ellipticine and doxorubicin have shown IC_{50} of 0.88 and 0.05 µg/mL respectively. In another study by Reddy *et al.* (2012)[227] using MTT assay explored that ethyl acetate extract (ranging from 0.1- 1000 µg/mL) treatment for 24 hrs on skin cancer cell liens (A431) shown IC_{50} value 220 µg/mL whereas, the treatment extended upto 48 hrs exhibits the IC_{50} 78 µg/mL . Further, the extract also inhibited the 12 R LOX enzyme by dose dependent manner (50-300 µg/mL). Similarly an experiment with MTT, ethanolic extract alone and its formulation as casein-chitosan micro particles at 20-70 µg/mL have been shown the effect on prostate cancer cell lines (PC3) by releasing LDH enzyme. Interestingly, both were shown similar cytotoxicity up to 24 hrs but micropaticles significantly more effective when incubated up to 72 hrs.[228] In addition to this, synthesized silver and gold nanoparticles with whole plant aqueous extract (100 µg/mL) have been showed anti-breast cancer (using MDA-MB-231 cell line) effect by showing 40% cytotoxicity, apoptotic changes with elevation of caspase-3 enzyme (more effect was shown by gold nano particles) and DNA damage.[229] Sivaraj *et al.* (2014)[230] reported that copper oxide nanoparticles from whole plant aqueous extract exhibited potential anti-breast cancer activity (97% cytotoxicity on MCF-7 cancer cell lines at 100 µg/mL).

Wound healing property

Topical application of total plant ethanolic extract (10%) on wounds of male rats noticed that healing of excision wound per day was 18%, whereas breaking strength of incision wound was 279.75 g (breaking strength of control is 63.523 g).[231] In another study, 1 % hot water extract applied on excision wound for 19 days in either sex rats exhibited potential healing property (44%) than standard povidone-iodine ointment (28%). In incision wound, the extract treatment for 10 days showed the tensile strength 82.387 g nearer to the standard povidone-iodine of 86.113g.[232] Ganeshkumar *et al.* (2012)[233] have also beenbeen carried out experiments on similar wound models of male rats. Topical application of 50% ethanolic extract (40 mg/kg) of leaves healed the wounds by increasing percentage of collagen, DNA, protein, hexosamine (basic substance for collagen synthesis), uronic acid, TNF-α, TGF-β1, collagen 1α (I), collagen 3α (I) and decreasing lipid peroxidation. Further histopathological observation of treated tissues illustrated the fair deposition of fibroblast cells, cellular infiltration and collagen deposition,

is an indicative sign of wound healing. Experiment on angiogenesis, which is an important event being occurred in wound healing has been conducted with 1 % hot aqueous extract (0.1 mg/μL) of leaves in chick chorioallantoic membrane model. Extract treatment formed 10 blood capillaries whereas the standard vascular endothelial growth factor was resulted 13 capillaries in the duration of 72 hrs.[232] Hence, further purification of bioactive compounds from these extracts would help the scientists for the preparation of natural drugs in future.

Antifertility activity

Petroleum ether and ethanol extracts of 600 mg/kg given to 7 days pregnant female rats for ten days treatment significantly inhibited the pregnancy progression by decreasing 75% and 62.5% of implantations respectively. Extracts also caused unfavourable conditions for fertility through increasing diameter of uterus, thickness of endometrium, height of the endometrial and epithelium weight. Moreover, extracts increased the uterine weight by effecting 37% and 32 % of ethinyl estradiol levels respectively. Confirmation to this, female rats delivered healthy pups when discontinued the treatment with extracts.[234] Further, bioactive compounds isolation is required in the background of the established fact on petroleum ether and ethanol extracts to ascertain potential anti-fertility porperty.

Acute intravascular haemolysis prevention.

Clinically diagnosed patients characteristically showed low haemoglobin content, changes in peripheral blood, reticulocytosis, increased serum indirect bilirubin, haemoglobinuria and reduced levels of glucose-6-phosphate dehydrogenase enzyme confirmed that it is an acute intravascular haemolysis, when the same patients received *A.indica* leaves broth, they were recovered within 4 days by reestablishing of all hematological alterations. [5] This information gives a clarity that *A.indica* broth has capacity to reduce the acute intravascular haemolysis.

Antivenom property

An important aspect of *A.indica* is, its neutralizing ability on snake venom/poison as practiced by traditional healers of India and Srilanka.[23,27] The nullifying property of aqueous ethanol extract (95%) was studied on *Viper russelli* venom lethality (lethal dose of 61 μg/kg) in mice model; venom haemorrhagic (venom 340 μg/kg), mast cell degranulation (venom 61 μg/kg) and necrotic (venom 171 μg/kg) in rat models. Plant extract (750 mg/kg) treatment to venom affected rat models have recovered by significant inhibition of haemorrhage (from 10.1275 ± 8.53 to 3.1875 ± 6.57), necrosis and mast cell degranulation; decreased plasma lipid peroxidation (from 24.27 ± 2.46 to 10.5200 ± 0.17); and increased kidney GSH level and catalase enzyme activity. Interestingly, ethanolic extract (750 mg/kg) shown 100% survival rate of rats affected than venom antiserum (87.5%) (Shirwaikar *et al.* 2004). In another study with petroleum ether, benzene, chloroform and acetone extracts of leaves on *Viper russelli* venom, the acetone extract only at 500 mg/kg increases the survival rate upto 87 % which is equal to the positive control venom antiserum (87.5 %).[235] Beside these, *in vitro* experiments such as venom induced cardiac arrest on frog heart and neurotoxicity (1-4 μL of venom) in abdominus muscle of frog have significantly protected by ethanol extract with a dose of 1.6 mg/mL. Acetone extract (0.4 mg/mL) also protected the venom (0.1 mg/mL) induced haemolysis about 77.9%.[223,235] These results reveal that *A.indica* has potential antivenom phytochemical constituents.

Antitoxic effect

Along with snake venom neutralization, *A.indica* also nullified the Puffer fish muscle poison in mice. Hot water extract (5 g/L) of stem and leaves given to mice nullified the 1% acetic acid extracted poison of puffer fish (*L. lunaris*) muscle. Plant extract reduced the toxicity by increasing body weights, ALT, AST, and ALP activities and HDL-C while decreasing CRE, UA, TC, TG, LDL-C, T Bil, D Bil, ALB, GLB, TP and GLU in serum; elevating antioxidant enzymes (SOD, CAT and GPx) in kidney, heart and liver; decreasing liver lipid peroxidation. Histopathology evidence of liver, kidney and heart tissues showed that extract protected these from fish muscle toxicants.[236]

Analgesic activity

Methanolic extract of *A. indica* total plant tested in mice (20-25g, 30 days age) to define its analgesic (pain perception) property. Writhing reflexes caused by 0.7% acetic acid was inhibited upto 51.1% and 57.2 % by 200 and 400 mg/kg of extract respectively whereas the standard aminopyrine showed 89.9% inhibition at 50 mg/kg.[98] In another hot plate method, polyphenolic fraction (400 mg/kg) was increased the latency period upto 3 hrs in mice (20-25 g) whereas the standard diclofenac sodium (0.13 mg/kg) maintained upto 6 hrs. Tail-flick method for the same fraction revealed that it decreases the pain threshold of tail upto 6 hrs in rats (180-220 g) while diclofenac sodium showed significant results than fraction. The authors concluded that this property of fraction is due to the presence of polyphenol and flavonoid compounds.[82] The results obtained from these experiments shows that this plant is a good source for analgesic compounds for further isolation.

Anti-inflammation property

The carrageenan (1%) induced paw edema in rats (140-160 g) was inhibited by 125 and 250 mg/kg of methanolic extract of *A.indica* to an extent of 21.51% and 30.64 % respectively but this is lower than (37.55%) that of phenylbutazone of 100 mg/kg.[98] Godipurge *et al.* (2015)[82] reported that 400 mg/kg of polyphenolic rich extract exhibited potential inhibition of paw volume (92.3%) than standard diclofenac sodium (61.5 %) of 0.9 mg/kg by the action on prostaglandin E2 production. The same authors conducted *in vitro* experiment with polyphenolic rich extract (250 μg/mL) which stabilized the membrane about 20 % in hypo saline induced inflammation on human red blood cells, is nearer to the diclofenac sodium (21%). In another *in vitro* experiment, 0.1 mg/mL dose of ethyl acetate and hexane extracts have potentially showed anti-inflammation activity by inhibiting COX-2 and 5-LOX enzymes whereas, hexane extract shown more effect on COX-1.[227] Fatima *et al.* (2017)[237] reported that ethyl acetate and water extracts at 0.3 mg/mL showed inhibitory activity on 12R-LOX in *in vitro*, are equal to the standard drug Zileuton (0.07 mg/mL) activity. Having obtained all results about inflammation, it is clear indication that *A.indica* is a potential source for anti-inflammation drug development.

Kidney stones digestion

In male rats, ethylene glycol (0.75%) induced kidney stones were digested with ethanolic extract of *A. indica* (200 mg/kg). It was observed a decrease in AST, ALT, ALP and ACP enzyme activities in urine and serum whereas the same were increased in kidney. At the same time, extract also brings back membrane bound enzymes (Na+ K+, Ca+ and Mg+ ATPases) in kidney, equal to standard drug thiazide (150 μg/kg). The authors concluded that this kidney stones digestion of *A.indica* extract was due to the presence of antioxidant compounds. [238] The chemical constituents responsible and mechanism of action involved in the digestion of kidney stones is to be unraveled for further clinical trials in this area of research.

Cardio protective property

The cardioprotective property of flavonoid rich methanolic extract of *A. indica* leaves (200 mg/kg) studied in isoproterenol (ISO) (85 mg/kg) induced myocardial ischemia rats. The extract protected the myocardium by decreasing total cholesterol, triglycerol, low-density lipoprotein cholesterol, very low density lipoprotein cholesterol, fatty acids and phospholipids, and by increasing high density lipoprotein cholesterol in plasma, hepatic and cardiac tissues.[239,240] In another study, pre and post treatment of 70% methanolic extract (500 mg/kg) of leaves given to ISO induced female rats protected the cardiac tissue by inhibiting over expression of serum marker enzymes (LDH, AST, ALT and CK-MB); decrease in serum CRP and Troponin T levels and MDA content; elevated anti-oxidant enzymes (SOD and CAT) and prevented caridiac tissue damage. In addition to this, it prevented the cardiac death caused by furosemide (10 mg/kg) and potassium chloride (10 mEq/kg) by reverting CRP, CK-MB and troponin levels; decreasing serum, urine electrolytes (K+ and Na+) and urine output ; protecting architecture of left ventrical tissue; gaining of body weight; and maintaining of glucose levels.[84]

Antidiabetic activity

Aqueous ethanolic (80%), hydro alcoholic (50 %), chloroform soluble fraction of hydro alcoholic, n-butanol soluble fraction of hydro alcoholic and butanol insoluble fraction of hydro alcoholic extracts with a dose of 400 mg/kg and methanol: acetone fraction (70:30) with a dose of 500 mg/kg of *A.indica* have been nullified the alloxan induced diabetes complications in rats with an evidence of recovered body weight and dropped blood glucose levels.Of these extracts, the aqueous ethanolic only maintained the glucose levels (296.5 to 153.83) which was nearer to the standard glibenclamide (10 mg/kg) treated glucose levels (296.5 to 142.7) of rats.[80,221,241] In streptozotocin induced diabetic neonate rats (5 days age), methanolic extract (100 mg/kg) showed antidiabetic potentiality by decreasing blood glucose levels upto 57%, whereas 67% was observed in standard glibenclamide (5 mg/kg) treatment.[242] Rani, (2014)[126] reported potentiality of 100% ethanolic extract (500 mg/kg) on STZ induced diabetic matured rats. The extract reverted the complications by reducing glucose; decreasing DNA, RNA, glucose-6-phosphatase, ALP, ACP, AST, ALT, LDH, lipid profiles (total cholesterol, free chlolesterol, triglycerides, phospholipids, free fatty acids, HDL-cholesterol, LDL- cholesterol, VLDL- cholesterol); and elevating glycolytic enzymes (Hexokinase and Phosphoglucoisomerase), TCA cycle enzymes (succinate dehydrogenase, malate dehydrogenase), GSH, vitamin A, vitamin C and vitamin E. The extract also recovered the liver and kidney architecture to near normal state under diabetic condition. In another STZ induced experiment, the polyphenolic fraction (100 mg/kg) of leaves, methanolic extract of stem (600 mg/kg) and ethanolic extract of total plant (500 mg/kg) alleviate the oxidative stress in liver by elevating cellular antioxidant enzymes (SOD,CAT, GPx, GST, GR and G6PDH) equal to glibenclamide (20 mg/kg) and metformin (10 mg/kg) treatment in rats.[126,243,78]

The methanolic extract (600 mg/kg) of stem was tested for postprandial antihyperglycemic in maltose (2 g/kg), glucose (2 g/kg) and sucrose loaded rats which are also induced by STZ. Extract lowered the glucose levels upto 70.41% in maltose alone rats whereas extract and standard acarbose (5 mg/kg) lowered the glucose levels up to 69.10% and 44.87% respectively in maltose plus STZ rats. It was observerd that, 52.7% of glucose levels were dropped in sucrose loaded rats whereas 80.35% and 40.93% dropped by extract and acarbose respectively in sucrose with STZ rats. Further it was noticed that, the extract not suppressed the postprandial hyperglycemic condition in diabetic rats which are loaded with glucose. The extract (300 mg/kg) also protected the liver damage by decreasing liver markers SGOT, SGPT, ALP, and TB in serum.[243] Nandhakumar *et al.* (2009)[8] have reported *in vitro* anti-amylase (a marker enzyme for diabetes) activity of ethanol, chloroform and hexane extracts. The chloroform and hexane extracts (0.1 mg/mL) inhibited the enzyme upto 75.32% and 84.51% respectively, whereas ethanol extract (0.001-0.1 mg/mL) didn't show any activity. From these reports, it is very clear that the extracts of *A.indica* have potential anti-diabetic property on alloxan and streptozotocin induced animals.

Anthelmintic activity

Pheretima posthuma is an Indian earthworm belongs to Annelida and having anatomically, physiologically resemblance with intestinal round worm parasite of humans. Treatment with 70% hydro alcoholic extract (10, 25 and 50 mg/mL) of roots induced the paralysis and death of annelidan in a dose dependent manner. The extract (50 mg/mL) caused the paralysis at 20 min of time and death within 30 min whereas the standard albendazole (10mg/ml) achieved the same condition at 20 min and 46 min respectively.[244]

Antiarthritic activity

Ethanolic and water extracts (250 mg/kg) of *A.indica* exhibited anti-arthritic activity on heat killed *Mycobacterium tuberculosis* (0.5 mL of 5%) induced chronic arthritic rats (130- 150 g). Ethanolic extract inhibited swelling of paw upto 7.85%, water extract showed 41.96% whereas standard drug ibuprofen exhibited 49.10% by decreasing the levels of alkaline phosphatase.[245]

Hepatoprotective activity

A.indica extracts and synergy with other plants/bioactive compounds shown protective effect on thioacetamide, paracetamol, CCL4, rifampicin-isoniazid and hypoxia induced hepato toxicity in experimental animals. Methanolic extract (300 mg/kg) and methanolic fraction (250 mg/kg) protected the thioacetamide (100 mg/kg) induced hepatic tissue in wistar strain albino rats by decreasing SGOT, SGPT, ALKP, total cholesterol and total bilirubin; increasing albumin and total protein in serum; recovered the architecture of hepatic tissue.[81] In paracetamol (1 g/kg) induced male rats, 70% hydroalcoholic and ethanolic extracts (100 and 200 mg/kg) of leaves recovered the architecture of hepatic tissue by decreasing AST, ALT, ALP and lipid peroxidation; and elevating the levels of cellular antioxidants (SOD and GSH).[246,247] Vijayabhaskar *et al.* (2013)[248] have been stated hepatoprotective property of 70% alcoholic extract (300 mg/kg, post treatment for 10 days) of whole plant in CCL4 induced rats with an evident in drastic reduction of SGPT, SGOT and ALP in serum than silymerin (100 mg/kg), a standard drug.

Synergytic effect of methanolic extracts (70%) of *A.indica (*200 mg/kg*)* and *Centella asiatica* (150 mg/kg) have been protected the hepatic tissue of rats growing under hypoxia condition (10 % O_2 and 90 % N_2) by decreasing lipid peroxidation whereas standard vitamin C (100 mg/kg) didn't show any protection.[249] In another experiment, 70% ethanolic extract (150 mg kg) with piperine compound (20 mg) protected the rifampicin-isoniazid (50 mg/ kg) induced hepatic tissue of rats equal to silymerin (100 mg/kg) with a mark of decreased SGPT, SGOT and ALP in serum.[248]

Antiulcer activity

Anti-ulcer property of 80% ethanolic extract of *A. indica* leaves and roots (100 and 200 mg/kg each) studied on pylorus ligated, acetyl salicylic acid (200 mg/kg), cold stress (4°C for 2 hrs) and 40% ethanol induced peptic ulcers. Root extract (200 mg/kg) shown 66.62 % defence against pylorus ligated ulcers by improving pH, reducing acidity/gastric volume whereas standard ranitidine exhibited 67.24%. Acetyl salicylic acid induced ulcer was reduced (55.61 %) by higher concentration of root extract whereas standard ranitidine showed 70.25%. Cold stress induced ulcers was

relaxed with the root extract (200mg/kg) by 58.14 % whereas 74.06 and 70.25 % were exhibited by diazepam (1mg/ kg) and ranitidine (50 mg/kg) respectively. Ethanol induced gastric lesions reduced 64.55 % by higher concentration of root extract while standard ranitidine reduces 68.19%. In all these studied experiments on ulcers, leaf extract didn't show any protentiality but root has comparatively equal with the standard drugs.[250]

Metal accumulation property

The phytoextraction or hyper accumulation and translocation of metal ions (zinc, iron, copper, lead and cadmium) examined with *A.indica*. Olowu *et al.* (2015)[251] have identified heavy metals accumulation in leaves, stem and root tissues of *A. indica* growing at dump areas of Ibadan Metropolis, South West Nigeria. More accumulated metals found were: iron, zinc, and copper whereas moderately accumulated were: lead and cadmium followed by less accumulated nickel and chromium. It was also observed that the metals were more accumulated in leaves than other parts. In another experiment, accumulated metal ions resulted alterations of this plant have been reported. Different concentrations (0, 100, 200, 300, 400, 500 mg L^{-1}) of Pb ion supplementation to *A.indica* for 12 days revealed that greater accumulation of Pb observed in root (121.6 mg g^{-1} DW) than shoot (17.5 mg g^{-1} DW). Accumulation decreases the length of root and shoot upto 49.9% and 50.9% respectively; the growth tolerance index of roots and shoots decreased upto 44.5% and 52.3% respectively; chlorophylls (chl a, chl b, chl a/b) and carotenoids content decreased in leaves. MDA levels (lipid peroxidation) increased in leaves by 117% and 151.4% at 100 mg L^{-1} and 500 mg L^{-1} concentrations respectively. Antioxidant enzymes (SOD, POX, CAT and APX) alteration also caused in leaves and roots. Protein banding analysis of leaves with higher concentration of Pb revealed that it causes disappearance of protein bands and decrease in protein intensity over the control plants. The RAPD-PCR profile of DNA of leaves exhibited that Pb induced the DNA damage, absence of bands and amplification of new bands.[252] It was observed that, *A.indica* plant has been struggled from metal toxicity however, its accumulation in this plant parts is helpful for the measurement of heavy metal toxicity, aswell as phyto remediation in water and soil polluted environments.

A.indica roots as cat attractant

For the protection of native endangered species of Christmas Island from cats, yellow crazy ants and black rats, a research group conducted an experiment to attract the cats using *A.indica* roots. Many cats attracted towards roots and chewed them (Figure 2). GC-MS analysis of dichloromethane and ethanol extracts of roots revealed two Iridoids such as (4R,4aR,7S,7aR)-isodihydronepetalactone and (4R,4aS,7S,7aR)-isoiridomyrmecin. Interestingly, these two compounds are known to have effects on behavioural activities of cats.[253]

Nanoparticles synthesis

Water and ethanol extracts of *A. indica* have been used by many research groups to synthesize metal based particles including silver, gold, palladium, copper oxide, yttrium oxide, zinc oxide and zirconium dioxide nanoparticles; and chitosan-casein micro particles. [228-230, 254-261] The biological properties of these particles are discussed in antimicrobial and cytotoxicity sections of this review.

Antibacterial activity

Table 10 presents the antibacterial properties of solvent extracts of *A. indica*. Mainly three methods have been carried out to define the antibacterial property which includes dilution, well diffusion and disc diffusion. Various extracts have been exerted notable antibacterial activity on both gram positive (*Staphylococcus auereus, Bacillus subtilis, Bacillus cereus, Bacillus megaterium, Staphylococcus epidermidis and Streptococcus faecalis*) and gram negative (*Escherichia coli, Proteus vulgaris, Salmonella typhi, Pseudomonas aeruginosa, Priteus mirabilis, Klebsiella pneumonia, Enterobacter aerogenes, Enterobacter cloacae* and *Vibrio cholerae*.) strains of test organisms, human pathogens and multidrug resistance bacteria. [74,77,169,225,262,-266] The dilution method was done only for the leaves and total plant, the resulted MIC values were ranging from 0.004 mg (acetone insoluble fraction on *Staphylococcus auereus*) to > 5 mg and 0.02 mg (ethanol extract on *E.coli*) to 1 mg respectively.[77, 267] Here, we review few potential extracts with MIC values: Gopalakrishnan *et al.* (2000)[77] have reported that acetone insoluble and soluble fractions showed potential activity against *Staphylococcus auereus* (MIC: 0.004 mg) and *Salmonella typhi* (MIC: 0.05 mg) respectively. In another study, Govindarajan *et al.* (2008)[262] have been confirmed the MIC for chloroform, ethyl acetate, hexane and methanol extracts of leaves. The MIC of chloroform and hexane extracts on *Streptococcus faecalis* was 0.312 mg and 0.156 mg respectively whereas, the MIC of ethyl acetate on *Staphylococcus auereus and Streptococcus faecalis* was 0.312 mg. In all cases of dilution method, the activity was not compared with any standard drugs.

The disc diffusion method was performed by Poornima and Prabakaran, (2012),[74] Govindarajan *et al.* (2008),[262] Solomon *et al.* (2005)[169] and Shanmugapriya *et al.* (2011)[225] for antibacterial activity of leaves extracts. Among all, Govindarajan *et al.* (2008)[262] have been only reported the bacterial inhibition maximum at concentration of 5 mg by Ethyl acetate, chloroform, hexane and methanol extracts on *Staphylococcus aureus, Staphylococcus epidermidis, Bacillus cereus, Streptococcus faecalis* and *Pseudomonas aeruginosa.* Comparison with standard streptomycin disc (0.01 mg/mL), the 5 mg/mL of above extracts successfully showed similar activity. *A.indica* leaves water extract at 4% v/v inhibited the growth of *Mycobacterium tuberculosis* H37Rv, multi drug resistance strains such as DKU-156 and JAL-1236 about 68%, 95%, and 68% respectively. The same extract has not exhibited inhibition on fast growing *M. fortuitum* (TMC-1529) strain.[268]

Identification of antibacterial effective dose through well diffusion method is very difficult for extracts of leaves, stem, root and total plant on bacterial species. Almost all extracts studied at 100 mg/mL concentration except ethyl acetate extract of total plant (0.05 mg). In concern of zone of inhibition, the acetone, chloroform, ethanol, ethyl acetate, methanol and petroleum ether extracts shown maximum at 100 mg/mL against *Escherichia coli, Salmonella typhi, Pseudomonas aeruginosa, Klebsiella pneumonia* and *Vibrio cholera*. [263-266] Along with extracts, synthesized silver and copper oxide nanoparticles have been also shown antibacterial potentiality on *E. coli*, *V. cholerae*, *P.aeruginosa*, *B.subtilis, P. fluorescens, P.vulgaris* and *S.aureus* at the microgram level.[230,254,269]

Antifungal activity

As shown in Table 11, the methanolic extract of *A.indica* leaves, stem and roots showed maximum activity against *Candida albicans* with the percent activity of 119%, 95% and 109% respectively whereas chloroform extract of leaves and roots have been shown 104% and 61% activity respectively and stem methanolic extract has 85% activity against *Aspergillus niger.* The authors have declared that the antifungal activity of extracts was due to having a bioactive compound clotrimazole.[169] In another experiment, minimum fugicidal concentrations (MFC) of hexane, methanol and ethanol extracts of *A.indica* whole plant against 12 fungals species (Table 11) revealed that hexane extract only shown maximum activity at 0.5 mg/mL against *Trichophyton rubrum* PSSF57/01, *Trichophyton tonsurans* PSSF46/01 and *Epidermophyton floccosum* PSSF73/01 whereas other extracts MFC were not better than hexane extract. In this study, the authors compared the results with standard drugs indirubicin, fluconazole

Table 10: Antibacterial effective doses and MIC values of various extracts prepared from *A.indica* and its parts.

S.No	Extracts	Method	Micro-organism tested and effective dose (MIC values/Effective Concentration-Zone of inhibition)															
			Leaves															
			EC	PV	SA	BS	BC	ST	BM	SE	PA	PM	KP	EA	ECl	SF	VC	References
1	Acetone insoluble fraction of methanol	Dilution	MIC: 0.125 mg	-	MIC:0.004 mg	MIC: 0.15 mg		MIC: 0.05 mg	-	-	MIC: 0.15 mg	-	MIC: 0.125 mg	-	-	-	-	[77]
2	Acetone soluble fraction of methanol	Dilution	MIC:0.25 mg	-	MIC: 0.15 mg	MIC: 0.15 mg		MIC:0.05 mg	-	-	MIC: 0.15 mg	-	MIC: 0.25 mg	-	-	-	-	[77]
3	Chloroform	Dilution	MIC: 0.4 mg	-	MIC: 0.4 mg	MIC: 0.4 mg		MIC: 0.4 mg	-		MIC: 0.4 mg	-	MIC: 0.4 mg	-	-		-	[77]
			MIC: > 5mg	-	MIC: 0.625 mg	-	MIC: 0.625 mg	-	-	MIC: : 1.25 mg	MIC: 2.5 mg		MIC: > 5 mg	-	-	MIC: 0.312 mg	-	[262]
4	Ethyl acetate	Dilution	MIC: > 5 mg	MIC: > 5 mg	MIC: 0.312 mg	-	MIC: 0.625 mg	-	-	MIC: 1.25 mg	MIC: 5 mg	-	MIC: > 5 mg	-	-	MIC: 0.312 mg	-	[262]
5	Hexane	Dilution	MIC: >5 mg	MIC: >5 mg	MIC: 0.312 mg	-	MIC: 0.312 mg	-	-	MIC: 1.250 mg	MIC: 5 mg	-	MIC: >5 mg	-	-	MIC: 0.156 mg	-	[262]
6	Methanol	Dilution	MIC: >5 mg	MIC: >5 mg	MIC: 0.156 mg	-	MIC: 0.156 mg	-	-	MIC: 0.625 mg	MIC: 2.5 mg	-	MIC: > 5 mg	-		MIC: 0.156 mg	-	[262]
7	Diethyl ether	Disc diffusion	100 mg- NA	100 mg-	100 mg- 27 mm	100 mg- 14 mm	-	-	-	100 mg- NA	100 mg- NA	-	100 mg- NA	-	-	-	-	[74]
8	Ethanol	Disc diffusion	100 mg- NA	100 mg- NA	100 mg- NA	100 mg- NA	-	-	-	100 mg- NA	100 mg- NA	-	100 mg- NA	-	-	-	-	[74]
9	Ethyl acetate	Disc diffusion	100 mg- 10 mm; 5 mg- NA	100 mg- 12mm; 5 mg- NA	100 mg- NA; 5 mg-14.6 mm	100 mg- 20 mm	5 mg-15 mm	-	-	100 mg- 15 mm ; 5 mg- 13.8mm	100 mg- 15 mm; 5 mg-10 mm	-	100 mg- 12 mm; 5 mg-NA	-	-	5 mg-15 mm	-	[74, 262]
10	Chloroform	Disc-diffusion	5 mg- NA	5 mg- NA	5 mg- 14.6 mm	-	5 mg- 15.0 mm	-	-	5 mg- 13.8mm	5 mg- 10 mm	-	5 mg- NA	-	-	5 mg- 15.0 mm	-	[262]
11	Clotrimazole	Disc-diffusion	0.001 mg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[169]
12	Hexane	Disc-diffusion	5 mg: NA	5 mg: NA	5 mg- 12.8 mm		5 mg- 13.8mm		-	5 mg- 11.0mm	5 mg- 9.7 mm	-	5 mg: NA	-		5 mg-12 mm	-	[262]

Continued....

Table 10: Continued....

13	Methanol	Disc-diffusion	5 mg-NA; 40 mg-6 mm; 100 mg- NA	5 mg-NA; 100 mg- NA	5 mg-15.8 mm; 30 mg-8 mm; 100 mg- NA	40 mg-NA; 100 mg- NA	15 mg-14 mm; 40 mg-9 mm	40 mg-6 mm	-	5 mg-14 mm; 100 mg- NA	5 mg-12.7 mm; 100 mg-NA	-	5 mg-NA; 100 mg-NA	-	-	5 mg-16.5	-	[74, 225, 262]
14	Acetone	Well diffusion	100 mg-35 mm	-	100 mg-23 mm	-	-	100 mg-30 mm	-	-	100 mg-35 mm	-	100 mg-28 mm	-	-		100 mg-29	[263]
15	Chloroform	Well diffusion	100 mg-30 mm	-	100 mg-20 mm	-	-	100 mg-28 mm	-	-	100 mg-33mm	-	100 mg-25 mm	-	-		100 mg-27 mm	[263]
16	Ethanol	Well diffusion	100 mg-30 mm	-	100 mg-12mm	100 mg-30 mm	100 mg-15 mm	100 mg-20 mm, 25 mm	-	-	100 mg – 30 mm	-	100 mg-20 mm	-	-	100 mg-25 mm	100 mg-20 mm	[264, 265]
17	Ethyl acetate	Well diffusion	75 mg-25 mm; 100 mg-23 mm	-	100 mg-2.7 mm, 15 mm	100 mg-1.9 mm, 13 mm ; 75 mg-13mm	75 mg-13 mm; 100 mg-11 mm	75 mg-20 mm; 100 mg-18 mm	-	-	100 mg-NA	-	100 mg-3.5 mm75 mg-20 mm	-	-	100 mg-15 mm	75 mg-13 mm; 100 mg-13 mm	[264-266]
18	Hexane	well diffusion	100 mg-20 mm	-	100 mg-9mm, 0.8 mm	100mg-10. mm	-	100 mg-18 mm	-	-	100 mg-20 mm	-	100 mg-10 mm, 0.9 mm	-	-	-	100 mg-15 mm	[263, 266]
19	Methanol	Well diffusion	100 mg-35mm	-	100 mg-1.1 mm, 26mm	100 mg-1.3 mm	-	100 mg-32 mm	-	-	100 mg-35 mm	-	100 mg-1 mm, 33mm	-	-	-	100 mg-30 mm	[263, 266]
20	Petroleum ether	Well diffusion	100 mg-25 mm	-	100 mg-14 mm	-	-	100 mg-22 mm	-	-	100 mg-25 mm	-	100 mg-20 mm	-	-	-	100 mg-22 mg	[263]
								Roots										
1	Methanol	Agar diffusion method	30 mg	-	30 mg	NA	30 mg	30 mg	-	-	-	-	-	-	-	-	-	[225]
2	Clotrimazole from Hexane, acetone, chloroform and methanol	Disc-diffusion	0.5 µg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[169]

Continued....

Table 10: Continued....

3	Ethyl acetate	Well diffusion	-	-	100 mg-2.1 mm	100 mg-1.7 mm	-	-	-	-	-	-	100 mg-3.3 mm	100 mg-3.3 mm	-	-	-	[266]
4	Hexane	Well diffusion	-	-	100 mg-1.1 mm	100 mg-1.2 mm	-	-	-	-	-	-	100 mg-0.8 mm	100 mg-0.8 mm	-	-	-	[266]
5	Methanol	Well diffusion	-	-	100 mg-1.2 mm	100 mg-1.5 mm	-	-	-	-	-	-	100 mg-1.2 mm	100 mg-1.2 mm	-	-	-	[266]
								Stem										
1	Clotrimazole from Hexane, acetone, chloroform and methanol	Disc-diffusion	0.01 mg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[169]
2	Hexane	Well diffusion	-	-	100 mg-1 mm	100 mg-1.2 mm	-	-	-	-	-	-	100 mg-1.2 mm	-	-	-	-	[266]
3	Ethyl acetate	Well diffusion	-	-	100 mg-0.8 mm	100 mg-1.1 mm	-	-	-	-	-	-	100 mg-1.1 mm	-	-	-	-	[266]
4	Methanol	Well diffusion	-	-	100 mg-0.8 mm	100 mg-1.2 mm	-	-	-	-	-	-	100 mg-1.2 mm	-	-	-	-	[266]
Total plant																		
1	Acetone	Dilution	MIC: 0.04 mg	-	MIC: 0.04 mg	-	-	-	-	-	-	MIC: 0.02 mg	MIC: 0.08 mg	1 mg	1 mg	-	-	[267]
2	Ethanol	Dilution	MIC:20 µg	-	MIC: 60 µg	-	-	-	-	-	-	MIC: 60 µg	MIC: 90 µg	-	-	-	-	[267]
3	Hydro alcoholic	Cup plate method	1 mg-10mm	-	-	-	-	0.5 mg -6 mm	1 mg-10 mm	1 mg-10mm	0.5mg-6mm	1 mg-9mm	0.5 mg-6 mm	0.5 mg-6mm	1.5 mg-11 mm	-	-	[76]
4	Hexane	Cup plate method	0.5 mg-7 mm	-	-	-	-	0.5 mg-9 mm	0.5mg-7 mm	0.5 mg-8mm	0.5 mg-7mm	0.5 mg-7 mm	0.5 mg-8 mm	0.5 mg-7mm	1mg-7 mm	-	-	[76]
5	Ethyl acetate	Cup plate method	0.5 mg-10 mm	-	-	-	-	0.5 mg -10 mm	0.5mg-8 mm	0.5 mg-10mm	0.5 mg-9 mm	0.5 mg-7 mm	0.5 mg-7 mm	0.5 mg-8mm	0.5-7mm mg	-	-	[76]
6	Methanol	Cup plate method	0.5 mg-7 mm	-	-	-	-	1 mg-8 mm	1 mg-9mm	1 mg-8mm	1 mg-9 mm	1 mg-7mm	1 mg-9mm	1 mg-9 mm	1 mg-7mm	-	-	[76]
7	Chloroform	Disc diffusion	300 µg-17 mm	-	300 µg-13 mm	300 µg-18 mm	-	-	-	-	300 µg-9 mm	-	-	-	-	-	-	[280]
8	Methanol	Well diffusion	50 µg-18mm	-	50 µg-8mm	-	-	50 µg-16 mm	-	-	50 µg-15 mm	-	-	-	-	-	-	[75]

-': Not tested; MIC: Minimum inhibitory concentration; NA: No activity; EC: *Escherichia coli*; PV: *Proteus vulgaris*; SA: *Staphylococcus auereus*; BS: *Bacillus subtilis*; BC: *Bacillus cereus*; ST: *Salmonella typhi*; BM: *Bacillus megaterium*; SE: *Staphylococcus epidermidis*; PA: *Pseudomonas aeruginosa*; PM: *Priteus mirabilis*; KP: *Klebsiella pneumonia*; EA: *Enterobacter aerogenes*; ECl: *Enterobacter cloacae*; SF: *Streptococcus faecalis*; VC: *Vibrio cholerae.*

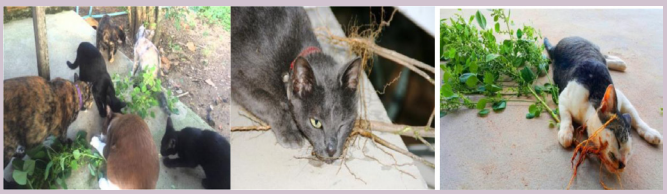


Figure 2: *A.indica* roots as cat attractant: chewing of roots by cats. [253]

and ketoconazole.[270] Experiments were conducted on six clinical isolates cum drug resistance *Candida albicans* strains with methanol, acetone, petroleum ether and water extracts of *A. indica* leaves. Among extracts, the methanol extract at 0.05 mg/mL showed good activity. The best activity concentrations are shown in Table 11.[271] Sakthi *et al.* (2011)[272] were also isolated 6 fungal species and their inhibition by ethanol and ethyl acetate extracts (100 mg/mL, 200 mg/mL and 300 mg/mL) of leaves revealed that the ethyl acetate extract at higher concentration (300 mg/mL) showed good antifungal property than ethanol. Somchit *et al.* (2010)[273] isolated four fungal strains which have sensitive to the chloroform extract at 30 mg/mL than ethanol and water extracts. The potential chloroform extract competed with fungicide ketoconazole but not with fluconazole and fraconazole. On other hand, *A.indica* leaves synthesized silver and copper oxide nanoparticles exhibited potential property on *C. albicans, A. alternate, S. sclerotiorum, M. phaseolina, R. solani, B. cinerea, C. lunata* and *A. niger.*[255, 269]

Endophytic fungi in plant parts of *A.indica*

The endophytic fungal species present in *A. indica* plant parts such as leaves, petiole, stem and roots have been isolated and identified by Kurandawad and Lakshman, (2014)[274] using potato dextrose agar and malt extract agar. The leaves allowed the colonization of *Aspergillus candidus* Link ex. Fries, *Aspergillus flavipes* Bainer and Sartory, *Bipolaris nodulosa* (Bert and Curt. ex. Sacc.) Shoemaker, *Fusarium oxysporum* Schlechtendahl. Screening of stem revealed fungal species include *Aspergillus candidus* Link ex. Fries, Aspergillus *niger* Tiegh, *Cunninghamella blacksleeana* Lender, *Fusarium oxysporum* Schlechtendahl, *Rhizopus nigricans* Ehrenberg and one unidentified species. The petiole has *Aureobasidium pullulans* (de Bary) Arnaud. Les and *Fusarium oxysporum* Schlechtendahl, *Penicillum purpurogenum* stoll species. Nanda and Nayak, (2015)[275] conducted experiment on leaves and reported the presence of *Alternaria alternate, Alternaria geophila, Alternaria tenuis, Botytis cinerea, Brown sterile mycelia, Cladosporium* sp, *Cladosporium herbarum, Colletotrichum falcatum, Curvularia lunata, Curvularia geniculata, Dreshlerea* sp, *Fusarium oxysporum,* Green sterile mycelia, *Geotrichum* sp, *Helminthosporium* sp, *Mortierella, Pencillium fumiculosum, Wallemia sebi,* white sterile mycelia, *Ulocladium langinosum* species in young, mature, yellow, infected and dry leaves of *A. indica*. It was observed that fungal species colonization in *A.indica* would be responsible for production of huge number of secondary metabolites, bioactive compounds and antimicrobial agents.

Larvicidal potential

Larvicidal potentiality of *A.indica* extracts has been studied on *Anopheles stephensi* Liston, *Aedes aegypti* and *Culex. Quinquefasciatus* and *Anopheles subpictus.* In a study, methanol extract showed LC_{90} concentration 36.32 ppm on *Anopheles stephensi* Liston larvae than benzene, chloroform, ethyl acetate extracts of leaves.[262] In another experiment on the same larvae, petroleum ether extract (LC_{90} of 447.19) was more active than hexane, ethanol, acetone and chloroform extracts but same extracts on *Aedes aegypti* and *Culex. Quinquefasciatus* revealed that hexane extract (LC_{90} of 230.40 ppm) and acetone extract (LC_{90} that of 411.48 ppm) have good activity on *Aedes aegypti* and Culex. *Quinquefasciatus* respectively.[49] In another observation, the hexane extract (1000 ppm) on early fourth instar larvae of *C. quinquefasciatus* showed highest mortality rate (about 66 %)[276] whereas Teklani and Perera, (2017)[95] have found highest mortality rate of acetone extract (100 % at 97 mg/mL) and water extract (100 % at 100 mg/mL). Santhoshkumar *et al.* (2012)[277] have reported that acetone extract (100 ppm) shown potential larvicidal activity on *Anopheles subpictus*.

Ovicidal activity

Ovicidal property of benzene, chloroform, ethyl acetate and methanol extracts of *A. indica* at different concentrations (25, 50, 75, 100, 125, 150, 175 and 200 ppm) on different ages (3, 6, 9, 12, 15 and 18 hrs) of *A. stephensi* eggs revealed that extracts at higher concentration affected the hatchability rate in younger eggs than older by 17.3%, 24.3%, 29.0% and 13.0 % respectively.[262]

Oviposition activity

Various concentrations (0.01 to 0.1 %) of ethanol extract of *A. indica* leaves prevented the deposition of eggs by *A. Aegypti, A. Stephensi* and *C. quinquefasciatus* female mosquitoes. High concentration (0.1 %) of extract prevented the percent laying of eggs about 99.4%, 98.0% and 97.5 % by *A. aegypti, A. stephensi* and *C. quinquefasciatus* respectively. [49] Govindarajan *et al.* (2008)[262] have reported the contrast results on attraction of *A. stephensi* for deposition of eggs instead of prevention of laying eggs. Hundread ppm of benzene, chloroform, ethyl acetate and methanol extracts of leaves was attracted the *A. stephensi* for deposition of eggs about 90.09%, 94.20%, 85.43% and 95.75% respectively.

Mosquito repellent activity

Hexane, ethyl acetate, acetone, methanol, water extracts and essential oils of *A. indica* leaves at 5% concentration repel the *Aedes aegypti*. Among, hexane extract from maceration method and ethyl acetate from sonication have potentially been played 50 % static repellent role for initial 2 hrs, next 3 hrs they maintained 20-30% spatial repellency. Other extracts have shown static repellency but they are failed in spatial repellency. In another experiment, the hexane extract (0.02 ppm) protected the people from *Culex quinquefasciatus, Aedes aegypti and Anopheles stephensi* bite upto 122, 119 and 116 min respectively.[95] Hence, hexane extract is a potential mosquito repellent of *A. indica* leaves

Anti-plasmodial property

Ethanolic extract of leaves, stem and root have shown anti-plasmodial property on *P. falciparum* (200 µL) cultured in red blood cells for 48 hrs with IC_{50} concentrations of 0.056, 0.043 and 0.069 mg/mL but this activity is lower than that of positive controls chloroquine (IC_{50} of 0.018 mg/mL) and artemether (IC_{50}: 0.005 µg/mL).[278]

Anti-tuberculosis activity

Anti-tuberculosis property of *A.indica* leaves was studied with water extract at 4% v/v revealed that the extract inhibited the growth of *Mycobacterium tuberculosis* H37Rv, multi drug resistance isolates such as DKU-156 and JAL-1236 about 68%, 95%, and 68% respectively. The same extract didn't exhibit inhibition on fastly growing *M. fortuitum* (TMC-1529) strain.[268]

Insecticidal property

Cotton seeds and leaves (50 g of each) soaked overnight in various concentrations (0.385-6%) of water extract of *A.indica* revealed the insecticidal property. *Dysdercus cingulatus* (Red cotton bug) fed with

Table 11: Antifungal effective doses of solvent extracts prepared from *A.indica* and its parts.

S.No	Plant part and extracts	Method	Organism tested and effective dose (ng/mL, µg/mL and mg/mL)																			References
			AN	CA	CG	AFu	AF	PC	CT	MC	TrM	TrP	TmP	TsP	TtP	EfP	ClP	SbP	CaM	CaP	CsP	
1	L-Acetone	Disc diffusion	-	0.05 mg-13 mm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[271]
2	L-Chloroform	Disc diffusion	-	30 mg-12.7	-	-	30 mg-8.7 mm	-	30 mg-10.3 mm	30 mg-13 mm	-	-	-	-	-	-	-	-	-	-		[273]
3	L-Ethanol	Well Diffusion	300 mg-NA	300 mg-18 mm	300 mg-11mm	300 mg-16 mm	300 mg-28 mm	300 mg-14 mm	-	-	-	-	-	-	-	-	-	-	-	-		[272]
4	L-Ethanol	Disc diffusion	-	30 mg-8.7 mm	-	-	30 mg-NA	-	30 mg-NA	30 mg-9.3 mm	-	-	-	-	-	-	-	-	-	-		[273]
5	L-Ethyl acetate	Well Diffusion	300 mg-NA	300 mg-13 mm	300 mg-NA	300 mg-15 mm	300 mg-18 mm	300 mg-10 mm	-	-	-	-	-	-	-	-	-	-	-	-		[272]
6	L-Methanol	Disc diffusion	-	0.05 µg-20 mm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[271
7	L-Petrolium ether	Disc diffusion	-	0.05 µg-17 mm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[271
8	L-water	Disc diffusion	-	30 mg-NA	-	-	30 mg-NA	NT	30 mg-NA	30 mg-NA	-	-	-	-	-	-	-	-	-	-		[273]
9	L-Water	Disc diffusion	-	0.05 µg-12 mm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[271]
10	TP-Chloroform	Dilution		MIC: 0.4 mg	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
11	TP-Clotrimazole	Disc diffusion	500 ng-22 mm	500 ng-20 mm	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		[169]
12	TP-Ethanol	Dilution	NA	-	-	-	-	-	-	-	MFC: NA	MFC: 8mg	MFC: 4 mg	MFC: NA	MFC: 8mg	MFC: NA	MFC: 4mg	MFC: NA	MFC: 2mg	MFC: 2 mg	MFC: NA	[270]
13	TP-Hexane	Dilution	NA	-	-	-	-	-	-	-	MFC: 4 mg	MFC: 0.5 mg	MFC: 2mg	MFC: NA	MFC 0.5 mg	MFC: 0.5 mg	MFC: NA	MFC: NA	MFC: 4mg	MFC: 4mg	MFC: NA	[270]
14	TP-Methanol	Dilution	NA	-	-	-	-	-	-	-	MFC: NA	MFC: 4 mg	MFC: NA	MFC: NA	MFC: 4 mg	MFC: 4 mg	MFC: NA	MFC: 4mg	MFC: 2mg	MFC: 2mg	MFC: 4mg	[270]

Mg: milli gram; ng: nanogram; '-': Not tested; MIC: Minimum inhibitory concentration; NA: No activity; AN: *Aspergillus niger*; CA: *Candida albicans*; CG: *Candida glabrata*; AFu: *Aspergillus fumigates*; AF: *Aspergillus flavus*; PC: *Penicillium chrysogenum*; CT: *Candida tropicalis*, MC: *Microsporum canis*; TrM: *Trichophyton rubrum* MTCC296; TrP: *Trichophyton rubrum* PSSF57/01; TmP:*Trichophyton mentagrophytes* PSSF66/01; TsP: *Trichophyton simii* PSSF110/02; TtP:*Trichophyton tonsurans* PSSF46/01; EfP: *Epidermophyton floccosum* PSSF73/01;ClP: *Curvularia lunata* PSSF46/01; SbP: *Scopulariopsis brevicaulis* PSSF101/01; CaM: *Candida albicans* MTCC227; CaP: *Candida albicans* PSSF71;CsP: *Cryptococcus* sp. PSSF68/04.

Table 12: Biological properties of *A.indica*.

S. No	Activity tested	Model used	Effective dose (Plant extract)	Effective dose (Standard drug)	Mechanism of action	Reference
			Total plant			
1	Analgesic	Male Mice	ED:400 mg/kg (Polyphenolic extract)	0.13 mg/ 25 kg (Diclofenac sodium)	Increased latency period	[82]
		Either sex rats	ED:400 mg/kg (Polyphenolic extract)	0.9 mg/200 kg (Diclofenac sodium)	Decreased pain threshold	[82]
		Either sex mice	ED:400 mg/kg (Methanolic extract)	50 mg/kg (aminopyrine)	Inhibited writhing reflexes	[98]
2	Antiinflammation	Either sex Rats	ED:250 mg/kg (Methanolic extract)	100 mg/kg (phenylbutazone)	Decreased paw volume	[98]
		Red blood cells of human	ED:400 mg/kg (Polyphenolic extract)	3.6 mg/kg (Diclofenac sodium)	Stabilized RBC membrane	[82]
3	Anti-Fertility	Female rats	ED:600 mg/kg (Ethanolic extract) and ED: 600 mg/kg (Petroleum ether extract)	Ethinyl estradiol (1 µg)	Increased ethinyl estradiol levels, diameter of uterus, thickness of endometrium, height of the endometrial and epithelium weight	[234]
4	Hepatoprotective	Rats	ED: 300 mg/kg (methanol), ED: 250 mg/kg (methanol fraction)	100 mg/kg (Silymarin)	Decreased liver function markers, total bilirubin, and total cholesterol. Increasing total protein and albumin. Tissue recovery from damage.	[81]
		Rats	ED: 300 mg/kg (70% Ethanol)	100 mg/kg (Silymarin)	Reduced SGOT, SGPT and ALP	[248]
		Rats	ED: 150 mg/kg (70% Ethanol)+ 20 mg/kg piperine	100 mg/kg (Silymarin)	Reduced SGOT, SGPT and ALP	[248]
		Rats	ED: 200 mg/kg (70 % methanol) + 150 mg/kg (70 % methanol-*Centella asiatica*)	100 mg/kg (vitamin C)	Decreased lipid peroxidation	[249]
5	Anti-diabetic	Male rats	ED: 400 mg/kg (80% Aqueous ethanolic extract)	10 mg/kg (glibenclamide)	Decreased blood glucose levels and increased body weights.	[221]
		Neonate rats	ED: 100mg/kg (Petroleum ether, chloroform, acetone and methanol extracts)	5 mg/kg (glibenclamide)	Decreased blood glucose levels	[242]
		Male rats	ED: 500 mg (methanol: acetone fraction (70:30)		Decreased blood glucose levels	[241]
		in vitro	ED: 0.1 mg/mL (Hexane and chloroform extracts)		Inhibited α- amylase activity	[8]
6	Anti-arthritic	Rats	ED: 250 mg/kg (Ethanolic extract) ED: 250 mg (water extract)	100 mg/kg (Ibuprofen)	Decreased paw volume. Alkaline phosphatases activity, SGOT and SGPT	[245]
7	Kidney stones digestion	Male rats	ED: 200 mg/kg (Ethanolic extract)	150 µg/kg (Thiazide)	Accelerated Ca^{2+}, Mg^{2+} Na^{+} and K^{+} ATPases. Decreasing ACP, ALP, AST and ALT.	[238]
8	Wound healing	Either sex rats	ED: 10% w/v (Ethanolic extract)	-	Heal of wound	[231]
		Either sex rats	ED: 1% (Hot water extract)	Povidone-iodine ointment	Heal of wound	[232]
		Chick chorioallantoic membrane	ED: 100 µg/µL (Water extract)	vascular endothelial growth factor	Formed of new blood capillaries	[232]

Continued....

Table 11: Continued....

9	Antioxidant	DPPH	IC_{50}: 616.32 µg/mL (hydro alcoholic), IC_{50}: 191.25 µg/mL (Ethyl acetate fraction), IC_{50}: 554.2 µg/mL (methanol fraction) and IC_{50}: 249.14µg/mL (hexane fraction)	IC_{50}: 22.0 µg/mL (Ascorbic acid)	Scavenged the DPPH radical by donating either hydrogen or electron followed by proton	[76]
10	Insecticdal	*Dysdercus Cingulatus*	ED: 6% and 2% Water extract	-	Influenced the mortality, alterated Na^+, K^+, Ca^+, changing glucose, protein levels of ovary and testes. Increased Aspertate levels in intestine and fat body	[279]
	Neutralization (toxicants from Lagocephalus lunaris fish)	Male mice	ED: 5g/L	-	Increased activities of ALT, AST, ALP, SOD, CAT, GPx and HDL-C levels. Decreased diarrhea, creatinine, uric acid, total cholesterol, triglyceride, LDL cholesterol, total bilirubin, direct bilirubin, albumin, globulin, total protein and Glucose. Liver, kidney and heart tissue recovered from damage	[236]
				Leaves		
1	Adulticidal	*Haemaphysalis bispinosa* and *Hippobosca maculate*	2000 ppm (Methanolic extract)	-	-	[277]
2	Anti ulcer	Either sex rats	200 mg/kg (80% ethanol extract)	50 mg/kg (Ranitidine) and 1 mg/kg (Diazepam)	Protected from acetyl salicylic acid, cold stress, ethanol induced and pylorus ligated ulcers by improving pH, reducing gastric volume, acidity and mean ulcer score	[250]
3	Antidiabetic	Either sex rats	ED:400 mg/kg (hydro alcoholic extract), ED:400 mg/kg (Chloroform soluble fraction), ED: 400 mg/kg (Butanol soluble fraction), ED:400 mg/kg (Butanol insoluble fraction)	50 mg/kg (Metformin)	Decreased blood glucose levels	[80]
		Rats	ED:500 mg/kg (Ethanolic extract)	5mg/kg Glibenclamide)	Prevented Nucleic acids decrement. Decreased blood glucose levels, gluconeogenic enzymes, ALP, ACP, AST, ALT, LDH and lipid profile. Elevation of cellular antioxidant, glycolytic and TCA cycle enzymes. Recovery of liver and kidney tissues	[126]
		Male Rats	ED:100 mg/kg (Polyphenolic fraction)	20mg/kg (Glibenclamide)	Elevated cellular antioxidant enzymes	[78]
4	Hepato protective	Male rats	100 mg/kg (70% alcohol)	-	Decreased AST, ALT, ALP, Lipid peroxidation and elevating antioxidants. Protecting tissue damage	[246]
		Male rats	200 mg/kg (Ethanolic extract)	-	Decreased AST and ALT	[247]

Continued....

Table 11: Continued....

5	Antioxidant	DPPH	IC_{50}:28.330 µg/mL, 330 µg/mL, 230 µg/mL, 7079 µg/mL; ED: 600 µg/mL (Methanol extract)	IC_{50}:2.69 µg/ mL, 4.106 (Ascorbic acid) IC_{50}: 3.91 µg/mL (Rutin); IC_{50}: 80 µg /mL (Trolax)		[78, 99, 224, 225]
			IC_{50}: 6019 µg/mL (Hexane extract)	IC_{50}: 80 µg /mL (Trolax)		[99]
			IC_{50}: 5.70 mg/mL (Chloroform extract)	IC_{50}: 80 µg /mL (Trolax)	Scavenged the DPPH radical by donating either hydrogen or electron followed by proton	[99]
			IC_{50}: 300.58 µg/mL (Poly phenolic fraction)	-		[78]
			IC_{50}: 476.19 µg/mL (Ethanolic extract); IC_{50}: 616.32 µg/mL (70%Ethanolic extract)	IC_{50}: 13.1 µg/mL(Tannic acid); IC_{50}: 22.0 µg/mL (Ascorbic acid)		[76, 126]
			IC_{50}: 179.82 µg/mL (Acetone extract)	179.59 µg/mL (Ascorbic acid)		[83]
			IC_{50}: 191.25 µg/ mL (Ethyl acetate fraction)	IC_{50}: 22.0 µg/mL (Ascorbic acid)		[76]
			IC_{50}: 554.2 µg/mL (Methanolic fraction)	IC_{50}: 22.0 µg/mL (Ascorbic acid)		[76]
			IC_{50}: 249.14 µg/mL (Hexane fraction)	IC_{50}: 22.0 µg/mL (Ascorbic acid)		[76]
		ABTS	IC_{50}: 6013 µg/mL (Hexane extract)	IC_{50}: 1.32 mg/mL (Trolax),		[99]
			IC_{50}: 6031 µg/mL (Chloroform extract)	IC_{50}: 1.32 mg/mL (Trolax),		[99]
			IC_{50}: 6037 µg/mL, 5.93 µg/mL (Methanolic extract)	IC_{50}: 1.32 mg/mL (Trolax), 0.52 µg/mL (Rutin), 11.25 µg/ mL (Ascorbic acid),		[99, 224]
			IC_{50}: 252.56 µg/mL (Acetone extract)	IC_{50}: 225 µg/mL (BHT)	ABTS radical conversion into its stable form	[83]
		Sugar damage by hydroxyl radicals	IC_{50}: 35.933 µg/mL (Methanolic extract)	5.278 µg/mL (Ascorbic acid)	Mitigated hydroxyl radicals	[78]
		Lipid peroxidation by hydroxyl radicals	IC_{50}: 84.775 µg/mL and >1000 µg/mL (Methanolic extract)	65.321 µg/mL (Ascorbic acid) and 95.00 µg/mL (BHA)	Mitigated hydroxyl radicals	[78, 224
		Hydrogen peroxide	IC_{50}: 703.88 µg/mL (Polyphenolic fraction)	-	Converted hydrogen peroxide into water	[226]
			IC_{50}: 84.415 µg/ mL, 193.33 µg/ mL (Methanolic extract)	IC_{50} : 57.560, 187.33 µg/mL, (Ascorbic acid); IC_{50} : 36.16 µg/mL (Rutin)		[78, 224]
			IC_{50}: 272.77 µg/mL (Acetone extract)	IC_{50} : 195 µg/mL (Ascorbic acid)		[83]
		Hydroxyl radical	IC_{50}: >1000 µg/mL (Methanolic extract)	IC_{50}>1000 µg/mL (Ascorbic acid), IC_{50}:205.83 µg/mL (Rutin), IC_{50}: >1000 µg/mL (BHA)	Mitigated hydroxyl radicals	[224]
			IC_{50}: 284.46 µg/mL (Acetone extract)	225.76 µg/mL (Ascorbic acid)		[83]
			IC_{50}: 574.71 µg/mL (Ethanolic extract)	IC_{50}: 38.3 µg/mL (Mannitol)		[126]

Continued....

Table 11: Continued....

		Superoxide radical	IC_{50}: 243.68 µg/mL (Acetone extract)	IC_{50}: 148.53 µg/mL (Ascorbic acid)	Scavenged superoxide radical	[83]
			IC_{50}: 568.18 µg/mL (Ethanolic extract)	IC_{50}: 52.1 µg/mL (Quercetin)		[126]
		Nitric oxide	IC_{50}: 14.77 µg/mL (Methanolic extract),	IC_{50}:68.44 µg/mL (Rutin)		[224]
			IC_{50}: 203.56 µg/mL (Acetone extract)	IC_{50}: 231.24 µg/mL (Ascorbic acid)	Scavenged nitric oxide	[83]
			and IC_{50}: 427.35 µg/mL (Ethanolic extract)	IC_{50}: 43.1µg/mL (Curcumin)		[126]
		Reducing power	ED:500 µg/mL (Polyphenolic fraction),	ED:500 µg/mL (Ascorbic acid)		[226]
			ED:100 µg/mL (Methanolic extract)	ED:100 µg/mL (Ascorbic acid)	Converted of Fe^{3+} to Fe^{2+}	[78]
			IC_{50}:202.86 (Acetone extract)	IC_{50}:244.52 µg/mL (Ascorbic acid)		[83]
		Total antioxidant	ED:1000 µg/mL (Polyphenolic fraction)	ED:1000 µg/mL (Ascorbic acid)	Reduced of Mo (VI) to Mo (V)	[226]
			ED:100 µg/mL (Methanolic extract)	ED:100 µg/mL (Ascorbic acid)		[78]
			IC_{50}: 2.86 µg/mL (Methanolic extract)	-		[224]
			IC_{50}: 231.48 µg/mL (Acetone extract)	IC_{50}: 196.80 µg/mL (Ascorbic acid)		[83]
6	Cytotoxicity/ Cancer	Small cell lung cancer	IC_{50}: 25 µg/mL (Methanolic extract)	IC50: 0.88 µg /mL (Ellipticine) and IC_{50}: 0.05 µg/mL (Doxorubicin)	Induced cell death	[99]
		Squamous skin cancer	ED:100 µg/mL (Hexane extract)	-	Cytotoxicity	[227]
			IC_{50}: 78 µg /ml (Ethyl acetate extract)	-	Cytotoxicity and inhibition of 12 R LOX	[227]
		prostate cancer	ED: 70 µg/mL (Ethanolic extract loaded casein-chitosan microparticles)	-	Cytotoxicity; LDH elevation	[228]
		Breast cancer	ED:100 µg/mL (Aqueous extract loaded silver and gold nanoparticles)	-	Cytotoxicity, apoptosis, DNA damage	[229]
			ED:100 µg/mL Aqueous extract loaded copper oxide nanoparticles	-	Cytotoxicity	[230]
7	Larvicidal	*Anopheles subpictus*	100 ppm (Acetone extract)	-	Lethality shown on laraval stage of mosquitoes	[277]
		Aedes aegypti	LC_{90}: 462.17 ppm (Acetone extract), LC_{90}: 1059.78 ppm (Chloroform extract), LC_{90}: 230.40 ppm (Hexane extract), LC_{90}: 396.75 ppm (Petroleum ether extract) and LC_{90}: 1198.85ppm (Ethanol extract)	-	Lethality shown on laraval stage of mosquitoes	[49]
			ED:97 mg/mL (Acetone extract from soxhlet method), ED:100 mg/mL (Water extract from sonication method)		Lethality shown on laraval stage of mosquitoes	[95]

Continued....

Table 11: Continued....

			ED: 1,000 ppm (Acetone, Chlorform, ethyl acetate, hexane, Methanol extracts)	-	Lethality shown on laraval stage of mosquitoes	[276]
		Culex quinquefasciatus	LC_{90}: 411.48 ppm (Acetone extract), LC_{90}: 760.38 ppm (Hexane extract), LC_{90}: 950.80 ppm (Petroleum ether extract), LC_{90}: 1181.55 ppm (Ethanol extract) and LC_{90}: 695.55 ppm (Chloroform extract).	-	Lethality shown on laraval stage of mosquitoes	[49]
		Anopheles stephensi	LC_{90}: 41.29 ppm (benzene extract), LC_{90}: 58.27 ppm, (chloroform extract), LC_{90}: 49.19 ppm (ethyl acetate extract), LC_{90}: 36.32 ppm (methanolic extract)	-	Lethality shown on laraval stage of mosquitoes	[262]
			LC_{90}: 1210.9ppm (chloroform extract), LC_{90}: 660.9 ppm (Hexane extract), LC_{90}: 447.19 ppm (Petroleum ether extract), LC_{90}: 1779.62 ppm (Ethanolic extract) and LC_{90}: 660.9 ppm (Acetone extract)	-	Lethality shown on laraval stage of mosquitoes	[49]
8	Ovicidal	*Anopheles stephensi*	200 ppm (Benzene, chloroform, ethyl acetate and methanolic extracts)	-	Killed the mosquitoes eggs	[262]
9	Oviposition	*Anopheles stephensi*;	100 ppm (Benzene, chloroform, ethyl acetate and methanol extracts)	-	Attracted the mosquitoes to laying of eggs.	[262]
		C. quinquefasciatus, A. stephensi and A. aegypti.	0.1 % (Ethanolic extract)	-	Greatly Reduced the laying of eggs	[49]
10	Mosquito repellent	*Aedes aegtpti, Anopheles stephensi and Culex. quinquefasciatus*	0.02 ppm (Hexane extract)	-	Repelled mosquitoes from biting. Spatial repellencies of mosquitoes	[49]

Continued....

Table 11: Continued....

		Aedes aegtpti	5 % (Hexane extract –Maceration), 1.5 % (Hexane extract- Soxhlet), 1.5 % (Hexane extract- Sonication), 1.5 % (Ethyl acetate extract- Maceration), 1.5 % (Ethyl acetate extract- Soxhlet), 5 % (Ethyl acetate extract – Sonication), 2 % (Acetone extract – Maceration), 1.5 % (Acetone extract – Soxhlet), 3 % (Acetone extract – Sonication), 1.5 % (Methanol extract- Maceration), 1.5 % (Methanol extract- Soxhlet), 2 % (Methanol extract – Sonication), 1.5 % (Water extract- Maceration), 1.5 % (Water extract- Soxhlet), 1.5 % (Water extract- Sonication) and 1 % (Steam distillation extract).			[95]
12	Cardio protective	Male rats	ED:200 mg/kg (Flavonoid rich extract)	-	Restored plasma, serum markers, antioxidant enzymes, lipid profiles and cardiac tissue dammage	[239, 240]
		Female rats	ED:500 mg/kg (70%Methanolic extract)	-	Restored serum markers, antioxidant enzymes and cardiac tissue damage	[263]
		Female rats	ED:500 mg/kg (70%Methanolic extract)	-	Reverted the CRP, CK-MB and Troponin; maintaining architecture of left ventrical tissue	[263]
13	Anti plasmodial	*Plasmodium falciparum*	56.89 81µg/mL (Ethanolic extract)		Showed antiplasmodial activity	[278]
14		Male Rats	ED:750 mg (Ethanolic extract)	Snake venom antiserum	Inhibited haemorrhage, necrosis and mast cell degranulation	[223]
		Male mice	ED:750 mg (Ethanolic extract)	Snake venom antiserum	Neutralized the venom	[223]
	Neutralization (snake venom)	Frog	ED:1.6 mg/mL (Ethanolic extract)	-	Inhibited venom on neuro and cardic cells	[223]
		Mice	ED: 500 mg/kg (Acetone extract).	Snake venom antiserum	Neutralized snake venom	[235]
		RBC	ED:0.4 mg/mL (Acetone extract)	-	Inhibited heamolysis	[235]
15	Wound healing	Male rats	ED:40 mg/kg (aqueous ethanol)		Mitigated oxidative stress, lipid peroxidation, increased ascorbic acid, improving cell proliferation ; positive action on TNF-α and TGF-β1, collagen synthesis, collagen 1 α and collagen 3 α.	[233]
16	Haemolysis	Humans	Broth		Caused changes in peripheral blood, reticulocytosis, increase levels of serum indirect bilirubin and haemoglobinuria	[5]

Continued....

Table 11: Continued....

18	Inflammation	*In vitro*	ED:0.1 mg/mL (Ethylacetate and Hexane and Ethanol extract	-	Inhibited 5-LOX, 15 LOX, COX-1 and COX-2 enzymes	[227]
			ED: 0.3 mg (Ethyl acetate and water extracts)	0.07 mg/mL (Zileuton)	Inhibited 12 R-Lox	[237]
	Roots					
1	Anti plasmodial	*Plasmodium falciparum*	IC_{50}: 69 µg/mL (Ethanolic extract)	-	-	[278]
3	Anti Ulcer	Either sex Rats	200 mg/kg (80% ethanol extract)	50 mg/kg (Ranitidine); 1 mg/kg (Diazepam)	Protected from acetyl salicylic acid, cold stress, ethanol induced and pylorus ligated ulcers by improving pH, reducing gastric volume, acidity and mean ulcer score	[250]
4	Anthelmintic	*Pheretima posthuma*	50 mg/mL (70% alcohol)	10mg/mL (Albendazole)	Caused paralysis and death	[244]
5	Antioxidant	DPPH	IC_{50} : 208.5 and ED: 600 µg/mL (Methanolic extract)	IC_{50}: 2.69 µg/mL (Ascorbic acid); IC_{50}: 3.91 µg/mL (Rutin)	Scavenged DPPH radical	[224, 225]
			IC50: 227.02 µg/mL (Acetone extract)	179.59 µg/mL (Ascorbic acid)		[83]
		ABTS	IC_{50}: 24.00 µg/mL (Methanolic extract)	IC_{50}: 11.25 µg/mL (Ascorbic acid); IC_{50}: 0.52 µg/mL (Rutin);		[224]
			and IC_{50}: 288.53 µg/mL (Acetone extract)	IC_{50}:288.53 µg/mL (BHT)	Scavenged AB TS radical	[83]
		Hydrogen peroxide	IC_{50} : 205.00 µg/mL(Methanolic extract)	IC_{50}: 187.33 µg/mL (Ascorbic acid); IC_{50}: 36.16 µg/mL (Rutin)	Converted hydrogen peroxide to water	[224]
			$IC5_0$: 293.11 µg/mL (Acetone extract)	IC_{50}: 195 µg/mL (Ascorbic acid)		[83]
		Hydroxyl radical	IC_{50} : >1000 µg/mL (Methanolic extract)	IC50: >1000 µg/mL, (Ascrobic acid); IC_{50}: 205.83 µg/mL (Rutin); IC_{50}: > 1000 µg/mL (BHA)	Scavenged hydroxyl radical	[224])
			IC_{50}: 288.61 µg/mL (Acetone extract)	IC50: 225.76 µg/mL		[83]
		Superoxide radical	IC_{50}: 277.78 µg/mL (Acetone extract)	IC_{50}: 148.53 µg/mL (Ascorbic acid)	Scavenged superoxide radical	[83]
		Lipid peroxidation	IC_{50} : 180.00 µg/mL (Methanolic extract)	IC_{50}: 95.00 µg/ml (BHA)	Mitigation of hydroxyl radicals	[224]
		Ferric reducing	IC_{50} : 224.13 µg/mL (Acetone extract)	IC_{50}: 244.52 µg/mL (Ascorbic acid)	Converted of Fe^{3+} to Fe^{2+}	[83]
		Total antioxidant	IC_{50} : 1.53 µg/mL (Methanolic extract)			[224]
			IC_{50}: 253.12 µg/mL (Acetone extract)	IC_{50}: 196.80 µg/mL (Ascorbic acid)	Reducted of Mo (VI) to Mo (V)	[83]

Continued....

Table 11: Continued....

		Nitric oxide	IC50 : >700 µg/mL (Methanolic extract)	IC_{50}: 68.44 µg/mL (Rutin)		[224]
			IC_{50}: 255.05 µg/mL (Acetone extract)	231.24 µg/mL (Ascorbic acid)		[83]
			IC_{50} : 315.46 µg/mL (Ethanolic extract)	IC_{50}: 103.59 µg/mL (Ascorbic acid)	Scavenged nitric oxide	[79]
			IC_{50}: 667.82 µg/mL (Aquoes extract)	IC_{50}: 103.59 µg/mL (Ascorbic acid)		[79]
	Stem					
1	Anti plasmodial	*P.falciparum*	IC_{50}: 43.81µg/mL (Ethanolic extract)		Showed antiplasmodial activity	[278]
2	Diabetes	Rats	ED:600 mg/kg (Methanolic extract)	5 mg/kg (Acarbose)	Suppressed postprandial glucose and sucrose elevation.	[243]
		Rats	ED:300 mg/kg (Methanolic extract)	10 mg/kg (Metformin)	Decreased liver markers and elevating antioxidant enzymes	[243]
3	Free radical scavenging	DPPH	IC_{50}: 212.83 µg/mL (Methanolic extract)	IC_{50}: 2.69 µg/mL (Ascorbic acid), IC_{50}: 3.91 µg/mL (Rutin)		[224]
			and IC_{50}: 218.28 µg/mL (Acetone extract)	179.59 µg/mL (Ascorbic acid)	Scavenged the DPPH radical	[83]
		ABTS	IC_{50}: 14.33 µg/mL (Methanolic extract);	IC_{50}: 11.25 µg/mL (Ascorbic acid); IC_{50}: 0.52 µg/mL (Rutin)	Scavenged ABTS radical	[224]
			IC_{50}: 323.09 (Acetone extract)	and IC_{50}:225 µg/mL (BHT)		[83]
		Lipid peroxidation	IC_{50}: 700.00 µg/mL (Methanolic extract)	IC_{50}: 95.00 µg/mL (BHA)	Mitigated hydroxyl radicals	[224]
		Hydrogen peroxide	IC_{50}: 380.00 µg/mL (Methanolic extract)	IC50: 187.33 µg/mL, (Ascorbic acid); IC50: 36.16 µg/mL (Rutin)	Converted hydrogen peroxide to water	[224]
			IC_{50}: 333.55 µg/mL (Acetone extract)	195 µg/mL (Ascorbic acid)		[83]
		Superoxide radical	IC_{50}: 308.61 µg/mL (Acetone extract)	IC_{50}: 148.53 µg/mL (Ascorbic acid);		[83]
		Ferric reducing	IC_{50}: 320.19 µg/mL (Acetone extract)	IC_{50}: 244.52 µg/mL (Ascorbic acid);	Converted Fe^{3+} to Fe^{2+}	[83]
		Hydroxyl radical	IC_{50}: 873.33 µg/mL (Methanolic extract)	IC_{50}: >1000 µg/mL(Ascorbic acid); IC_{50}: 205.83 µg/mL (Rutin) and IC_{50}: > 1000 µg/mL (BHA)	Scavenged hydroxyl radical	[224]
			IC_{50}: 317.33 µg/mL (Acetone extract)	IC_{50}: 231.24 (Ascorbic acid)		[83]
		Nitric oxide	IC_{50}: 490.00 µg/ml (Methanolic extract) and	IC_{50}: 68.44 µg/ml (Rutin)	Scavenged nitric oxide	[224]
			IC_{50}: 255.05 µg/mL (Acetone extract)	IC_{50}: 231.24 µg/mL (Ascorbic acid)		[83]
		Total antioxidant	IC_{50}: 2.27 µg/mL (Methanolic extract) and	IC_{50}: 196.80 µg/mL µg/mL	Reduced Mo (VI) to Mo(V)	[224]
			IC_{50}: 244.24 µg/mL (Acetone extract)	(Ascorbic acid)		[83]

ED: Effective dose; $IC_{50;}$ Fifty percent inhibitory concentration

leaves and seeds for 96 hrs shown 77.4% and 49.5% mortality at higher concentration respectively by causing alterations in intestine, fat body and reproductive system. The red bug fed with cotton seeds and leaves having 2% extract revealed that seeds decreased the gut Na^+ whereas leaves decreased the K^+ and Ca^+; both increased the glucose and protein levels in testes; seeds increased the aspertate in intestine and fat body.[279]

DISCUSSION

General information

A.indica has 20 synonyms which are available in "The plant database" and "Kew-Royal botanical garden". Due to the medicinal importance of this plant, many taxonomists have focused on it and given synonyms. At the same time, the local ethnics and accents of Asia and African countries have given many vernacular names. Especially, it has different vernacular names in Indian regional languages because it is a common weed growing in public places and the traditional healers used this plant for many health problems.

Traditional clues

In modern era, apart from synthetic drugs, most of the drugs are identified for diseases from traditional information of extracts/decoctions/paste etc., of plants/other natural sources or from skeleton moieties of plant compounds. Simply, building of modern medicine is constructed on pillars of traditional information of medicinal plants. The traditional information of *A.indica* existed with healers of African (Seychelles, Namibia, Mozambique, Réunion etc.,) and Asian countries (India, Srilanka, Nepal, Bangladesh etc.,) where they used this plant sources (whole plant, leaves, stem, root and seeds) as decoction, paste, juice, sap and others. These sources are used to treat asthma, bronchitis, burns, cough, diarrhea, dog bite, ear ache, epilepsy, skin infections, joint pains, rheumatoid arthritis, snake bite, ulcers, wounds, syphilis etc., (Table 1). Traditional information available on *A.indica* provides clue to the modern science for identification of potential medicine for respective ailments. Extensive research reports are also available on *A.indica* and strongly supported the traditional uses. All scientific evidences in connection with traditional data will be discussed in the following sections of this review.

Phytochemistry

People show importance to the plants majorly due to the presence of medicinally useful secondary metabolites. In this connection, *A.indica* has been used by traditional healers against many ailments, this is followed by the researchers started extraction of phytochemicals into methanol, diethyl ether, ethyl acetate, ethanol, aqueous alcohol, petroleum ether, chloroform and water from total plant, leaves, roots and stem. Consequently they found flavanones, flavonoids, phenols and saponins quantitatively. Among these findings, our research group[78] reported rich content of flavonoids, phenols and saponins in methanolic extract of *A.indica* leaves. We also identified methanol, ethanol, ethyl acetate and water extracts of *A. indica* leaves are hygroscopic in nature (unpublished data from our study). This query has been conquered by applying lyophilization method to get solid or powder forms and also taken further care in storage to get accurate weighing and results.

Isolation of bioactive compounds is very essential element in phytochemistry because it gives fruitful functional property of the plants. Accordingly, an attempt on *A.indica* total plant and leaves for isolation of bioactive compounds is more when compared with stem, root and inflorescences. This plant is very precise in having alkaloids and their glycosides because few of them are cynogenic glycosides, a class of toxic compounds. Flavonoids, tannins, coumarins, phenols, fatty acids, steroids and terpenes/terpenoids are othe constituents.

Cynogenic compound

In a list of 15 alkaloids, seven of them are cynogenic glycosides (1-4, and 9-11 in Table 4) which are identified higher in quantity from methanolic extract of leaves and inflorescence (0.35% on fresh weight basis) than roots and stem whereas no such toxic compounds are found in seeds.[87] These are considered as hydrogen cyanide (HCN) releasing phytotoxins, produced against pathogens, herbivores and are very harmful to humans if consumed.

After having information on phytochemistry and pharmacology of *A.indica*, everyone thought that why cyanide toxicity reports are not available on animal studies for phytoextracts of *A.indica*?. Hence, in this review we are providing some possible reasons i) As per WHO, cynogenic glycosides show toxicity when its range present in between 0.5 to 3.5 mg HCN per kg/b.w.[281] The *A.indica* extracts used for animal studies might have lower than 0.5 mg of HCN ii) Sulfur containing amino acids of rhodanase enzyme present in liver of animals detoxifies the HCN to thiocynide and thiocyanic acid which are excreted through urine. iii) The hydroxocobalamin (B12a vitamin) of liver converted into cynocobalamine (B12 vitamin) by the process of detoxification of HCN.[281] iv) Soaking, boiling, fermentation and drying of plant material also remove the cyanide.[282] Generally, sequential procedure of drying, phytoextraction with solvents by soaking, concentration using rotary evaporator at suitable boiling temperature of solvents and biological evaluation of *A.indica* plant/parts might reduce the cynogenic glycosides.

Polyphenols

Due to the presence of hydrogen bond donor and acceptors, polyphenols of plant playing crucial role in protection of biomolecules by stabilizing free radicals. Apart from they also act as inhibitors against therapeutic targets of deadly diseases. *A.indica* has 27 polyphenols including flavonoids (10 numbers), tannins (11 numbers), coumarins (3 numbers), hydroxy benzoate (2 numbers) and hydroxy cinnamic (1 number). Diseases management of these compounds is summarized in Table 3. *A.indica* extracts having rich content of polyphenols showed potential antioxidant activity against DPPH, Hydroxyl radical, Hydrogen peroxide, lipid peroxidation etc., (Table 12).

Volatile compounds

The volatility of plants is a sign of language, useful for the communication and interaction with surrounding environment. Flowers, leaves, and fruits being released the volatile compounds into air for attraction of pollinators and defense against herbivores, parasites, bacteria, and fungus whereas roots release into soil for the protection of pathogens. These volatiles are also giving major assistance in curing of diseases. GC-MS and HR-LC-MS analysis of *A.indica* provided volatile compounds which come under aldehydes, alkanes, esters, ethers and fatty acid derivatives (fatty acyls and fatty alcohols). The volatilization (smell) of *A.indica* also found when the plant leaves are crushed with hands as well extraction with low polar organic solvents.

Pharmacological properties

A.indica extracts from whole plant, leaves, stem and root have used for animals studies (Table 12). The abundant usage order of this plant extracts are leaves> total plant> roots> stem. The reason behind the choice of plant leaves is due to having plenty of secondary metabolites resulted from the stress of biotic and abiotic factors. Based on various biological activities of *A.indica,* we categorized them into stabilization, killing/inhibition, protection, reduction and neutralization.

Stabilization

Free radicals are the molecules having one or more unpaired electrons in their outer shell, so they pair/interact with adjacent moieties (biomolecules in biological system) to get stable form. It results the adverse effects like DNA damage, protein degradation, lipid peroxidation etc. In this scenario, *A.indica* stabilizeed various radicals (DPPH, hydroxyl, superoxide, etc., as summarized in Table 12) due to its anti-oxidant polyphenolic compounds. Antioxidants donate either electron or electron followed by hydrogen to the radicals. Among extracts and fractions of *A.indica*, the methanolic extract exhibited potential radical stabilization property, which is equal to the standard antioxidant (ascorbic acid). As per Do *et al*. (2014),[283] highly polar phenols extracted more into methanol than water and also mixing of high polar water to other solvents like methanol, ethanol and acetone reduce the extraction of phenols. This extraction procedure and stabilization properties are strongly support the quantified phenolic content (Table 2), isolated and identified polyphenolic (tannins, flavonoids, coumarins and phenols etc.,) compounds (see in phytochemistry description) of *A.indica*. On the whole *A.indica* could be used as alternative antioxidant medicine for the radicals associated deadly diseases.

Killing/ inhibition

A.indica unveiled growth inhibition or killing ability on disease causing cells/organisms like bacteria, fungus, cancer, mosquitoes larvae, round worm parasite resembled *Pheretima posthuma*, *Plasmodium falciparum* and *Dysdercus cingulatus* (Red cotton bug).

Various solvent extracts/ fractions from leaf, root, stem and total plant of *A.indica* exhibited antimicrobial and antifungal properties. Among, the dilution method is a very reliable and accurate for assessing effective concentrations than disc diffusion and well diffusion. Extracts potentially exhibited antimicrobial activity on bacteria (*E.coli* and *S. auereus* summarized in Table 10) and fungus (*C.albicans)*. Hence, to identify potentiality of extracts, researchers could choose dilution method/ other advanced methods and instruments.

The information available as on this date is insufficient to decide whether this plant possess cytotoxic/anticancer potentiality because of any *in vitro* report is not available on toxic effects of extracts on normal cells. Though, extracts at higher doses are not shown toxicity in invivo, its direct exposure to cells (cell lines, where no detoxification occurs) in *in vitro* may be possible. Moreover, all experiments on cancer have been conducted using cell lines and obtained positive results but many times the *in vitro* activities are failed in animal models. Hence, further extensive investigation on animal models with different dose ranges would clarify these remarkable queries.

Extracts of *A.indica* shown potential larvicidal and ovicidal activities at different concentrations (Table 12); hence, the synergistic study of *A.indica* extracts with other pesticides and mosquito predators would require to establish the toxic properties of this plant. Moreover, water extract of *A.indica* exhibited killing capacity on Red cotton bug (insect) with good mortality rate; ethanolic extract killed the *Plasmodium falciparum* cultured in RBC; and *Pheretima posthuma* has been killed by hydro alcoholic (70%) extract effectively than standard drug abendazole but in all cases, the results are not compared with standard drugs except in red cotton bug and *Pheretima posthuma.* Researchers who done work on this plant also not isolated any active compounds (except L-Quebrachitol isolated from leaves by Sanseera *et al*. (2012) from bioactive extracts. Hence, the comparative study on other solvent extracts of leaves, roots and stem of *A.indica* with reference drugs would help in isolation of future toxic constituents.

Protective property

A.indica shown protective property on cardiac, hepatic, liver and kidneys damage induced in experimental animals as follows: i) Methanolic and hydro methanolic (70%) extracts of leaves protected the isoproterenol, furosemide and potassium chloride induced cardiac damage in rats. ii) The leaves broth protected the intra vascular haemolysis in glucose-6-phosphate dehydrogenase enzyme deficient humans. iii) In STZ induced diabetic condition, ethanolic extract protected the liver and kidney tissues. iv) Alongside, thioacetamide, paracetamol and CCL_4 induced liver damage is protected by methanolic extract from methanolic fraction and hydro alcoholic extracts of leaves and whole plant. Among the above results, 70% alcoholic extract (300 mg/kg) is a very potential cardio protective comparatively with standard silymerin (100 mg/kg) but other extracts are not reached upto the activities of standard drugs. Hence, the hydro alcoholic extracts of *A.indica* to be used in the preparation of herbal drug/ identifiaction of active moieties for the treatment of cardiac damage in future.

Reduction

Biological experiments on *A.indica* proved that it has reduction potentiality on wounds, pains and inflammation. It is a potential wound healer than standard ointment povidone, good analgesic agent and anti-inflammatory source. Generally, there is an interconnection between wounds, pain and inflammation. These properties also supported by traditional information on this plant as wound healing agent on animals, treatment for joint pains and arthritis, antiseptic etc (Table 12). Through phytochemistry, the reduction of inflammation is strongly supported by having anti-inflammatory compounds such as n-(2hydroxyethyl)palmitamide (Propylene glycol), catechin, quercetin 3-0-β-D-glucoside, rutin, kaempferol, n-tris[hydroxymethyl]methyl2-aminoethanesulfonic acid, gallic acid, caffeic acid, sulindac sulfide, dimethylglycine, ibuprofen, beta-sitosterol and stigmasterol (Table 3). Usually, majority of anti-inflammatory compounds can reduce the pain. Gathering, this reduction property of *A.indica* is due to active phytochemical compounds, isolation would be taken up, evaluated in experimental animals and further studies may be extended to human beings.

Neutralization

Snake bite is aone of the public health problem in India, 2 Lakh people are being preyed, among 35 to 50 thousand death cases have been recorded annually. Traditional healers have used plant medicine against snake bites, like wise *A.indica* used traditionally as venom neutralizer, also been proved in biological experiments (Table 1). The same has been executed experimentally in animals. Shirwaikar *et al.* (2004)[223] and Rajendran *et al.* (2010)[235] have reported that *A.indica* works equal to the anti-snake venom. To date, the potential neutralizing extracts (aqueous ethanol an acetone) reported on this plant but no one identified active constituents of these extracts. So, future researchers should take up and cover this scientific gap by isolation and evaluation of venom neutralizing compounds from bioactive extracts of *A.indica.*

Presence of endophytic fungal species in *A.indica* is helpful to the plant but it consumption by humans is not safe. Hence, people may be advised to use this plant source with the help of organic solvents or heat resulted decoction.

The bioremediation is emerging, ecofriendly, lesser cost technology for the removal of environmental pollutants such as dyes and heavy metals to improve the quality of environment. Biosorption of dyes by *A.indica* helps the environmentalists to get effective solution for removal of hazardious dyes (carcinogens, mutagenic and effects on aquatic biota) and heavy metals. Further step should be taken to cultivate *A.indica* at highly polluted areas to reduce toxic effects.

CONCLUSION

The current review article reports detailed information about *A.indica* traditional knowledge, phytochemistry and pharmacological properties. *A.indica* has been used by local/ traditional healers of Asia, Africa and American countries for wound healing, snake bites, asthma, cough, bacterial infections, dog bite etc. (Table 1). In India all parts of the plant/ total plant are being used for treating of various diseases. Traditionally, the effectiveness of this plant also considered to increase when it combined with other plant/ plant products. It is rich in phenolic content, as well as flavonoids. The phytochemistry of this plant revealed that it has mostly polyphenols (phenols, flavonoids, tannins and coumarins), alkaloids and their glycosides (few of them are toxic), volatile compounds and fatty acids. So far there is no evedance for toxic property on this plant even at higher concentration in animal studies, which might be due to elimination of such toxic agents during processing (at extraction, drying of extracts and detoxification in animal body) to use and detoxicfication in animal body. Biological or pharmaceutical studies showed that *A.indica* is a potential anti-microbial, anti-diabetes, anti-inflammation, larvicidal, anti-oxidant, wound healing and venom neutralizing agent.

Scientific gaps

Several scientific gaps need to be highlighted based on this review about *A.indica* i) Geographical distribution of *A.indica* and published traditional knowledge is not correlated. The published reports available are only from few Asian (India, Srilanka, Nepal, Bangladesh, Indonesia and Thailand) and African (Seychelles, Namibia, Djibouti, Mozambique, Reunion, Madagascar and Mauritius,) countries but is occupied many areas as described elsewhere in this review hence, research on other places where this plant is distributed to be carried out and to be published to support the pharmaceutical evaluations against diseases. ii) The biological evaluation of the isolated compounds is in many cases lacking. The potentiality of the plant can only proved when biological evaluation of isolated compounds from bioactive extracts are done focusing on the relevant diseases. Clinical studies, mechanism of action and effective doses for the bioactive extracts, pharmacokinetic and pharmacodynamics evaluation to the bioactive compounds are lacking. iii) Many traditional uses (Table 1) have not been evaluated experimentally yet, including asthma, burns, diarrhoea, dog bite, epilepsy, haemorrhoids, constipation, aches of stomach/ear/head, syphilis, wheezing etc., of traditional information based experiments to be conducted in future at preclinical then clinical stage to explore the strength of *A.indica* in pharmacy/medicine. iv) The extracts which showed potential activity will be properly utilised for development of drug candidates. v) All pharmacological properties except few (see in pharmacological properties) are reported with preliminary evidences, so these activities must be extended extensively with different dosage studies, various modes of experimentation, molecular mechanism, and phytochemicals responsible. vi) *A.indica* has been utilized by traditional healers as antifertility agent, also was proven in experimental animals pharmaceutically, hence it is suggested that, pregnant women should avoid this plant as remedy to treat any health issues to them.

In future, this plant would be utilized and highly beneficial for pharmacological evaluataions of the overlooked traditional applications particularly on snake bites, oragan specific aches, asthma and microbial related issues. The effective crude extracts could be utilized for bioactives isolation to assist in therapy of diseases and drug development. Isolation and extract detoxification process of cynogenic compounds of this plant need to be explored to prove this plant is non-toxic for further clinical applications in the interest of human health.

Authors' contribution

The first and second authors played substantial role in data acquisition, analysis, interpretation and manuscript preparation. The other co-authors contributed their efforts equally towards acquiring additional data making script in good way by their expertise in their respective research fields. The corresponding author critically revised and finalized the manuscript for publication.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

HR-LC/Q-TOF/MS: High resolution liquid chromatography/ Quadruple time-of-flight/ mass spectrometer; **ALT:** Alanine aminotransferase; **AST:** Aspartate aminotransferase; **ALP:** Alkaline Phosphatase; **CRE:** Creatinine; **UA:** Uric Acid; **TC:** Total Cholesterol; **TG:** Triglyceride; **T Bil:** Total Bilirubin; **D Bil:** Direct Bilirubin; **ALB**: Albumin; **GLB:** Globulin; **TP:** Total protein; **GLU:** Glucose; **RP- HPLC:** Reverse phase high-performance liquid chromatography; **MIC:** Minimum inhibitory concentration.

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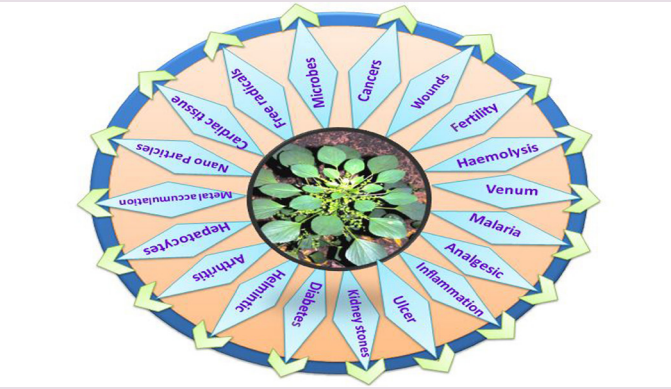
GRAPHICAL ABSTRACT



SUMMARY

- Traditionally, *A.indica* formulations have worked against microbial infections, stomach ulcers, snake bites, pains, wounds, liver/kidney problems, and rheumatism etc.
- Scientific evidences proved that *A.indica* is a good source of anti-microbial, anti-diabetes, anti-inflammation, larvicidal, anti-oxidant, wound healing and venom neutralizing agent.
- Traditional and pharmaceutical properties of *A.indica* is due to the presence of phytochemical such as phenols, flavonoids, tannins, coumarins, alkaloids and their glycosides, and saponins.

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