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Research Article

GCMS Profile of Bioactive Secondary Metabolites with Therapeutic Potential in the Ethanolic Leaf Extracts of *Azadirachta indica*: A Sacred Traditional Medicinal Plant of INDIA

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Abstract

Neem (*Azadirachta indica*) a member of Meliaceae plays an immense role in human health and disease which is attributed to its composition of Bioactive Secondary Metabolites (BASM). It has been widely used in Indian Traditional Systems of Medicine that includes Ayurveda, Siddha, Unani, Homeopathy and other Folklore Systems of Medicine practiced in the Indian Subcontinent for the treatment and prevention of various diseases. Current global health perspectives and medical practice in the post COVID era has no other way but to seek to merge alternative systems of medicine with evidence-based therapeutic aspects for a better understanding of the metabolic process and its effects in the human body. The studies based on animal model established that neem and its chief constituents play pivotal role in anticancer management through the modulation of various molecular pathways including p53, pTEN, NF-κB, PI3K/Akt, Bcl-2, and VEGF. Besides, NEEM plays a vital role in the management of diabetics and its associated long term complication through ROS scavenging and ameliorative potentials to restore oxidative injury/ inhibit enzymes linked to. Overall NEEM is considered as GRAS medicinal plant that modulates metabolic inflammations without side effects. Though it has been confirmed that neem and its constituents play role in the scavenging of free radical and prevention of disease pathogenesis, a clear scientific basis of its pharmacoinformatics is still lacking. Gas Chromatography–Mass Spectroscopy (GC–MS) analysis of the fractions revealed the presence of 62 metabolites.

Keywords: *Azadirachta indica*; NEEM; GCMS; Bioactive Secondary Metabolites; GRAS; Medicinal Plants

INTRODUCTION

Azadirachta indica A. Juss commonly known as Neem or Margosa belongs to the family Meliaceae[1]. Popular as Miracle tree it is a natural drugstore/ store-house of phyto-drugs since the dawn of civilization[2,3]. This tree is one of the most versatile plant across the country and elsewhere known for its use in various Indigenous/ Traditional Systems of Medicine. Kumar et al[4]. described Neem as a tree of drugs from prehistory to contemporary medicinal uses to humankind. *A. indica* has its origin from India and is commonly distributed in the South East Asian (SEA) Region (Bangladesh, Srilanka, Bhutan, Myanmar, Pakistan, and Nepal)[5], it has been attempted for global, distribution, through introduction and cultivation, in particular the tropical and sub-tropical regions[6]. Neem is a perennial, small to medium-sized (10 to 15 m) and fast-growing tree and grows well in locations with temperature to a maximum of 48-50 °C, the plant needs low annual rainfall (400 – 800 mm/annum).

Being the storehouse/ repository of wide array of bioactive secondary metabolites, Neem tree remains the ideal target of interest for research[7,8]. As most of the bioactive secondary metabolites are localised in the leaves and seeds, destruction of whole plant is not required for the isolation/ extraction of bioactive secondary metabolites. Furthermore, being perennial annual replenishment of leaves and seeds prevents whole-plant harvest. Bioactive secondary metabolites of Neem contain high proportion of water-soluble substances that favours DIY extraction and application. Moreover, majority of these compounds are eco-friendly bioactive compounds (EFBAC) that are of biodegradable nature adhering to GRAS standards, therefore harmless to man and environment[9].

A. indica shows therapeutics potential in healthcare and management as herbal remedies[10] due to rich source of

various types of ingredients[2,11,12]. The most important active constituent is azadirachtin is known for its biological activities and medicinal properties[3] and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin. Leaves contain Limonoids[13-15] such as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, nimbiol[16-22] and Tetranortriterpenoids from the seeds[15,23]. Awolu et al.[24] Optimized solvent extraction protocol for oil from neem *Azadirachta indica* and characterised the compounds.

Used for centuries in India and SEARC region as a natural remedy for cancer, neem compounds present in bark, leaves, flowers, and seed oil have been shown to possess properties such as chemopreventive[25], apoptotic activities[26], immunomodulatory[27] effects, and induction of p53-independent apoptosis. To date, of more than 140 compounds isolated from Neem at least 35 biologically active principles have shown antitumor activity. They suppress tumor by interfering with the carcinogenesis process. Likewise, leaf and bark extracts of Neem have been explored for their antioxidant activity and it has been indicated that leaf and bark extracts of neem grown in the foothills have significant antioxidant properties than others, further it has been indicated that high degree of variation is in chemical content exists.

Rahmani et al.[11] (2018) described the pharmacological and therapeutic potential of neem and pointed out that since antiquity all parts of the plant, including root, stem, bark, leaves, fruits, and seeds are used to cure various ailments in humans and other applications such as insect-pest control[28-30]. Gupta et al.[31] described Neem as an Indian traditional panacea with modern molecular basis[32]. Profile of bioactive compounds in medicinal plants provides an understating to the type and level of bioactive secondary metabolites in different parts of the plant.[33-36] In fact, therapeutic applications attributed to Neem[37-41] include abortive[42], analgesic[43], antibacterial[44], antimicrobial[45] anticancer[46,47], anticandidal[48], antidermatophytic[39], antidiabetic[49], antifeedant[9], antifungal[50], anti-helminthic, anti-hyperglycemic, anti-inflammatory, antimalarial, antipyretic, antispasmodic[51], anti-spermatogenic(Seriana), antiviral[52], diuretic, contraceptive[53], hepatoprotective[54], hypercholesterolemic[55], immuno-modulatory activities[27], contraception/ aborticide, dental plaque, dengue[56]; diabetes, fever, head lice, heart disease, insect repellent, malaria, pesticide, psoriasis, skin diseases[57], ulcers, stomach upset, stomach-ache, intestinal worms, and wound healing[58]. Recently, Azadirachtin – A, bioactive secondary metabolite from *A. indica* has been identified as potential inhibitor of SARS-CoV-2 main protease[59-61] and is expected to play a major role in the management of COVID-19 once through with clinical trials. Furthermore, pharmacological characterization, and ADMET profiling[62-65] is expected to validate this natural drug lead.

MATERIALS AND METHODS

Class	:	Equisetopsida C. Agardh
Subclass	:	Magnoliidae Novák Ex Takht.
Superorder	:	Rosanae Takht.
Order	:	Sapindales Juss. Ex Bercht.
Family	:	Meliaceae Juss.
Genus	:	*Azadirachta* A. Juss.
Species	:	*Azadirachta indica* A. Juss.
Common Name	:	Neem
Vernacular Name	:	Vempu (Tamil)

Botanical Description

Tree, up to 15 m tall; Branches glabrous; Leaves imparipinnate, pulvinus at the base; leaflets alternate to opposite, 2.5 - 7.0 cm long, 1.5 - 4.0 cm broad, ovate, subsessile, acuminate; Flowers white, sweet-scented; Sepals obovate, 1.5 mm long, puberulous, imbricate. Petals 6 mm long, obvoate to oblong, white, margin ciliate; Staminal tube 5 mm long, puberulous, 10-striate, 10-toothed; teeth 2-lobed; anthers oblong, basifixed; Ovary sub-globose; style linear 2.5 mm long; stigma trifid. Fruit: Drupe oblong, 1.3 - 2.0 cm long, greenish-yellow, Seed: 1-seeded.

Collection of Plant material

A. indica leaf samples (twigs) collected from the foothills of Alagar Hills, Alagarkovil Reserve Forest, Dindigul District, Tamil Nadu, India and identity of the plant was confirmed by Botanical Survey of India, Southern circle, Coimbatore, Tamil Nadu. The collected leaves samples were rinsed with tap water dried and powdered and then stored at 4 °C. Plant extracts preparation 5g of each sample was extracted with 100 ml of ethanol using Soxhlet apparatus as previously reported[34]. The extract was filtered and ethanol was evaporated by rotary evaporator and stored at 4°C until future use.

Phytochemical Screening

Ethanolic leaf extracts of Neem were subjected to chemical tests for the detection of different phytoconstituents using standard procedures.

Test for Phenols

To 1 ml of the extract, 3 ml of distilled water followed by few drops of 10% aqueous Ferric chloride solution was added. Formation of blue or green colour indicates the presence of phenols.

Test for Flavonoids

To 2 ml of the extract, 1 ml of 1% ammonia solution was added. Appearance of yellow colour indicates the presence of flavonoids.

Test for Tannins

To 1 ml of the extract, 1 ml of 0.008 M Potassium ferricyanide was added and then add 1ml of 0.02 M Ferric chloride containing 0.1 N HCl. Appearance of blue-black colour indicates the presence of Tannins.

Test for Alkaloids

Approximately, 1 ml of crude extract was mixed with 2 ml of Wagner's reagent. Reddish brown colour precipitate indicates the presence of alkaloids.

Test for Carbohydrates

Fehling's test Equal volume of Fehling A and Fehling B reagents were mixed together and then add 2ml of crude extract in it and gently boiled. A brick red precipitate appeared at the bottom of the test-tube indicates the presence of reducing sugars.

Benedict's test1 ml of crude extract was mixed with 2ml of Benedict's reagent and boiled. A reddish brown precipitate was formed which indicates the presence of the carbohydrates.

Test for Proteins

Millon's test1 ml of crude extract was mixed with 2ml of Millon's reagent white precipitate appeared which turned red upon gentle heating confirmed the presence of protein.

Ninhydrin test1 ml of crude extract was mixed with 2ml of 0.2% solution of Ninhydrin and boiled. A violet colour precipitate was appeared suggesting the presence of amino acids and proteins.

Test for Cardiac glycosides (Keller-Kiliani test)

5 ml of extract was treated with 2 ml of glacial acetic acid containing one drop of ferricchloride solution. This was underlayed with 1 ml of concentrated sulphuric acid. A browning of the interface indicates a deoxy sugar characteristic of cardenolides. A violet ring may appear below the brown ring, while in the acetic acid layer, a greenish ring may form just gradually throughout thin layer.

Test for Saponins

2 ml of crude extract was mixed with 5 ml of distilled water in a test tube and it was shaken vigorously. Add some drops of olive oil. The formation of stable foam was taken as an indication for the presence of saponins.

Test for Coumarin

10 % Sodium hydroxide was added to the extract and chloroform was added. Formation of yellow color shows the presence of Coumarin.

Test for Terpenoids (Salkowski test)

5 ml of extract was mixed with 2 ml of chloroform and 3 ml of concentrated sulphuric acid was carefully added to form a layer. A reddish brown colouration of the inter face was formed which indicates the presence of terpenoids.

Test for Steroids

2 ml of acetic anhydride was added to 0.5 ml of crude extract containing 2 ml of sulphuric acid. The colour changed from violet to blue or green in samples indicates the presence of steroids.

Test for Quinones

Diluted sodium hydroxide was added to the 1 ml of crude extract. Blue green or red coloration indicates the presence of quinones.

Test for anthraquinones (Borntragers test)

0.5 g of each extract was boiled with 10% hydrochloric acid for few minutes in water bath. It was filtered and allowed to cool. Equal volume of $CHCl_3$ was added to the filtrate. Few drops of 10% ammonia was added to the mixture and heated. Formation of rose – pink color indicates of n-hexane, chloroform, ethyl acetate and methanol of the presence of the anthroquinones.

GC-MS Analysis

Neem leaf samples collected from the foothills of Alagar Hills, Alagarkovil Reserve Forest, Dindigul District, Tamil Nadu, India. Phyto-components were identified using GC–MS detection system as described previously[34], however with modification, whereby portion of the extract was analysed directly by headspace sampling. GC–MS analysis was accomplished using an Agilent 7890A GC system set up with 5975C VL MSD (Agilent Technologies, CA, USA). Capillary column used was DB-5MS (30×0.25 mm, film thickness of 0.25 µm; J&W Scientific, CA, USA). Temperature program was set as follows: initial temperature 50°C held for 1 min, 5°C per min to 100°C, 9°C per min to 200°C held for 7.89 min, and the total run time was 40 min. The flow rate of helium as a carrier gas was 0.811851 mL/ min. MS system was performed in electron ionization (EI) mode with Selected Ion Monitoring (SIM). The ion source temperature and quadruple temperature were set at 230°C and 150°C, respectively. Identification of phyto-components was performed by comparison of their retention times and mass with those of authentic standards spectra using computer searches in NIST 08.L and Wiley 7n.l libraries[34].

RESULT

Phytochemical screening of leaf extracts of *A. indica* revealed the presence of Carbohydrates; Flavonoids; Phenols; Proteins; Terpenoids; Alkaloids; Saponins and Anthraquinones; Cardiac Glycosides; Coumarins; Quinones; Steroids; Tannins were absent in the leaf ethanolic extract of *A. indica* on the other hand Anthraquinones; Carbohydrates; Coumarins; Proteins; Terpenoids; Saponins were present Alkaloids; Cardiac Glycosides; Flavonoids; Phenols; Quinones; Steroids; Tannins in the leaf aqueous extract of *A. indica* (Table 1).

GCMS analysis revealed the presence of the following compounds in the Ethanolic Leaf Extracts of *Azadirachta indica* - Thiazole, 4,5-dihydro-2-methyl- (MF - C_4H_7NS; MW - 101.170); Peak area - 0.3631; 2-Hexenoic acid (MF - $C_6H_{10}O_2$; MW - 114.1424); Peak area - 0.4441; 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl- (MF - $C_6H_8O_4$; MW - 144.1253); Peak area - 4.1847; Isopropyl isothiocyanate (MF - C_4H_7NS; MW - 101.170); Peak area - 0.2569; N-Aminopyrrolidine (MF - $C_4H_{10}N_2$; MW - 86.1356); Peak area - 0.2128; Benzofuran, 2,3-dihydro- (MF - C_8H_8O; MW - 120.1485); Peak area - 0.4228; 2(1H) Pyrimidinone,4-amino-1,N-dimethyl- (MF - $C_6H_9N_3O$; MW - 139.1552); Peak area - 0.1826; 2,6-Octadienal, 3,7-dimethyl-, (Z)- (MF - $C_{10}H_{16}O$; MW - 152.2334); Peak area - 0.1549; Geraniol OR 2,6-Octadien-1-ol, 3,7-dimethyl-, (E)- (MF - $C_{10}H_{18}O$; MW - 154.2493); Peak area - 0.2256; Malic Acid (MF - $C_4H_6O_5$; MW - 134.0874); Peak area - 0.3247; 2-Methoxy-4-vinylphenol (MF - $C_9H_{10}O_2$; MW - 150.1745); Peak area - 0.2593; 1H-Cycloprop[e]azulene, 1a,2,3,4,4a,5,6,7b-octahydro-1,1,4,7-tetramethyl-, [1aR-(1a.α.,4.α.,4a.β.,7b.α.)]- (MF - $C_{15}H_{24}$; MW -

204.3511); Peak area - 0.2434; trans-Cinnamic acid (MF - $C_9H_8O_2$; MW - 148.1586); Peak area - 0.1914; .γ.-Elemene OR γ-Elemene (MF - $C_{15}H_{24}$; MW - 204.3511); Peak area - 0.2789; L-Proline, 1-acetyl- (MF - $C_7H_{10}NO_3$; MW - 156.1592); Peak area - 0.1632; Dodecanoic acid (MF - $C_{12}H_{24}O_2$; MW - 200.3178); Peak area - 0.1893; Cyclohexane, 1-ethenyl-1-methyl-2-(1-methylethenyl)-4-(1-methylethylidene)- (MF - $C_{15}H_{24}$; MW - 204.3511); Peak area - 0.3327; Carbamic acid, methylphenyl-, ethyl ester (MF - $C_{10}H_{13}NO_2$; MW - 179.2157); Peak area - 0.4281; .β.-D-Glucopyranoside, methyl (MF - $C_7H_{14}O_6$; MW - 194.1825); Peak area - 0.3267; Sorbitol (MF - $C_6H_{14}O_6$; MW - 182.1718); Peak area - 0.2506; Galactitol (MF - $C_6H_{14}O_6$; MW - 182.1718); Peak area - 0.2716; Palmitoleic acid (MF - $C_{16}H_{30}O_2$; MW - 254.4082); Peak area - 0.2894; n-Hexadecanoic acid (MF - $C_{16}H_{32}O_2$; MW - 256.4241); Peak area - 7.4241; Hexadecanoic acid, ethyl ester (MF - $C_{18}H_{36}O_2$; MW - 284.4772); Peak area - 2.0398; Heptadecanoic acid (MF - $C_{17}H_{34}O_2$; MW - 270.4507); Peak area - 0.1899; 3-Heptanol, 3,5-dimethyl- (MF - $C_9H_{20}O$; MW - 144.2545); Peak area - 0.4054; Phytol (MF - $C_{20}H_{40}O$; MW - 296.5310); Peak area - 21.563; 9,12,15-Octadecatrienoic acid, (Z,Z,Z)- (MF - $C_{18}H_{30}O_2$; MW - 278.4296); Peak area - 15.7212; Octadecanoic acid (MF - $C_{18}H_{36}O_2$; MW - 284.4772); Peak area - 2.5401; Octadecanoic acid, ethyl ester (MF - $C_{20}H_{40}O_2$; MW - 312.5304); Peak area - 0.3292; 1-Heneicosyl formate (MF - $C_{22}H_{44}O_2$; MW - 340.5836); Peak area - 0.2169; Eicosanoic acid (MF - $C_{20}H_{40}O_2$; MW - 312.5304); Peak area - 0.6416; Cyclo-tetradecane, 1,7,11-trimethyl-4-(1-methylethyl)- (MF - $C_{20}H_{40}$; MW - 280.5316); Peak area - 0.2073; Eicosane (MF - $C_{20}H_{42}$; MW - 282.5475); Peak area - 0.2459; Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (MF - $C_{19}H_{38}O_4$; MW - 330.5026); Peak area - 2.0186; Glycerol 1-palmitate (MF - $C_{19}H_{38}O_4$; MW - 330.5026); Peak area - 0.2548; Bis(2-ethylhexyl) phthalate (MF - $C_{24}H_{38}O_4$; MW - 390.5561); Peak area - 0.2199; Docosanoic acid (MF - $C_{22}H_{44}O_2$; MW - 340.5836); Peak area - 0.2299; Nonadecanoic acid, ethyl ester (MF - $C_{21}H_{42}O_2$; MW - 326.5570); Peak area - 0.6983; Cyclopentadecanone, 2-hydroxy- (MF - $C_{15}H_{28}O_2$; MW - 240.3816); Peak area - 0.2932; 9,12,15-Octadecatrienoic acid, ethyl ester, (Z,Z,Z)- (MF - $C_{20}H_{34}O_2$; MW - 306.4828); Peak area - 0.2054; Ethanol, 2-(octadecyloxy)- (MF - $C_{20}H_{42}O_2$; MW - 314.5463); Peak area - 5.8689; Linolenic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (Z,Z,Z)- (MF - $C_{21}H_{36}O_4$; MW - 352.5081); Peak area - 4.9763; Benzene, 1,2-dimethoxy-4-nitro- (MF - $C_8H_9NO_4$; MW - 183.1614); Peak area - 0.8062; Fumaric acid, pent-4-en-2-yl tridecyl ester (MF -; MW -); Peak area - 0.5631; Octacosane (MF - $C_{28}H_{58}$; MW - 394.7601); Peak area - 2.3197; Squalene (MF - $C_{30}H_{50}$; MW - 410.7180); Peak area - 0.1787; Nonacosane (MF - $C_{29}H_{60}$; MW - 408.7867); Peak area - 3.6131; Octacosyl acetate (MF - $C_{30}H_{60}O_2$; MW - 452.7962); Peak area - 0.1721; 1-Nonadecene (MF - $C_{19}H_{38}$; MW - 266.5050); Peak area - 0.2752; Tetracosane (MF - $C_{24}H_{50}$; MW - 338.6538); Peak area - 3.7204; Triacontyl acetate (MF - $C_{32}H_{64}O_2$; MW - 480.8494); Peak area - 0.2446; .γ.-Tocopherol (MF - $C_{28}H_{48}O_2$; MW - 416.6795); Peak area - 0.1834; Vitamin E (MF - $C_{29}H_{50}O_2$; MW - 430.7061); Peak area - 0.9945; Octadecane (MF - $C_{18}H_{38}$; MW - 254.4943); Peak area - 3.0663; Campesterol (MF - $C_{28}H_{48}O$; MW - 400.6801); Peak area - 0.4544; Stigmasterol (MF - $C_{29}H_{48}O$; MW - 412.6908); Peak area - 0.8867; γ-Sitosterol (MF - $C_{29}H_{50}O$; MW - 414.7067); Peak area - 2.0986; Eicosane (MF - $C_{20}H_{42}$; MW - 282.5475); Peak area - 2.2165; 4,22-Stigmastadiene-3-one (MF - $C_{29}H_{46}O$; MW - 410.6749); Peak area - 0.4248; Stigmast-4-en-3-one (MF - $C_{29}H_{48}O$; MW - 412.6908); Peak area - 0.7263; Cannabidiol (MF - $C_{21}H_{30}O_2$; MW - 314.4617); Peak area - 0.7689 (Table 2). Further, the cytoscape network analysis of phytoconstituents of *A. indica* indicates that the bioactive secondary metabolites in NEEM hold significant therapeutic potential (Fig. 2).

DISCUSSION

Literature reveals that most of the bioactive secondary metabolites identified in the crude extracts of Neem leaves are of therapeutic potential[64]. Literature contains lots and lots of information on the chemical and biological investigations on *Azadirachta indica*[66]. A large number of bioactive secondary metabolites have been identified and characterized in organic crude extracts of neem than any other medicinal plant species[67]. It has been pointed out earlier that such identified bioactive compounds are plays a vital role in plant defense systems. Some of the bioactive compounds isolated in crude extracts are used as natural antioxidant, antimicrobial agents and in the formulation of different medicines for pharmaceutical industries. However, ADMET characterization[62,63] of such compounds is warranted so as to make it a competent marketable drug.

CONCLUSION

The results of the present study do not depict the chemical compound is responsible for bioactivity pertaining to metabolic inflammations. GC–MS analysis has revealed the presence of 62 bioactive compounds in the ethanolic leaf extract of *A. indica*. Most of the compounds in the list have been indicated as good source of antioxidant. Further studies are needed for the isolation and identification of individual compounds from the plant crude extracts also in vivo studies are mandatory for better understanding of their mechanism of action as antioxidant along with their ADMET pharmacoinformatics.

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Table 1 Phytochemical screening of leaf extracts of *A. indica*

Phytochemical Class of Compounds	LEEAI	LAEAI
Alkaloids	++	–
Anthraquinones	–	+
Carbohydrates	+	+
Cardiac Glycosides	–	–
Coumarins	–	+
Flavonoids	+	–
Phenols	+	–
Proteins	+	+
Quinones	–	–
Saponins	+++	+++
Steroids	–	–
Tannins	–	–
Terpenoids	+	+

Table 1 GCMS analysis of Ethanolic Leaf Extracts of *Azadirachta indica*

SNO	RT	IUPAC name of compound	MF	MW	Area %
1.	6.85	Thiazole, 4,5-dihydro-2-methyl-	C_4H_7NS	101.170	0.3631
2.	8.00	2-Hexenoic acid	$C_6H_{10}O_2$	114.1424	0.4441
3.	10.43	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	$C_6H_8O_4$	144.1253	4.1847
4.	10.88	Isopropyl isothiocyanate	C_4H_7NS	101.170	0.2569
5.	11.42	N-Aminopyrrolidine	$C_4H_{10}N_2$	86.1356	0.2128
6.	11.76	Benzofuran, 2,3-dihydro-	C_8H_8O	120.1485	0.4228
7.	12.04	2(1H)Pyrimidinone,4-amino-1,N-dimethyl-	$C_6H_9N_3O$	139.1552	0.1826
8.	12.23	2,6-Octadienal, 3,7-dimethyl-, (Z)-	$C_{10}H_{16}O$	152.2334	0.1549
9.	12.47	Geraniol OR 2,6-Octadien-1-ol, 3,7-dimethyl-, (E)-	$C_{10}H_{18}O$	154.2493	0.2256
10.	13.42	Malic Acid	$C_4H_6O_5$	134.0874	0.3247
11.	13.67	2-Methoxy-4-vinylphenol	$C_9H_{10}O_2$	150.1745	0.2593
12.	15.56	1H-Cycloprop[e]azulene, 1a,2,3,4,4a,5,6,7b-octahydro-1,1,4,7-tetramethyl-, [1aR-(1a.alpha.,4.alpha.,4a.beta.,7b.alpha.)]-	$C_{15}H_{24}$	204.3511	0.2434
13.	15.75	trans-Cinnamic acid	$C_9H_8O_2$	148.1586	0.1914
14.	15.94	.gamma.-Elemene OR γ-Elemene	$C_{15}H_{24}$	204.3511	0.2789
15.	17.96	L-Proline, 1-acetyl-	$C_7H_{10}NO_3$	156.1592	0.1632
16.	18.08	Dodecanoic acid	$C_{12}H_{24}O_2$	200.3178	0.1893
17.	18.19	Cyclohexane, 1-ethenyl-1-methyl-2-(1-methylethenyl)-4-(1-methylethylidene)-	$C_{15}H_{24}$	204.3511	0.3327
18.	18.78	Carbamic acid, methylphenyl-, ethyl ester	$C_{10}H_{13}NO_2$	179.2157	0.4281
19.	20.22	.beta.-D-Glucopyranoside, methyl	$C_7H_{14}O_6$	194.1825	0.3267
20.	21.54	Sorbitol	$C_6H_{14}O_6$	182.1718	0.2506
21.	22.53	Galactitol	$C_6H_{14}O_6$	182.1718	0.2716
22.	23.91	Palmitoleic acid	$C_{16}H_{30}O_2$	254.4082	0.2894
23.	24.33	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256.4241	7.4241
24.	24.63	Hexadecanoic acid, ethyl ester	$C_{18}H_{36}O_2$	284.4772	2.0398
25.	25.54	Heptadecanoic acid	$C_{17}H_{34}O_2$	270.4507	0.1899
26.	25.80	3-Heptanol, 3,5-dimethyl-	$C_9H_{20}O$	144.2545	0.4054
27.	26.31	Phytol	$C_{20}H_{40}O$	296.5310	21.563
28.	26.71	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	$C_{18}H_{30}O_2$	278.4296	15.7212
29.	26.89	Octadecanoic acid	$C_{18}H_{36}O_2$	284.4772	2.5401
30.	27.25	Octadecanoic acid, ethyl ester	$C_{20}H_{40}O_2$	312.5304	0.3292
31.	28.06	1-Heneicosyl formate	$C_{22}H_{44}O_2$	340.5836	0.2169
32.	29.28	Eicosanoic acid	$C_{20}H_{40}O_2$	312.5304	0.6416
33.	30.78	Cyclotetradecane, 1,7,11-trimethyl-4-(1-methylethyl)-	$C_{20}H_{40}$	280.5316	0.2073
34.	30.82	Eicosane	$C_{20}H_{42}$	282.5475	0.2459
35.	30.96	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	$C_{19}H_{38}O_4$	330.5026	2.0186
36.	31.07	Glycerol 1-palmitate	$C_{19}H_{38}O_4$	330.5026	0.2548
37.	31.41	Bis(2-ethylhexyl) phthalate	$C_{24}H_{38}O_4$	390.5561	0.2199
38.	31.55	Docosanoic acid	$C_{22}H_{44}O_2$	340.5836	0.2299
39.	31.87	Nonadecanoic acid, ethyl ester	$C_{21}H_{42}O_2$	326.5570	0.6983
40.	32.64	Cyclopentadecanone, 2-hydroxy-	$C_{15}H_{28}O_2$	240.3816	0.2932
41.	32.70	9,12,15-Octadecatrienoic acid, ethyl ester, (Z,Z,Z)-	$C_{20}H_{34}O_2$	306.4828	0.2054
42.	32.95	Ethanol, 2-(octadecyloxy)-	$C_{20}H_{42}O_2$	314.5463	5.8689
43.	33.01	Linolenic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (Z,Z,Z)-	$C_{21}H_{36}O_4$	352.5081	4.9763
44.	33.17	Benzene, 1,2-dimethoxy-4-nitro-	$C_8H_9NO_4$	183.1614	0.8062
45.	33.48	Fumaric acid, pent-4-en-2-yl tridecyl ester			0.5631
46.	33.96	Octacosane	$C_{28}H_{58}$	394.7601	2.3197
47.	34.31	Squalene	$C_{30}H_{50}$	410.7180	0.1787
48.	34.96	Nonacosane	$C_{29}H_{60}$	408.7867	3.6131
49.	35.19	Octacosyl acetate	$C_{30}H_{60}O_2$	452.7962	0.1721
50.	35.25	1-Nonadecene	$C_{19}H_{38}$	266.5050	0.2752
51.	35.91	Tetracosane	$C_{24}H_{50}$	338.6538	3.7204
52.	36.14	Triacontyl acetate	$C_{32}H_{64}O_2$	480.8494	0.2446
53.	36.50	.gamma.-Tocopherol	$C_{28}H_{48}O_2$	416.6795	0.1834
54.	37.29	Vitamin E	$C_{29}H_{50}O_2$	430.7061	0.9945
55.	37.81	Octadecane	$C_{18}H_{38}$	254.4943	3.0663

56.	38.36	Campesterol	$C_{28}H_{48}O$	400.6801	0.4544
57.	38.74	Stigmasterol	$C_{29}H_{48}O$	412.6908	0.8867
58.	39.46	gamma-Sitosterol	$C_{29}H_{50}O$	414.7067	2.0986
59.	40.21	Eicosane	$C_{20}H_{42}$	282.5475	2.2165
60.	40.48	4,22-Stigmastadiene-3-one	$C_{29}H_{46}O$	410.6749	0.4248
61.	41.36	Stigmast-4-en-3-one	$C_{29}H_{48}O$	412.6908	0.7263
62.	41.93	Cannabidiol	$C_{21}H_{30}O_2$	314.4617	0.7689

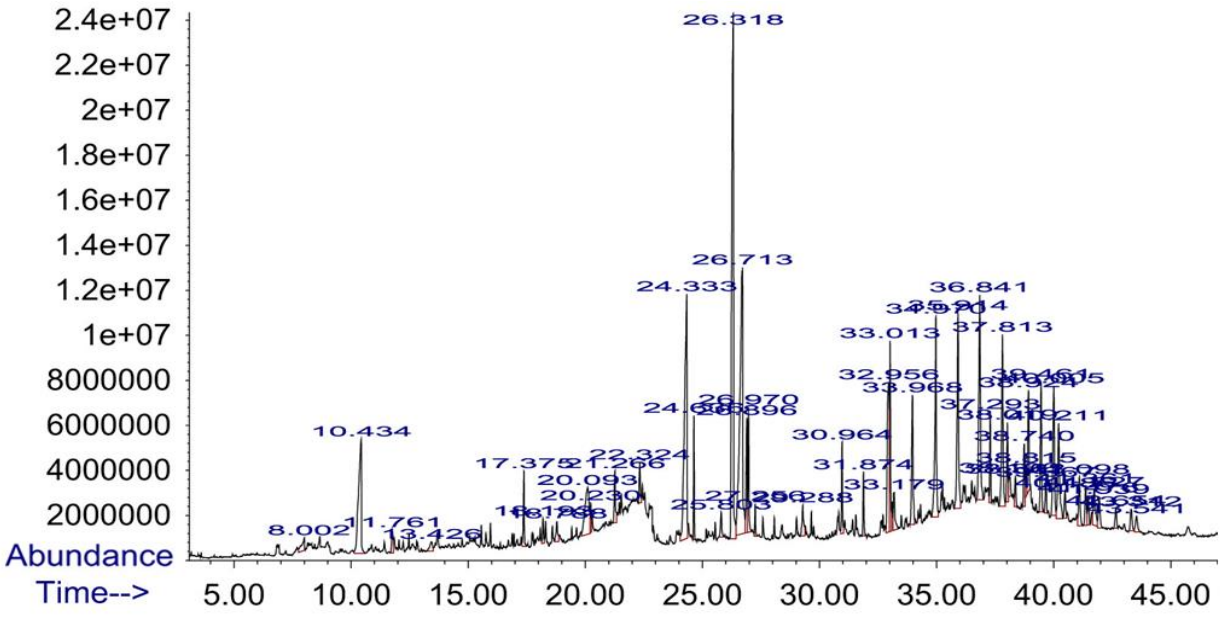

Fig. 1 GCMS Profile of Bioactive Phytoconstituents in ethanolic extracts of *A. indica*

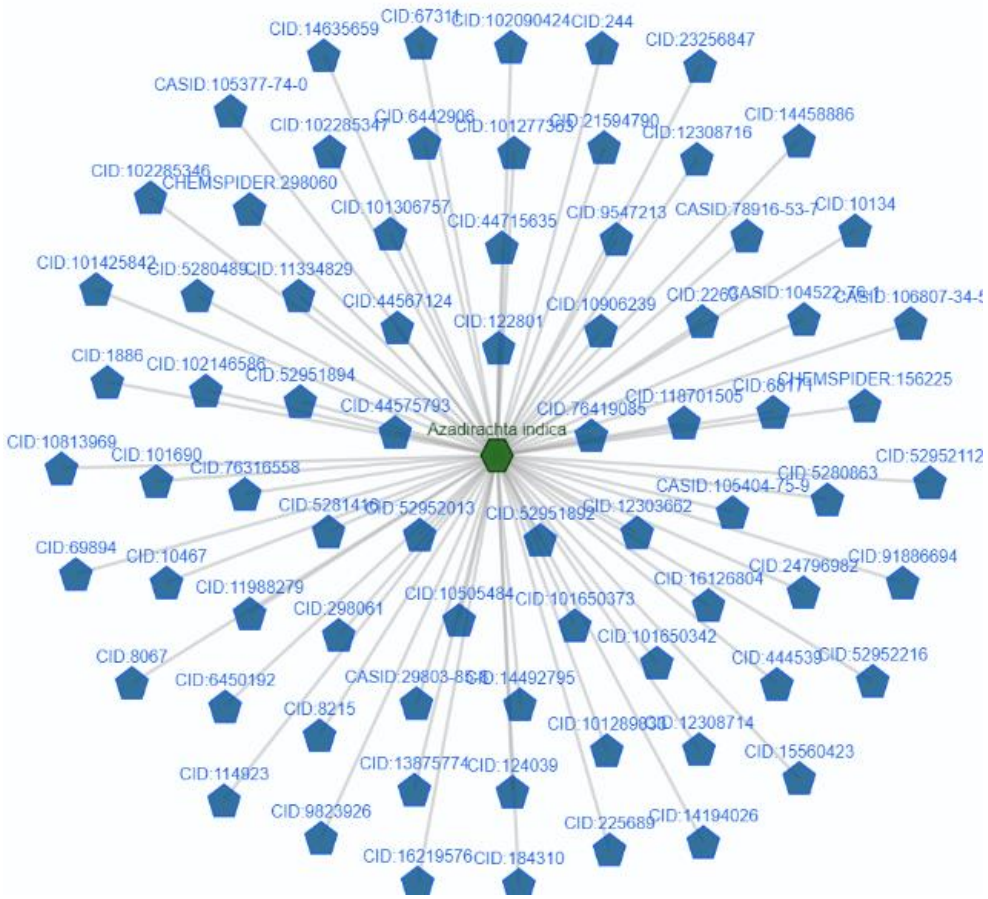

Fig. 2 Cytoscape Network of Phytoconstituents of *A. indica* with therapeutic potential