**Review of Literature**

The family Lauraceae commonly called Laurel family, comprising about 55 genera with 3000 species is distributed world-wide, mostly in warm temperate or tropical regions, prominently in Southeast Asia and South America (Mabberley, 2008; Bhuniya *et al.*, 2010a).

The systematic relationships within the Litsea complex of family Lauraceae, consists of *Litsea, Lindera, Neolitsea, Actinodaphne, Dodecadenia, Alseodaphne, Parasassafras, Sinosassafras, Umbellularia* and *Laurus*. The cladogram highlights the general integration of *Litsea* and *Lindera* and show that most genera in the complex are polyphyletic (Li and Christophel, 2000).

*Litsea* is one of the largest genus of the family Lauraceae. The genus *Litsea* consists of more than 300 species distributed in tropical Asia and in islands of Australia, New Zealand, North and Central America and form an important component of tropical forests (Ngernsaengsaruay *et al.*, 2011). In India, there are 45 species of *Litsea* found growing in the evergreen or semi-evergreen forests at the elevation of 2000-3650 m and richly distributed in north-eastern states and Western Ghats (Table 1). Of the 45 species, four are endemic to north-east India and 14 are endemic to peninsular India including Western Ghats (Bhuniya *et al.*, 2010b). 12 of the 45 species are found in Karnataka with species diversity of *L. floribunda* high in Western Ghats and Madikeri (Saldanha 1996; Srinivas and Krishnamurthy 2016b).
Table 1. Distribution of *Litsea* species in India

<table>
<thead>
<tr>
<th>Species</th>
<th>Distribution of forest types</th>
<th>Location</th>
<th>Reference</th>
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<tr>
<td><em>Litsea assamica</em> Hook.</td>
<td>Evergreen forests and low hills of north-eastern India</td>
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<td>Bhuniya <em>et al.</em>, 2010a and Singh, 2015a</td>
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<tr>
<td><em>Litsea beddomei</em> Hook.</td>
<td>Evergreen forests</td>
<td>Kerala and Tamil Nadu</td>
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<td><em>Litsea coriacea</em> (Nees) Hook.</td>
<td>Evergreen and mixed forests of Western Ghats</td>
<td>Maharashtra, Goa, Karnataka, Kerala and Tamil Nadu</td>
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<tr>
<td><em>Litsea membranifolia</em> Hook.</td>
<td>Sub-tropical forests of North-east India</td>
<td>Arunachal Pradesh and Nagaland</td>
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<tr>
<td><em>Litsea mishmiensis</em> Hook.</td>
<td>Sub-tropical forests - Mishmi Hills of North-east India</td>
<td>Arunachal Pradesh</td>
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<td><em>Litsea oleoides</em> (Meisn.) Hook.</td>
<td>Evergreen forests of Western Ghats</td>
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<tr>
<td><em>Litsea oreophila</em> Hook.</td>
<td>Sikkim Himalayas on rocky soil in Sikkim</td>
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<td><em>Litsea stocksii</em> (Meisn.) Hook.</td>
<td>Deciduous, semi-evergreen and evergreen forests of Western Ghats</td>
<td>Maharashtra, Goa, Karnataka, Kerala and Tamil Nadu</td>
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<td><em>L. wightiana</em> (Nees) Benth. and Hook.</td>
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<td><em>Litsea mysorensis</em> Gamble</td>
<td>Evergreen and mixed forests of Western Ghats</td>
<td>Karnataka, Kerala and Tamil Nadu</td>
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<td><em>Litsea laevigata</em> (Nees) Gamble</td>
<td>Evergreen and mixed forests</td>
<td>Karnataka, Kerala and Tamil Nadu</td>
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<td><em>Litsea nigrescens</em> Gamble</td>
<td>Evergreen forests of Western Ghats</td>
<td>Kerala and Tamil Nadu</td>
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<td><em>Litsea floribunda</em> (Bl) Gamble</td>
<td>Evergreen and semi-evergreen forests of Western Ghats</td>
<td>Maharashtra, Karnataka, Kerala and Tamil Nadu</td>
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<tr>
<td><strong>Litsea ghatica</strong> C. J. Saldanha</td>
<td>Evergreen and semi evergreen forests of Western Ghats</td>
<td>Maharashtra, Karnataka, and Kerala</td>
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<td><strong>Litsea travancorica</strong> Gamble</td>
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<td><strong>Litsea keralana</strong> Kost.</td>
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<td><strong>Litsea cubeba</strong> (Loureiro) Pers.</td>
<td>Evergreen forests</td>
<td>Arunachal Pradesh, Assam, Meghalaya, West Bengal and Sikkim</td>
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<tr>
<td><strong>Litsea elonagata</strong> (Nees) Hook.</td>
<td>Mahananda Wild Life Sanctuary</td>
<td>Arunachal Pradesh, Assam, West Bengal, Himachal Pradesh and Sikkim</td>
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<tr>
<td><strong>Litsea glutinosa</strong> (Loureiro) C.B. Rob.</td>
<td>Semi-evergreen forests of Eastern Ghats</td>
<td>Arunachal Pradesh, Assam and Andhra Pradesh</td>
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**Ethnomedicinal uses of the family Lauraceae**

Healing with medicinal plants is as old as mankind itself. The connection between man and his search for drugs in nature dates from the far past, of which there is ample evidence from various sources: written documents, preserved monuments, and even original plant medicine (Petrovska, 2012). As per the report of World Health Organization (WHO), nearly three fourth of the world’s population depends on plants for their preliminary health care medicines. Some 14–28% of the total number of plant species estimated (250,000) to occur around the world are used as medicinal plants (Mamedov, 2012).

Plants have formed the basis of traditional medicine practices in China, India, and many other countries. Use of plants as drugs is found in the earliest records like Artharvaveda, which forms the basis for Ayurvedic medicine in India (dating back to 2000 BCE), the clay tablets in Mesopotamia forming the basis for traditional medicine in Mesopotamia, and the Eber Papyrus in Egypt forming the basis for traditional medicine in Egypt. Other popular literature sources on medicinal plants
include – “De Materia Medica”, and “Pen Ts‘ao Ching Classic of Materia Medica”. Plant-based traditional medicines or phytotherapeutics usage is increasing steadily over years and they are often termed complementary or alternative medicine (CAM) in developed countries (www.science20.com/news_articles/herbal_dietary_supplement).

The following genera of family Lauraceae include best known species with commercial value; *Cinnamomum*: Cinnamon and Camphor Laurel, *Laurus*: Bay Laurel, *Lindera*: Spice bush, *Persea*: Avocado, *Sassafras* and *Litsea*. There are three main economical uses for this family. A high content of essential oils are found in many that are important for spices and perfumes. Avocados are important oil-rich fruits, and many are used as medicinal plants but are in danger of extinction due to over exploitation as medicinal plants because of their unique phytochemistry. Many genera of Lauraceae like *Persea*, *Cinnamomum*, *Ocotea*, *Litsea*, and *Nectandra* have been proved as plants of high medicinal value.

The leaf, bark, fruit, seed and flower extracts of Lauraceae have been used in traditional medicine from ancient times for relieving pain, wound healing, arousing sexual power, diarrhea, dysentery, antidote for snake bite, in treating rheumatism, sprains, bruises, paralysis, mental disorders like hysteria, in treating cough and bronchitis as expectorant and to promote digestion (Lohita *et al.*, 2010a).

*Persea americana* commonly known as avocado is a valuable species within the Lauraceae family. It is low in sugar, rich in fats and proteins and highly nutritious, providing lot of vitamins A, B, C, D, and E. Avocados have been eaten by humans for at least ten thousand years. The stem bark, fruit and leaf of *P. americana* are used in traditional medicine in South America, West Indies and Africa for the treatment of ailments such as menorrhagia, blood pressure, stomach pain, bronchitis, diarrhoea, and diabetes (Adeyemi *et al.*, 2002; Lawal *et al.*, 2010). The leaf paste of *P. macrantha* (Nees) Kosterm, improves hair growth and cooling sensation (Girishkumar *et al.*, 2014).

*Cassytha filiformis* is a traditional remedy for cancer, various human birthing issues, kidney ailments, in the treatment of gonorrhoea, eczema, urethritis, dysentery and as a diuretic. It is medicinally used as an antiplatelet, vasorelaxant,
alphaadrenoreceptor and as antitrypanosomal agent (Jain and Srivastava, 2005; Mythili et al., 2011). Decoction of *C. filiformis* in northern Thailand is used in the treatment of jaundice (Tangjitman et al., 2015).

The genus *Cinnamomum* exhibits number of biological activities validating their use in traditional medicine. Crude extracts and constituents from about 30 species of *Cinnamomum* displayed significant antibacterial, antifungal, antiseptic, antiviral, anti-inflammatory, antipyretic, antioxidant, chemopreventive, cytotoxic, antidiabetic, hypolipidemic, antispasmodic, antiulcer, antiplatelet, anodyne, choleretic, immunostimulant, anaesthetic and sedative activities (Balijepali et al., 2016). The essential oil, aqueous/alcoholic extracts, cinnamaldehyde and proanthocyanidins were reported to be mainly responsible for biological activities displayed by *Cinnamomum*. The decoction of stem bark of *C. cerum* Presl. is taken internally to treat cough, dysentery and to keep the body cool (Muthu et al., 2006). *C. zeylanicum* bark and oil is used in the treatment of bronchitis, asthma, cardiac disorder and fever. *C. assamicum* leaf and bark paste is applied locally for the treatment of scabies (Purkayastha and Nath, 2006). *C. camphora* is used in the traditional medicine for inflammation related diseases such as rheumatism, sprains, bronchitis and muscle pains (Lee et al., 2006). *C. tamala* Nees & Eberm. is used in treating cough, cold, bronchitis, asthma, tuberculosis and menstrual disorders (Singh, 2015b).

*Laurus nobilis* commonly called Bay tree is used for the treatment of bronchitis and influenza. Leaves have antiseptic, narcotic and stimulant properties in folk medicine. Fruits are used in the treatment of bruises and sprains. The essential oil from leaves has antimicrobial activity (www.naturalmedicinalherbs.net/herbs/Laurus). The infusion of *L. nobilis* in folk medicine is used as stomachic and carminative for the treatment of gastric diseases (Dall’Acqua et al., 2009).

*L. benzoin* commonly called spice bush is used as a household remedy in the treatment of cold, dysentery and intestinal parasites. The leaves and stem bark are reported to have vermifuge properties, used as diaphoretic, febrifuge, tonic, stimulant, anthelmintic, astringent and diaphoretic, where as the oil from fruits have been used in the treatment of bruises and rheumatism (www.naturalmedicinalherbs.net/herbs/lindera-benzoin=spicebush.php). *Lindera* root is used to treat abdominal pain and hernia in Chinese herbal medicine (www.chineseherbshealing.com/lindera-root).

The inner bark of root of *Sassafras* is used as a stimulant, alterative, diaphoretic and diuretic. It purifies blood, cleanses whole system, will relieve gas, used in the treatment of colic and all types of skin diseases, in kidney and bladder trouble and taken as tonic after child birth. The oil of *Sassafras* acts as excellent painkiller when applied to the aching tooth (www.chineseherbshealing.com/sassafras-root).

**Ethnomedicinal uses of *Litsea* species**

*Litsea*, an important genus of the family Lauraceae comprises 300 species, with 45 found in Indian subcontinent, eight species in China, 12 in Nepal, 11 in Bhutan, six in Bangladesh, Myanmar, four in Sri Lanka and two in Pakistan (Bhuniya *et al*., 2010a).

Seeds of *L. cubeba* are eaten raw to promote digestion and to treat cough and bronchitis, as an expectorant in China, where as bark and leaf decoction is taken to cure mental disorders like hysteria and forgetfulness (Perry, 1980). Decoction of *L. cubeba* fruit is given orally in colic and heart diseases and its stem bark paste is applied in scabies and eczema (Nath, 1996). Plant extract is used to treat athlete's foot and other skin diseases in Taiwan, where as in Indonesia, fruits are used as substitute of cubeb piper, *Piper cubeba* L. (Oyen and Dung, 1999). *L. cubeba* decoction of fruit is given orally in colic and heart diseases and paste of the stem bark is applied in case of scabies and eczema (Bhuniya *et al*., 2010b).

Plant parts of the genus *Litsea* are used in traditional medicine. *L. cubeba* seeds are eaten in China to promote digestion, as expectorant where as, leaf and stem decoction is used to cure mental disorders like hysteria and forgetfulness (Bhuniya *et al*., 2010c). *L. liuyingi* H. Liu leaves and bark are used to treat leucorrhoea. *L. wightiana* (Nees) Hook. f. leaf improves hair growth, cleanses hair and cooling
sensation. *L. floribunda* (Bl.) Gamble and *L. coriacea* Heyne ex Meisner Hook. f. leaf improves hair growth, cleanses hair and provides cooling sensation (Hossan *et al.*, 2010; Girishkumar *et al.*, 2014).

Ghosh and Sinha (2010) reported that, the powdered bark and roots of *L. polyantha* Juss. is used to treat pains, bruises, and for fractures in animals by the traditional healers of Oraon and Munda community of Jharkhand. *L. glaucescens* infusion is used for the treatment of diarrhoea, vomit, pain in the bones, to treat anger, sadness and nervousness. *L. guatemalensis* leaves are used to treat fever, headache, diarrhea, vomit, arthritis, fever, chill, pain in case of fractures etc. *L. nessiana* leaves are in treating fever and throat infection where as, *L. parvifolia* infusion is used against gastric problems (Jumenez-Perez *et al.*, 2011).

Bark, fruit, root, flower and wood of *L. chinensis* are used as medicine since ancient times. Decoction of these parts is used to cure burns, sprains, indigestion, cough, infection, wound healing and diarrhoea amongst tribal people of Assam and Arunachal Pradesh. Meghalayan tribal people use bark and leaf for wound healing (Bhatt and Pandya, 2012a). *L. gaucescens* is used in Mexican traditional medicine for treating sadness, the essential oil of this species has antidepressant like activity (Guzman-Gutierrez *et al.*, 2012). Fresh paste of bark from *L. monopetala* (Roxb.) Pers. is used as a plaster for cattle fractures (Chandra *et al.*, 2013).

*L. glutinosa* bark is used in healing of wound, dysentery, inflammation, skin diseases and in sprains. Leaf is used in cold, as emollient, antispasm, in nervous attack, headache, emmenagogue, intestinal parasites. Stem is used in bone fractures, inflammation, dysentery and sprains (Jain and Srivastava, 2005). *L. glutinosa* leaf paste mixed with turmeric rhizome is applied for 3-4 days in case of bone fracture or muscle pain (Majumdar *et al.*, 2006). *L. glutinosa* stem bark paste is plastered on the fractured bone with the help of a piece of cloth for about 10-15 days (Behera *et al.*, 2006). The bark and leaves of *L. glutinosa* are used as demulcent, mild astringent, antispasmodic, emollient, in the treatment of diarrhoea and dysentery, in treating muscular bleeding, in wound healing process and also for the treatment of spontaneous and excessive flow of semen in young boys in traditional medicine. The roots of *L. glutinosa* are used to poultice sprains and bruises. The leaf paste of *L. glutinosa* is applied to get relief from respiratory diseases (Pattnaik *et al.*, 2009;
Pradeepa et al., 2011; Bhowmick et al., 2014). It is reported that the bark of *L. glutinosa* is one of the most popular native drugs capable of relieving pain, arousing sexual power, good for stomach and used in the treatment of gonorrhea, to produce soothing effect on the body, arrest bleeding and also as demulcent and emollient ((Lohita et al., 2010b; Hosmath, 2011). *L. glutinosa* stem bark is used in treatment of bone fractures, inflammation, sprains, wound healing where as leaf is used in the treatment of cold, cough, diarrhea, as antispasm, in nervous attack, in sore throat and as emmenagogue (Ambasta, 1986; Ramana and Raju, 2017).

Species of *Litsea* is used in traditional medicines for the treatment of various gastrointestinal disorders, inflammation, arthritis, traumatic injury, central nervous system disorders (Kong et al., 2015).

**Phytochemistry of family Lauraceae**

Phytochemicals are defined as ‘non-nutritive plant chemicals that have protective or disease preventive properties’. Though phytochemicals are nonessential nutrients, they are required for sustaining human life and have potential health benefits (www.phytochemicals.info).

Plant secondary metabolites are an important group of phytochemicals which include alkaloids, cyanogenic glycosides, glucosinolates, flavonoids, saponins, steroids and terpenoids that help in protecting plants against pathogens, pests and environmental stress. Phytochemicals have health benefits like antioxidant, anti-inflammatory, antimicrobial, cancer preventive, antidiabetic, antihypertensive, antidepressant, nootropic and other biological properties (Maobe et al., 2012).

Essential oils, terpenoids, benzyl benzoates, and propenilfenols are found widely distributed in the family Lauraceae. Lignans, neolignans and flavonoids such as s-methyl 5-O, proanthocyanidins, cinamoilamidas, estirilpironas, polyketides (acetogenins), furanosesquiterpenes and sesquiterpenes are reported in *Litsea* species. Lactones reported are: germanacrolidous, elemanolidous, eudesmanolidous and guayanolidous. These phytochemicals found in Lauraceae have a wide range of biological properties such as antioxidant, anti-inflammatory, anti-feedant and antimalarial activities (Wang et al., 2010b).
The traditional medicinal applications of the *Cinnamomum* species have inspired many pharmacological investigations. The ethanolic, methanolic and aqueous extract of stem bark of *C. zeylanicum* showed the presence of phenolic compounds and exhibited antioxidant activity measured with linoleic acid system (Mancini-Filho *et al.*, 1998). Hot water and ethanolic extracts of *C. cassia* showed a greater inhibition than alpha-tocopherol on FeCl$_2$-ascorbic acid induced lipid peroxidation of liver homogenate in Winstar rats (Lin *et al.*, 2003). The leaf methanolic extract of *C. tamala* exhibited good radical scavenging activity comparable to butylated hydroxyl toluene (BHT) (Devi *et al.*, 2007). *C. camphora* methanolic extracts exhibited antibacterial and antifungal activities against *Escherichia coli*, *Shigella flexenari*, *Staphylococcus aureus*, and *Yersinia aldovae* (bacteria) and *Saccharomyces cerevisiae*, *Aspergillus parasiticus*, *Trichophyton rubrum*, and *Candida* (fungi) (Jagtap *et al.*, 2014). The essential oils extracted from the leaves, bark, stems and roots of *C. zeylanicum*, *C. burmannii* and *C. iners*, were analyzed by Gas Chromatography-Mass Spectroscopy (GC-MS). The major chemical compositions in *C. zeylanicum* were eugenol, camphor, tetradecanal and cinnamyl acetate. The chemical compositions in the oils of *C. burmannii* were rich in benzyl benzoate, (+)-2-bormanone, tetradecanal and caryophyllene. *C. iners* was having (+)-2-bormanone and hexadecanoic acid as the major compounds (Hasan *et al.*, 2009). Cinnamon is used as a traditional medicine to control blood pressure, tumor growth, diabetes, Alzheimer’s and Parkinson’s diseases with main bioactive compounds being polyphenols and cinnamaldehyde (Rebeiroyo-Santos *et al.*, 2017).

The *in-vitro* anti-inflammatory effects of seven known lignans and one dihydrochalcone isolated from *Pleurothyrium cinereum* and *Ocotea macrophylla* have been proved to be anti-inflammatory compounds. Chemicals like alkaloids, flavonoids, sesquiterpenoids, lignans, and essential oils have been extracted from this genus with proven bioactivities like antiinflammatory and antioxidant etc. Three active compounds namely asarone, galgravin and veraguensis isolated from crude leaf extract of *Nectandra megapotamica* have been proved to be analgesic and anti-inflammatory (Filho *et al.*, 2004; Coy-barrera and Cuca-suarez, 2011). Two flavonol glycosides namely rhamnosylquercetine and rhamnosylaempferol have been extracted from *N. grandiflora* with antioxidant activity (Filho *et al.*, 2006).
The essential oil of *Ocotea* fruit exhibited *in vitro* antioxidant property in 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay. It also exhibited antibacterial and antifungal activity (Bruni *et al*., 2004). Forty four compounds were identified from the essential oils in fruit calyces of *Ocotea quixos* by GC-MS analysis with main components transcinnamaldehyde (27.9%), methylcinnamate (21.6%), 1,8-cineole (8.0%), benzaldehyde (3.6%), and b-selinene (2.1%). The aqueous extract of *Lindera strychnifolia* has potent antioxidant activity as it exhibited potent scavenging activity against reactive oxygen species, reactive nitrogen species in DPPH and Nitric oxide (NO) assays (Noda and Mori, 2007). The essential oils from the leaf of *L. strychnifolia* exhibited strong *in vitro* cytotoxicity in three human cancer cell lines - A549, HeLa and Hep G2 in a modified MTT assay and antibacterial activity against *Staphylococcus aureus* in agar disc diffusion method. The constituents of the essential oils from the leaves of *L. strychnifolia* were analyzed by GC-MS (Yan *et al*., 2009). Furanodienone and curzerenone identified in the leaf essential oil of *L. pulcherrima*, exhibited good radical scavenging activity in DPPH assay and also potential antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* (Joshi and Mathela, 2012).

Lin *et al.* (2007) reported that *Neolitsea parvigemma* has strong antioxidant activity with IC$_{50}$ value of 5.73 µg/ml in the DPPH assay. Phytochemical screening of *Laurus nobilis* with semipreparative HPLC resulted in the isolation of 10 flavonoids which exhibited antioxidant activity in two *in vitro* assays-Briggs-Rauscher oscillating reaction test and Trolox equivalent antioxidant capacity test (Dall’Acqua *et al*., 2009). Phytochemicals like alkaloids, terpenoids, glycosides, flavonoids, coumarins were extracted from the aqueous and methanolic extract of leaf and fruits of *Persea americana* exhibiting diverse biological activities like analgesic, anti-inflammatory, antifungal, hypotensive, hepatoprotective, wound healing effects and antioxidant activities (Yasir *et al*., 2010).

A dichloromethane extract of stem bark of *Cryptocarya nigra* exhibited strong *in vitro* inhibition of *Plasmodium falciparum* with high antioxidant activity in DPPH assay and ferrous reducing ability of plasma (FRAP) assays. A phytochemical study on dried bark of *C. nigra* was known to contain alkaloids, -N-methylisococlarine, atherosperminine and 2-hydroxyatherosperminine which may be responsible for
strong inhibition of *in vitro* growth of a chloroquine resistant strain of *Plasmodium falciparum* (Nasrulla *et al.*, 2013).

A sesquiterpene - Isolinderalactone showed antitumour activity *in vitro* against tumor cells like “KB, P-388, A-549 and HI-29”. B-caryoplyllene and a-cardinal present in the essential oil extracted from the leaf of *Neolitsea variabililima* exhibited anti-cancer activity in HeLa cell with an IC₅₀ value of 4.0 µm (Su *et al.*, 2013). Genus *Neolitsea* is rich in sesquiterpenes, flavonoids, triterpenes, alkaloids, steroids and essential oils exhibiting biological activities like antioxidant, antibacterial, vasoconstricting, antitumour, anti-inflammatory and cytotoxicity. A sesquiterpene - Neoliacine isolated from the leaves of *N. aciculata* exhibited cytotoxic activity *in vitro* in HeLa cell culture (Qing *et al.*, 2014).

**Phytochemistry of Litsea species**

Extensive phytochemical work has been done on different species of *Litsea* such as *L. cubeba, L. polyantha, L. japonica, L. acutineva, L. cassiaeefolia, L. rotundifolia, L. monopetala, L. grandis, L. akoensis, L. glutinosa, L. pungens, L. deccanensis, L. guatemalensis, L. laevifolia, L. laeta, L. verticillata and L. pallidofolia* by extracting, characterizing and reporting their bioactivities.

The bark of *L. cubeba* yielded many compounds namely a-pinene, camphene, P-pinene, limonine, citronellol, linalool, geraniol, citral-a and b of which the major compound is citral. Essential oils from fruits on distillation yielded a pale yellow essential oil, containing citral, methyl heptenone, d-limonine, I-sabinene and terpenes and lauric acid. Distillation of plant parts yielded a yellow coloured oil with fresh lemony fragrance and contained essential oil cis-a-ocimene (25.11 %), 3,7-dimethyl-1,6-octadiene-3-ol (16.85%) and trans-nerolidol (13.89%) that finds its use in aromatherapy (Chopra *et al.*, 1956).

Previous phytochemical studies have indicated that *Litsea* species contain a number of biologically active compounds such as alkaloids, flavonoids, terpenoids and fatty acids (Agarwal *et al.*, 2011). An alkaloid isolated from the bark of *L. laeta* was identified as 2-hydroxy-1-methyl 10, 11-methylenedioxy noraporphine. N, O-Dimethylharnovine and glaucine were isolated from the bark of *L. laeta* and alkaloids dicentrinone and nordecentrine from the leaves of *L. salicifolia* (Rastogi and Borthakur, 1980). Alkaloids such as vilastonine, oxycanthine and barberine were
isolated from *L. pallidifolia* which proved to have strong antimalarial activities (Congdon *et al.*, 1981). Six new lactones from *L. japonica* namely litsenolide D₁, litsenolide D₂, litsenolide D₃, litsenolide E₁, litsenolide E₂, hamabiwalactone A and hamabiwalactone B were isolated whose structures were elucidated on the basis of spectroscopic evidence (Tanaka *et al.*, 1989). A novel phenanthrene alkaloid lитеbaine, was isolated from the woods of *L. cubeba*. The structure of the compound was elucidated by spectral analysis (Wu *et al.*, 1991).

Hakim *et al.* (1993) isolated sesquiterpenes namely isocurcumol and diepoxygermacranolide from *L. cassiaefolia* and Valene-1(10)-ene-8,11-dol from *L. excelsa* and their structures have been determined by X-ray crystallographic methods. Quaternary alkaloids were isolated using centrifugal partition chromatography and ion-pair reversed phase from *L. cubeba*, with their structural elucidation done by spectral analysis. Lee *et al.* (1996) isolated two quaternary alkaloids were isolated from *L. cubeba* namely, litcubine A and B and their structures were elucidated by spectral analysis and chemical correlation.

*L. cubeba* and *L. glutinosa* fruits, flowers and bark are rich in essential oils (Choudhary *et al.*, 1996, 1997; Wang *et al.*, 1999; Amer and Melhorn, 2006). The bark of *L. akoensis* is rich in butanolides, coumarin and syringaldehyde (Tsai *et al.*, 2000). The biological activity of the extracts of *L. acutineva* were studied and further investigated with bioassay guided fractionation procedures for the isolation and identification of active principles (Ahmad, 2000). The isolated alkaloids oxycanthine and obaberine of *L. acutineva* are reported to have anti-malarial activity. *L. rotundifolia var. oblongifolia* showed the presence of 37 constituents in the essential oil of roots with terpenoids and alkaloids as the major compounds (Yan *et al.*, 2000).

Cheng *et al.* (2001) reported the presence of butanolides in the leaves of *L. acutineva*. Six new compounds, including one nor-neolignan and five butanolides, litseakolide D, E, F, G and isolincomolide D were isolated from the leaves and their structures were elucidated from spectral analysis. Min *et al.* (2003) isolated two lactones, litsealactone A and B, from the leaves of *L. japonica* with known three lactones. Of these, Hamabiwalactone B and akolactone B exhibited significant anti-complement activity in *in vitro* anti-complement assay, with IC<sub>50</sub> values of 149 and 58 M respectively. Six sesquiterpenes and five butanolides were isolated from the leaves.
of *L. verticillata* (Zhang et al., 2005), of which three sesquiterpenes; isolitseanes A, B, C were new and the other three were known sesquiterpenes. New isolitseanes were identified as oxyphyelodiol B,1,2,3,4-tetrahydro-2,5-dimethyl-8-(1-methyl-ethyl)-1,2-naphthaleinediol and chromolaevanediol. One novel butanolide: litseabutenolide isolated was structurally elucidated based on spectroscopic studies such as 1D-NMR analyses. A new acetylenic ketone: 13-tetradecyn-2 was isolated from the stem bark of *L. rotundifolia* var. *oblongifolia*. *L. coreana* (Zhao et al., 2005) and Lee et al. (2005) reported flavonoids in the leaves of *L. japonica*.

A new diol, oblongifolinol was isolated from the stem bark of *L. rotundifolium* (Zhao et al., 2006) with its structural elucidation done by spectroscopic methods. Arfan (2006) isolated four phenolic compounds from the bark extracts of *L. monopetala* and the fractions were evaluated for antioxidant, antiradical scavenging and reducing power activities. The analysis of essential oils extracted from *L. cubeba* by gas chromatography-mass spectrometry led to identification of 16 compounds of which geranial, eugenol, isoeugenol and methyl isoeugenol were tested for nematicidal activity (Park et al., 2007). A new butanolide - acutilactone and a new lactone-4-nonacosyl-dihydroxyfuran were isolated from the chloroform and n-hexane fractions of the leaves of *L. acutivena* along with 15 known compounds (Tsai et al., 2007).

Chang et al. (2008b) isolated three new racemic butanolides, majorenolide majorynolide, and majoranolide, from the root of *L. akoensis* along with 10 ten known butanolides, litsenolide A2, B2, C1, C2, hamabiwalactone A and B, litseakolide A and B, isoobtusilactone, and obtusilactone; one lignan, (±)-syringaresinol, two flavans, (+)-catechin, and (-)-epicatechin, one coumarin, scopoletin, and four steroids. The structures were elucidated by spectroscopic analysis based on 1D-NMR data. Of these, nine butanolides showed antimycobacterial activities against *Mycobacterium tuberculosis* H37Rv, with MIC values of 15-50 μg/ml.

Two new isoquinoline alkaloids were isolated from *L. cubeba* (Feng et al., 2009), along with 11 known alkaloids from the alkaloid extracts of aerial parts by bioassay fractionation methods. Out of eleven alkaloids, two showed antimicrobial activities and their structures were analysed by spectroscopic methods. A new amide,
N-trans-sinapolymethoxytyramine was isolated from the leaves and twigs of *L. auriculata*, along with three known amides and two known flavanols. The structure was elucidated by spectroscopic analysis (Tanaka et al., 2009). A novel compound aryltetralone lignan was isolated from the leaves and twigs of *L. pedunculata*. The lignan isolated was pedunculine and its structural elucidation was done based on spectral analysis and single crystal X-ray diffraction (Wang et al., 2009).

A flavone glycoside was isolated from *L. glutinosa* C.B. Roxb. (Wang et al., 2010a) with four known compounds. The structure was identified on the basis of spectroscopic analysis. Ghosh and Sinha (2010) identified two compounds for the first time in the bark extracts of *L. polyantha* using GC-MS analysis and reported the presence of eugenol and chalcone and its derivatives which supported the use of *L. polyantha* as an analgesic in the traditional medicine. Ko et al. (2010) extracted essential oils from the fruits of *L. salicifolia* by hydrodistillation method and isolated two major compounds; E-citrol and Z-citrol by GC-MS analysis.

Cheng et al. (2010) isolated a new butanolide - litsealiicolide, along with seven known compounds, linderanolide, isolinderanolide, secolincomolide, secokotomolide, (+)-β-eudesmol, trans-phytol, and (−) matairesinol from the leaf chloroform extracts of *L. lii var. nunkaotahangensis* with their structural elucidation done by spectral analysis. 50-53 compounds were identified in the fruit oil of *L. cubeba*, of which the main compound in the fruit oil was citral and it exhibited cytotoxic activity against human lung, liver and oral cancer cells (Ho et al., 2010). A new C9 monoterpenoid acid ‘litseacubebic acid’ along with three known compounds was isolated with bioassay-guided purification from the fruit extract of *L. cubeba*. The structure of the compound was elucidated by spectral data as 2,6-dimethyl-6-hydroxy-2E,4E-hepta-2,4-diene acid (Yang et al., 2010).

Nadia et al. (2011) isolated alkaloids namely bisbenzylisoquinoline, lancifoliaine from the bark of *L. lancifolia* which showed a moderate vasorelaxant activity on rat aorta. Hasan (2011) extracted essential oils from the leaves, barks, stems and roots of *L. gracilipes* and *L. resinosa* and were analyzed by GC-MS. The chemical composition in the oil of *L. gracilipes* was caryophyllene and spathulenol while the oil of *L. resinosa* contained o-cymene, caryophyllene, and 3-methylacetophenone as the major constituents.
Ciral, lauric acid and oleic acid were isolated from the leaf of *L. chinensis*. Various biological activities such as antioxidant activity, anti-inflammatory and anthelminthic activities are reported from the ethanolic extract of *L. chinensis* (Bhatt and Pandya, 2012b). The essential oil of *L. cubeba* was obtained by hydro distillation and 59 different compounds were identified by GC-MS analysis. The major compounds present in the oils were neral, geranial, α-pinene, methylheptenone, β-myrcene, linalool, citronellal, verbenol, isopulegone, and caryophyllene oxide with citral being the abundant component (Si *et al.*, 2012). Primary phytochemical screening of the methanolic extraction of bark powder of *L. glutinosa* showed the presence of alkaloids, flavonoids, glycosides, phenols, tannins and saponins. The presence of Androstane, Androsta-trione, Thio-coumarin and phytoestrogens justify the aphrodisiac and osteoprotective effect of *L. glutinosa* (Parikh and Rangrez, 2012).

Agarwal *et al.* (2013) isolated four butanolides from the methanolic extract of heart wood of *L. glutinosa*. The isolated new compounds were characterized and structurally elucidated based on the spectral studies. The isolated butanolides are 3R, 4S, 5S-2-hexadecyl-3-hydroxy-4-methylbutanolide, litsealactone C, and litsealactone D and litsealactone. Aporphine alkaloids boldine and laurotetanine were isolated from the crude extract of *L. cubeba* using high-speed counter-current chromatography and the chemical structures were confirmed using electrospray ionization-mass spectrometry, ¹H-NMR and ¹³C-NMR (Sun *et al.*, 2015). Preliminary phytochemical tests showed the presence of flavonoids, coumarins, alkaloids, tannins, terpenoids, anthraquinones, phenols, reducing sugars and carbohydrates in the methanolic extract of powdered leaves of *L. quinqueflora* (Johny and Anilkumar *et al.*, 2015).

37 compounds were identified by the GC-MS analysis in the stem bark essential oil of *L. glutinosa*. Of the 37 compounds, 9, 12-octadecadienoic acid (62.57%), hexadecanoic acid (12.68%), stigmast-5-en-3-ol (6.87%) and vitamin E (2.51%) were the major constituents representing 84.63% of the oil (Arunodaya *et al.*, 2016). Leaf powder of *L. cubeba* rich in linalool was proved to be bactericidal against *Aeromonas hydrophila* when fishes were fed with 4% *L. cubeba* doses by increasing nonspecific immunity of common carp-*Cyprinus carpio* (Nguyen *et al.*, 2016). Plant parts of genus *Litsea* are a rich source of bioactive compounds and nearly 407 secondary metabolites are reported from *Litsea* species with alkaloids, terpenoids,
flavonoids and essential oils showing a wide spectrum of *in vitro* and *in vivo* pharmacological activities like anti-cancer, anti-inflammatory, antimicrobial, antioxidant, antidiabetic, anti-HIV, insecticidal etc (Wang *et al.*, 2016).

Jia *et al.* (2017) reported the presence of polyphenols, essential oils, and numerous flavonoids in phytochemical studies and showed that the compounds exhibit remarkable bioactivities, such as hepatoprotection, anti-inflammation, antioxidation and antibacterial in *L. coreana*. Their study reported the major constituents of phytochemicals as flavonoids.

**Biological activities of *Litsea* species**

Previous reports reveal that the genus *Litsea* exhibits various biological activities such as antioxidant, cardioprotective, analgesic, anti-diarrheal, germicidal, anti-inflammatory, cytotoxic, wound healing, antimicrobial, antimalarial, hepatoprotective and anti-termite and nematicidal activities as represented in Fig. 2.

![Biological activities of Litsea species](image)

**Fig. 2 Biological activities of Litsea species**
Antioxidant activity

Recently, much attention is given to natural antioxidants of plant sources and their association with health benefits as they act as reducing agents, hydrogen donors and singlet oxygen quenchers. The physiological processes taking place in the human body produce free radicals and other reactive oxygen species as byproducts, the overproduction of which cause oxidative damage to biomolecules leading to many chronic diseases, such as cancer, diabetes, ageing, and many other degenerative diseases in humans. Plants contain a wide variety of antioxidants such as phenolic compounds, vitamins, terpenoids and others rich in antioxidant activity. It is reported that many of these antioxidant compounds possess anti-inflammatory, antitumor, anticarcinogenic and antimicrobial activities to a considerable extent (Cai et al., 2004).

Hwang et al. (2005) tested the antioxidant activity of L. cubeba and the results showed that the methanol extract of L. cubeba and its fractions exhibited strong antioxidant activity with scavenging potential having IC$_{50}$ value of 34.22 µg/ml and 176.23 µg/ml for DPPH and H$_2$O$_2$ radicals respectively compared to alpha-tocopherol and ascorbic acid which were used as reference standards.

The four fractions of phenolic compounds isolated from the bark extracts of L. monopetala were separated and evaluated for their antioxidant, antiradical scavenging and reducing power activities (Arfan et al., 2006). Fraction I and II were reported to have strong antioxidant activity with total phenolics ranging from 169 mg/g to 753 mg/g. Fraction II and IV showed condensed tannins with total antioxidant activity from 1.90 mmol Trolox/g and 7.06 mmol Trolox/g respectively. Fractions II and III were reported to be having strong reducing powers whereas fraction III was having high antiradical activity against DPPH with EC$_{50}$ value 0.011 mg/assay. Reverse Phase-High Performance Liquid Chromatography (RP-HPLC) confirmed the presence of phenolic compounds.

Kshirsagar and Upadhya (2009) reported that stem bark methanolic extract of L. glutinosa exhibited maximum percentage of antioxidant activity i.e. 90.57% with an IC$_{50}$ value of 0.10 % (µg/ml) tested against standards like curcumin, catechin and trolox. Leaf and bark extracts were tested for their antioxidant activity by DPPH and
H₂O₂ radical scavenging assays using BHT and ascorbic acid as reference standards. Both the extracts exhibited scavenging potential with IC₅₀ value of 30.24 µg/ml and 216.53 µg/ml for DPPH and H₂O₂ radicals respectively and thus proved to be antioxidant in nature (Devi and Meera, 2010).

*Litsea* is a rich source of antioxidants containing structurally diverse and biologically active phytochemicals with broad-spectral biological activities (alkaloids, terpenoids, flavonoids, saponins and tannins) showing antioxidant, anti-inflammatory, wound healing, antidepressant, antibacterial, antifungal, analgesic, anti-diabetic, anti-HIV activity, cardioprotective and cytotoxic activity (Agarwal *et al.*, 2011). Limonene (18.5%) and thymol (10.1%) isolated from the leaf essential oil of *L. akoensis* were proved to be having excellent antioxidant properties as indicated by IC₅₀ value of 5.797±0.07% (µg/ml) in DPPH radical scavenging assay (Ho *et al.*, 2011).

The leaf and bark extracts of four *Litsea* spp. *L. monopetala*, *L. assamica*, *L. glutinosa* and *L. laeta* were evaluated for in vitro antioxidant activities (Choudhury *et al.*, 2013) by various antioxidant assays like DPPH and reducing power potency along with phytochemical screening and estimation of total phenol and flavonoid contents. The methanolic leaf extracts of *L. glutinosa* exhibited strong antioxidant activity DPPH scavenging activity (low IC₅₀ value) compared to extracts from bark except *L. monopetala*. The bark extracts of *L. glutinosa* showed high reducing capacity than leaf extracts of all the species with high reducing power (0.02 mg ascorbic acid Eq/gm). The study also showed that IC₅₀ value of the bark extract of *L. glutinosa* and *L. laeta* for metal chelating activity were 15.25 and 16.14 mg/ml which was higher than the other extracts. The study of nitric oxide radical scavenging activity showed that *L. monopetala* had better nitric oxide radical scavenging activity than other extracts.

Wang *et al.* (2013) evaluated the essential oil of *L. cubeba* for antioxidant activity and radical scavenging potential by using citral (major component in the essential oil of *L. cubeba*), ascorbic acid, BHT and propylgallate (PG). The results showed that the essential oil IC₅₀ values of hydroxyl radical scavenging activity were 0.19, 0.28, 0.50, 0.79 and 1.07 mg/ml, and IC₅₀ values of scavenging superoxide were 0.45, 0.64, 0.67, 1.08 and 0.51 mg/ml, respectively. Two new compounds were isolated from the bark of *L. costalis* namely biseugenol A and B and were tested for in
vitro antioxidant activity by DPPH assay with an IC$_{50}$ value of 4.77±0.006% (μg/ml) (Hosseinzadeh et al., 2013).

The total phenolic content of *L. polyantha* was determined by using the Folin-Ciocalteu reagent and aluminum chloride colorimetric method was used for the determination of total flavonoids (Ghosh et al., 2014). The content of phenolics in 100 g (dry weight) extract of *L. polyantha* Juss. was 511.472 ± 22.304 mg gallic acid equivalent (GAE), while total flavonoid content was 230.785 ± 5.439 mg/g quercetin equivalent in methanol extracts from *L. polyantha* Juss. proving that the plant is a good source of phenolic and flavonoids compounds. Wang et al. (2014) reported that the methanol extracts of root and stem of *L. elliptica* and *L. resinosa* potent antioxidant property as indicated by their low IC$_{50}$ values in DPPH radical scavenging assay.

Bhowmick et al. (2015) evaluated the antioxidant properties of the extracts of *L. glutinosa* with DPPH assay, reducing power assay and determination of total phenolic content. The high phenolic content (69.00±0.58 mg/g of gallic acid equivalent), low IC$_{50}$ value (9.68±0.15) and maximum reducing capacity (257.67±4.04) of the tested extract showed that extracts have strong antioxidant property.

The antioxidant activity of essential oil of *L. glutinosa* was measured by DPPH, 2, 2-azinobis-3-ethylbenzothiazoline-6-sulphonate radical cation (ABTS) and β-carotene bleaching assay. The stem bark essential oil with major constituent 9,12-octadecadienoic acid, exhibited good radical scavenging activity in DPPH assay with IC$_{50}$ value 4.540±0.06 μg/ml, ABTS assay with IC$_{50}$ value 256.02±0.06 μg/ml and β-carotene bleaching assay (%I: 78.51±0.42 %) and thus proved to have antioxidant property (Arunodaya et al., 2016).

**Antimicrobial activity**

Phytochemicals and plant extracts with known antimicrobial properties is of great significance in therapeutic treatments. With the rise in the incidence of new and emerging infectious diseases and the microorganisms developing resistance to antibiotics, there is a need to discover new antimicrobial compounds with novel mechanisms of action. It is advisable to develop new antimicrobial drugs which can
either inhibit the growth of pathogens or kill them and have no or least toxicity to host cells (Lohita et al., 2010a; Haque et al., 2014).

The aqueous, methanolic and ethanolic leaf and stem bark extracts of *L. guatemalensis* and *L. neesiana* exhibited antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* (Caceres et al., 1987). Citral contained in *L. cubeba* possesses antimicrobial property apart from its effectiveness in coronary heart diseases (Nath, 1996).

The essential oil extracted from the fruits of *L. laevigata* exhibited antimicrobial activity against *Streptococcus albus* and *Aspergillus niger*. The ethanolic extract of *L. glutinosa* exhibited strong *in vitro* antibacterial activity against *S. aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Enterococcus faecalis* and *E. coli* at the concentrations of 500 and 250 μg/ml by disc diffusion assay method (Prusti et al., 2008).

Areekul et al. (2009) subjected aqueous, ethanolic, ethyl acetate and hexane extracts of different species of *Litsea* plants for *in vitro* antimicrobial screening. The ethanolic leaf extract of *L. cubeba* inhibited the growth of bacteria *Bacillus subtilis* and *Listeria innocua*, whereas, leaf ethanolic extracts of *L. glutinosa* inhibited *S. aureus*. The ethanolic extracts were selected to determine the minimum inhibitory concentration (MIC) using broth dilution method and it showed MIC values of 0.39 - 25 mg/ml.

The preliminary bioassays conducted with the fruit extracts of *L. cubeba* showed that the terpenoids present in the extract had good fungicidal activity against *Sclerotinia sclerotiorum*, *Thanatephorus cucumeris*, and *Colletotrichum gloeosporioides*. The essential oil also exhibited good fungicidal activity against *Thanatephorus cucumeris* and *Sclerotinia sclerotiorum*, with IC<sub>50</sub> values of 115.58 and 151.25 μg/ml (Yang et al., 2010).

Hosmath (2011) reported that petroleum ether, ethanolic and aqueous extracts of *L. glutinosa* bark have antimicrobial and antifungal activities. Antibacterial activity of ethanolic extracts against Gram +ve *Staphylococcus aureus* was proved using reference standard Procain pencillin. The ethanolic extract showed effective antibacterial activity against Gram -ve bacteria *Escherichia coli*. Petroleum ether and
ethanolic extracts showed antibacterial activity against *Pseudomonas aeruginosa* using reference standard Streptomycin sulphate.

Pradeepa *et al.* (2011) tested the antibacterial activity of petroleum ether, chloroform and ethanol extracts of stem bark and leaf of *L. glutinosa* by agar well diffusion method against Gram-positive *S. aureus, Bacillus subtilis* and Gram-negative *E. coli, P. aeruginosa, Klebsiella pneumoniae, S. typhi, Salmonella paratyphi* and *Proteus* sp. The stem bark ethanolic extract showed antibacterial activity with 2.5 mg/ml MIC against *B. subtilis* (19.20 ± 1.52), *E. coli* (16.40 ± 0.55) and *S. aureus* (15.20 ± 0.84) which proved that the extract can be used in the treatment of diarrhea and dysentery. Leaf ethanolic extract also exhibited antibacterial activity against *K. pneumoniae* (16.40 ± 0.80) that could be used in the treatment of respiratory disorders.

Isoquinoline alkaloids isolated from *L. cubeba* showed antibacterial activity against *Streptococcus aureus* and antifungal activity against *Alternaria alternata* and *Colletotrichum nicotianae* (Zhang *et al.*, 2012). Total saponins of *L. coreana* (25 mg/ml) showed antibacterial activity against *Enterobacter aerogenes* and *P. vulgaris* (Wang *et al.*, 2012).

Wong *et al.* (2014) evaluated the antimicrobial property of hexane extract from stem of *L. resinosa* using agar well diffusion assay. The stem bark hexane extract of *L. resinosa* exhibited the largest inhibition zone in *P. aeruginosa* and *E. coli*, while chloroform extract from inner bark of *L. elliptica* showed major inhibition towards *B. subtilis*. The essential oils of the root extracts of *L. resinosa* ans *L. elliptica* showed significant antifungal activities. Cruz *et al.* (2014) reported that the essential oils and ethanolic extracts of *L. guatemalensis, L. glaucescens* and *L. neesiana* showed antibacterial activity against *B. subtilis* and *M. smegmatis*.

*L. cubeba* leaf essential oil showed the presence of linalool which was evaluated against strains of bacteria like *Aeromonas hydrophila, Edwarsiella tarda* and *Vibrio furnissi* and exhibited antibacterial activity against *Aeromonas hydrophila* in carps (*Cyprinus carpio*) (Nguyen *et al.*, 2016).

The *in vitro* antibacterial activity of the compound 9, 12-octadecadienoic acid isolated from the stem bark essential oil of *L. glutinosa* was investigated against eight
human pathogenic bacterial clinical isolates using agar disc diffusion method and MIC value was determined by modified resazurin microtitre-plate assay. The determination of in vitro antibacterial activity of stem bark essential oil resulted in significant inhibition zone (15.00±0.57 mm) and MIC value (0.15±0.15×10⁻² mg/ml). L. glutinosa stem bark essential oil showed potential antibacterial activity against Vibrio cholerae. The results of this investigation supported the ethnomedical claim of essential oil as a demulcent, antidiarrheal and antioxidant drug, against the pathogenic bacteria V. cholerae followed by P. aeruginosa and S. typhi (Arunodaya et al., 2016).

Cyriac and Thomas (2016) evaluated the fresh leaf ethanolic extract of L. ligustrina for antibacterial activity against eight strains of bacteria namely; Vibrio parahaemolyticus, S. typhi, B. cereus, Enterobacter spp, S. paratyphi, V. cholerae, S. aureus, E. coli and Streptococcus haemolyticus in disc diffusion method. The extract showed significant antibacterial activity against all the selected strains of bacteria. But petroleum ether, acetone and ethanol extracts prepared in the gradient of increasing polarity did not show antibacterial activity which confirms the role of heat liable compounds in the antibacterial activity of ethanolic extract. Flavonoids isolated from L. coreana (40 mg/ml) exhibited strong antimicrobial activity against Bacillus anthracis, Proteusbacillus vulgaris, S. aureus, and B. subtilis (Jia et al., 2017).

**Cytotoxic activity**

Uncontrolled proliferation is a universal property of tumor cells. Investigation of the cellular growth control mechanism has contributed to the understanding of carcinogenesis and to the identification of compounds with specific antitumoral activity. Mankind has been provided with many anticancer agents by nature, both from microorganisms and plants. But the search for new cytotoxic agents from natural - microbial, marine and plant-sources continues (Ruffa et al., 2002). Cancer is the third leading cause of mortality next to heart and vascular diseases. Research on plant natural products has actively contributed to drug development against cancer and thus, screening of medicinal plants and the isolation of natural products is a dire need to develop novel, and effective anticancer drugs to treat cancer (Tantengco and Jacinto, 2015). Chemotherapy, one of the commonly used methods of treatment in the treatment of cancer has many adverse side effects, ranging from nausea to failure of bone marrow and development of multidrug resistance (MDR). Hence, finding herbal
drugs from plant origin may provide an alternative to cancer treatment (Graidist et al., 2015).

Six new lactones isolated from *L. japonica* showed cytotoxic activities against HT-cell lines *in vitro* (Tanaka et al., 1989). The butanolides, litseakolide D, E, F, G and isolincomolide D isolated from the leaves of *L. akoensis* showed significant cytotoxic activity against P-388, A549 and HT-29 cell lines *in vitro* (Chen et al., 1998). Isolitseans isolated from *L. verticillata* were found to inhibit HIV-1 replication (Zhang et al., 2005). Butanolides isolated from *L. akoensis* were tested for cytotoxicity activity against human tumor cell lines. Of many compounds, only one i.e. butanolide B exhibited cytotoxicity against MCF-7, NCI- H460 and SF-268 cell lines *in vitro* (Wang et al., 2008a).

Tanaka et al. (2009) tested cytotoxic activity of the isolated amides and flavones from *L. auriculata* against HeLa cells. Out of six isolated compounds, five reduced the number of HeLa cells in the concentration range of 6.25–50 mg/ml. Three compounds reduced the cell number by 67–68% at 50 mg/ml and two compounds stimulated HeLa cells to decrease the cell number by 48 and 55% (50 mg/ml). The cytotoxic potency of the tetra and penta substituted oxygenation amides were stronger than that of the flavonol against HeLa cells. 50-53 compounds were identified from the fruit oil of *L. cubeba* of which Citral, the main compound in the fruit oil exhibited cytotoxic activity against human lung, liver and oral cancer cells (Ho et al., 2010).

A new megastigmene isolated from the leaves and twigs of *L. glutinosa* was evaluated for cytotoxic activity against human tumor cell lines for which it was proved to be inactive (Wang et al., 2011). The compounds isolated from the bark of *L. costalis* namely biseugenol A and B were tested for cytotoxic activity against cancer cells using MTT assay. Both the compounds exhibited excellent cytotoxic activity against HepG2, PC-3, and MCF-7 cell lines (Hosseinzadeh et al., 2013).

The leaf extracts of *L. glutinosa* showed antibacterial and cardiovascular activities. The extracts were evaluated for cytotoxicity using brine shrimp lethality bioassay. The bioassay results showed that all the extracts exhibited cytotoxic activity compared to Colchicine. Of all the extracts, the n-hexane fraction showed the highest
activity with LC$_{50}$ value, 30.32±0.46 µg/ml which was close to the standard LC$_{50}$ value, 30.11±0.30 µg/ml (Bhowmick et al., 2015).

Fourteen compounds with three new compounds, cubebanone, N-cis-3,4-methylenedioxy-3-methoxytropane and 9,9-o-di-(E)-feruloyl-(+)secoisolariciresinol were isolated by bioassay-guided fractionation of roots and stems of *L. cubeba*. These compounds exhibited anti-inflammatory and cytotoxic activity against LPS-induced murine microglia (BV-2) cell line and hepatocyte carcinoma (HepG2) cell lines (Guo et al., 2015).

**Anti-inflammatory activity**

A complex process associated with pain and involves the increase of vascular permeability, increase of protein denaturation and membrane alteration is inflammation. The response of a tissue to stress is inflammation which may be due to cell damage by microbes, physical or chemical agents that results in injury. Inflammation is characterized by redness, pain, heat, and swelling in the injured area depending on the site and extent of injury. Inflammation leads to increased blood flow to the injured site and forms one of the body’s nonspecific internal systems of defense. The caring of inflammation related diseases is a complex issue and the search is on for alternative drugs such as drugs produced from medicinal plants (Leelaprakash and Das, 2011).

Alkaloids extracted from *L. guatemalensis, L. laeta, L. japonica* and *L. cubeba* showed anti-inflammatory activities (Min et al., 2003). Methanolic extract of *L. cubeba* bark and its fractions (0.01 mg/ml) inhibited Nitric oxide and PGE2 production in lipopolysaccharide activated RAW 264.7 macrophages without significant cytotoxicity at less than 0.01 mg/ml concentration. The enzymatic activity of myeloperoxidase (0.05 mg/ml) was decreased by the extracts. The findings suggest that *L. cubeba* is active for inflammatory conditions and may contain compounds with anti-inflammatory properties (Bhuniya et al., 2010c). The extracts from *L. akoensis* exhibited significant anti-inflammatory activity as they inhibited the nitric oxide production in the lipopolysaccharides-induced (LPS) microphage assay in vitro at the dose of 25 µg/ml (Lin et al., 2007).
Flavonoids found in L. coreana exhibited anti-inflammatory activity in complete adjuvant-induced arthritis rat model, by suppressing the primary and secondary paw swelling, LPS-induced splenocyte proliferation, and pathological damage of knee joint (Wang et al., 2008b). CH$_2$Cl$_2$ fractions of L. japonica inhibited NO and PGE2 production primarily through the regulation of inducible nitric oxide synthase and cycloxygenase-2 gene expression). L. japonica may be a natural source of effective antioxidant and anti-inflammatory agents (Yoon et al., 2010).

Devi and Meera (2010) reported that the aqueous extract of L. glutinosa administered by oral route exhibited significant anti-inflammatory activity and inhibition of edema by 15.36% and 43.14%. The three sesquiterpenoids identified in the plant proved that they have significant anti-inflammatory and wound healing activities. Anti-inflammatory activity was studied in carragenan, histamine and dextrin-induced rats paw edema against Indomethacin as standard.

Bhowmick et al. (2014) conducted the anti-inflammatory activity test in the crude methanolic extracts of L. glutinosa which showed statistically significant anti-inflammatory activity (1.51 ± 0.04 and 1.47 ± 0.03 mm paw edema) where Ketorolac showed 1.64 ± 0.05 mm edema after 3 h of carrageenan injection. In the antipyretic activity assay, the crude extract showed notable reduction in body temperature (32.78 ± 0.46°C) at dose of 500 mg/kg-body weight, when the standard (at dose 150 mg/kg-body weight) exerted 33.32 ± 0.67°C temperature after 3 h of carrageenan administration.

Flavonoids, coumarins, alkaloids, tannins, terpenoids, anthraquinones, phenols, reducing sugars and carbohydrates were reported in the phytochemical screening of methanolic leaf extract of L. quinqueflora. The screening for anti-inflammatory activity using standard drug ibuprofen reported that maximum activity was in higher dose i.e. 2000 µg/ml of the extract and 95% inhibition of red cell lyses was observed in that dose (Johny and Anilkumar, 2015).

Song et al. (2016) tested the products of supercritical fluid extraction of L. japonica for the anti-inflammatory activity using supercritical carbon dioxide. The extract inhibited the production of inflammatory markers such as nitric oxide (NO), prostaglandin E2 (PGE2), and cyclooxygenase-2 (COX-2)] and proinflammatory
cytokines [tumour necrosis factor-α (TNF-α),] induced by lipopolysaccharide (LPS) treatment.

**Analgesic properties**

The sensation of pain is initiated in peripheral pain receptors (nociceptors) and its purpose is to draw attention to tissue damage. The impulses are transmitted to the dorsal horn, spinal cord, reticular formation and thalamus and finally to the cerebral cortex. Thus many parts of the brain are involved in the perception of pain. Analgesics can therefore work in several ways, and it is for this reason that they are often used in combination, mainly a narcotic-type with an anti-inflammatory or paracetamol. Narcotic analgesics work by mimicking natural neurotransmitter peptides known as endorphins and encephalin and others. There are several opioid receptors known, the main CNS receptors being (epsilon) receptors ε (sigma) and σ (mu), with others including the μ (delta), k (kappa) and μ (mu), with others including the σ (sigma) and ε (epsilon) receptors.

Many diseases in humans are manifested by common nonspecific reactions like inflammation and pain. Non-steroidal anti-inflammatory drugs (NSAIDs) and opiates are used in these conditions, but with adverse reactions such as gastrointestinal disturbances, renal damage, respiratory depression, and possible dependence (Shaojali et al., 2015).

International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage”. Aspirin and morphine are the common drugs used for pain relief in recent times. But these analgesic drugs, particularly opioids and nonsteroidal anti-inflammatory drugs (NSAIDs), relieve 50% of the pain in about 30% of patients and also cause serious side effects. Opioids cause side effects like physical dependency and addiction whereas, NSAIDs usually cause gastrointestinal disorders. Many of the herbs with analgesic activity have been used without any adverse effects and the research is on to discover other alternatives to treat pain (Fan et al., 2014).

The ethanolic extract of *L. glutinosa* at the dose of 100 and 300 mg/kg exhibited significant analgesic action showing increase in pain threshold in
hotplate, comparable to standard tramadol HCl using hotplate method in mice (Lohita et al., 2010b). Two compounds namely eugenol and chalcone and its derivatives were isolated from the bark extracts of *L. polyantha* (Ghosh et al., 2010) and showed their analgesic properties. Methanolic stem bark extract of *L. polyantha* exhibited marked inhibition on thermally induced hyperalgesia using animal models like tail flick method, tail immersion method and Eddy’s hot plate method. The extract proved significant analgesic activity at all dose levels where morphine (10 mg/kg b.w.) was used as standard drug.

Rhumzhum et al. (2012) reported that methanolic extract of *L. glutinosa* produced 70% and 87% writhing inhibition in acetic acid induced writhing model of mice, at the dose of 250 mg/kg and 500 mg/kg body weight respectively, whereas Diclofenac sodium produced 46% inhibition at the dose of 25 mg/kg. Thus the methanolic extract of *L. glutinosa* exhibited dose dependent analgesic activity in *in vivo* and antinociceptive effect in acetic acid induced writhing model in Swiss albino mice.

Bhowmick et al. (2014) reported that, the leaf extracts of *L. glutinosa* at a dose of 500 mg/kg showed the highest pain inhibitory activity (15.54 ± 0.37 sec) in hot plate method, compared to standard drug Ketorolac (16.38 ± 0.27 sec). In the acetic acid induced writhing test, the crude methanolic extract showed good analgesic potential (45.98 and 56.32% inhibition) compared to standard ketorolac (64.36% inhibition).

**Hepatoprotective activity**

The liver is a complex and vital organ which controls every physiological process of our body by protecting it from toxic metabolites particularly from xenobiotics. Liver diseases are posing a major global health problem. Liver damage is caused by excess use of antibiotics, chemotherapeutic agents, acetaminophen, exposure to peroxidised oils, aflatoxin, alcohol abuse, malnutrition, and exposure to high quantities of free radicals leading to oxidative stress which make liver vulnerable to disorders that account for high death rate in the world (Qureshi et al., 2010; Balne, et al., 2013).
The conventional drugs used in the treatment of liver disorders have serious side effects and therefore the focus on systematic research to evaluate scientific basis for traditional herbal medicines with hepatoprotective activity and with minimum side effects. Plants, natural products and traditional formulations have been used traditionally all over for prevention and treatment of liver diseases. Out of 600 formulations used world wide, India itself has 40 potential herbal formulations made from 95 medicinal plants used as hepatoprotective medicines (Girish et al., 2009; Lohan and Das, 2011).

Eidi et al. (2012), reported that the administration of stem bark ethanolic cinnamon extracts significantly reduced the impact of carbon tetrachloride toxicity on the serum markers of liver damage, aspartate amino transferase (AST), alanine amino transaminase (ALT) and Alkaline phosphatase (ALP) and also resulted in markedly increasing the levels of superoxide dismutase and catalase enzymes in rats. It is reported that the aqueous extract of Cinnamomum zeylanicum leaves and ethanolic extract of stem bark have shown significant hepatoprotection against alcohol induced hepatotoxicity in albino rats in reducing AST, ALT, ALP and levels of total bilirubin and total protein (Moselhy and Ali, 2009). The aqueous extract of leaves of Persea americana showed significant hepatoprotection against CCl₄-induced liver injury, in rats by reducing AST, ALT, ALP and levels of total bilirubin and total protein (Brai et al., 2014). The ethanolic leaf extract of Lindera communis, a member of Lauraceae, exhibited hepatoprotective activity by showing reduction in biochemical parameters with respect to control group in albino rats (Rajashekar an and Anandan, 2016).

Litsea coreana (Hawk tea) successfully prevented hepatic damage induced by CCl₄ in the rats. Serum levels of AST, ALT and lactate dehydrogenase (LDH) were significantly decreased when the rats were treated with 400 mg/kg concentration of Hawk tea compared with Silymarin (P<0.05) (Zhao et al., 2013). Oral administration of methanolic extract of Litsea glutinosa (100-200 mg/kg) exhibited protection against paracetamol and CCl₄-induced hepatotoxicity and restored the levels of the biochemical parameters to control levels in rats (Ghosh et al., 2016).
Anti-termite and nematicidal activities

Park et al. (2007) tested the essential oils extracted from *L. cubeba* for its nematicidal activity against pine wood nematode-*Bursaphelenchus xylophilus*. GC-MS analysis led to identification of 16 compounds from *L. cubeba* essential oils. Geranial, eugenol, isoeugenol and methyl isoeugenol were the compounds identified, tested and showed 100% nematicidal activity against pine wood nematode at 1.0 mg/ml concentration with LC$_{50}$ values of 0.120, 0.200, 0.210, 0.480, 0.517 and 0.525 mg/ml.

Jiang et al. (2009) in their comparative toxicity study of essential oils of *L. pungens* and *L. cubeba* and blends of their major constituents against the cabbage looper, *Trichoplusia ni* larvae, reported that both oils showed moderate activity against *T. ni* larvae with LD$_{50}$ values of 87.1 and 112.5 mg/larva, respectively. The essential oil - 1, 8-cineole from *L. pungens* an γ terpinene from the oil of *L. cubeba* were responsible for much of the toxicity on *T. ni* larvae.

The toxicity and antitermite activities of the essential oils extracted from the plant parts of *Cinnamomum* and *Litsea* were determined. All the essential oils showed inhibitory activity against the larvae of *Artemia salina* with the LC$_{50}$ value in the ranged of 3.02-56.23 μg/ml. The leaf oil of *C. burmannii* showed stronger biological activity against the larvae of *A. salina* and termites of *Coptotermes* sp. with LC$_{50}$ values of 3.02 μg/ml and 100% mortality after three days treatment at 1.0% concentration respectively. Other essential oil from *Cinnamomum* spp. exhibited moderate inhibitory activity towards termites *Coptotermes* spp. with 50-61% mortality at 10% concentration after three days of contact (Hasan, 2011).

Other biological activities

Poonia et al. (2006) proved the anti-diarrheal activity of higher doses of methanol extract of dried bark and aerial parts of *L. polyantha* in mice using castor-induced diarrhea and propulsive gut motility model in mice. Various alkaloids such as vilastonine, oxycanthine and barberine, extracted from *L. pallidifolia* are proved to be having strong antimalarial activities (Congdon et al., 1981; Min et al., 2003). The leaf ethanolic extracts of *L. glutinosa* was tested for wound healing activity in the form of an ointment by excision and incision wound models using Nitrofurazone ointment
(0.2% w/w) as the standard drug. The leaf extract applied in the form of simple ointment base at the concentrations of 3% and 5% w/w and exhibited noticeable response in both the models (Devi and Meera, 2010).

Ko et al. (2010) showed the insecticidal activity of essential oils extracted from the fruits of *L. salicifolia* against *Sitophilus zeamais* and *Trilobium castaneum* at the lowest rate 0.16 mg/cm-2. The essential oils also exhibited fumigant toxicity to *Sitophilus zeamais*, contact toxicity to both species and high antifeedant activity to *T. castaceum* than to *S. zeamais*. 200 mg/kg dose of *L. coreana* extract reduced the serum levels of ALT, AST, hyaluronic acid, procollagenase IV, leptin, and TGF-b1 in liver fibrosis rat model and thus exhibited remarkable hepatoprotective activity (Huang et al., 2010). Total flavonoids of *L. coreana* (400 mg/kg) reduced blood glucose level and relieved hyperglycaemia in a streptozotocin-induced type 2 diabetic rat model (Sun et al., 2010).

Kumar et al. (2011) in their study on the cardioprotective activity of *L. deccanensis* in rats by studying cardiac markers, opined that treatment with the extract prevented isoproterenol-induced oxidative stress in myocardial infarction by reducing the levels of biochemical markers and by inhibiting myocardial necrosis. The presence of phenolic and flavonoid compounds may be responsible for the high reducing power, potent free radical scavenging activity and pharmacological actions of the extract.

An essential oil obtained from the bark of *L. chinensis* by hydrodistillation process has good antiseptic germicidal activity and hypotensive effect (Bhatt and Pandya, 2012b). *L. gaucescens* is used in Mexican traditional medicine for treating of sadness and the essential oil of this species has antidepressant like activity (Guzman-Gutierrez et al., 2012). Strong insecticidal activity of ethanolic extracts of *L. cubeba* was reported against *Spodoptera exigua* (Lepidoptera; Noetuidae) larvae. *L. cubeba* leaf extract (10 mg/ml) exhibited strong antifeedant activity, as 96.64% FDI was produced when larvae were fed with the tested leaves (Feng et al., 2012).

The methanolic extract of *L. coreana* exhibited hepatoprotective activity in CCl₄ induced Sprague-Dawley rat models (Zhao et al., 2013). The hydroalcoholic extract of *L. glutinosa* leaves was evaluated for its thrombolytic activity. The results showed, a significant clot disruption at the dose of 1 mg/ml for all the extracts (n-
hexane, chloroform, ethyl acetate and methanolic) compared to the standard drug Streptokinase. The extracts showed 32.23 ± 0.26, 37.67 ± 1.31, 43.13 ± 0.85, and 46.78 ± 0.9% clot lysis, respectively, whereas the positive control streptokinase showed 93.35 ± 0.35% disruption at the dose of 30,000 I.U. (Bhowmick et al., 2014).

**Characterization of compounds using different chromatographic techniques**

The essential components that medicinal plants contain are bioactive compounds and the techniques of purification and isolation of bioactive compounds from plants have undergone new development in recent years. The searching for bioactive compounds is done with a method that can screen the source material for bioactivity. The primary steps to isolate and characterize a bioactive phytochemical is the selection of plant material, collection of ethno-botanical information about the plant and solvent extraction. Various chromatographic techniques are used to isolate individual phenols. Improved techniques such as high performance liquid chromatography (HPLC), Nuclear Magnetic Resonance (NMR), and Mass Spectroscopy (MS) are used for the structural elucidation of the compounds. Recently, Liquid chromatography-Mass spectroscopy (LC-MS) is used to analyse phenolic compounds. Further, Fourier transform infrared spectroscopy (FTIR) is done identify the chemical constituents and elucidate the structural compounds. Electrospray ionization/Mass spectroscopy (ESI-MS) is used as a preferred source due to its high ionization efficiency for phenolic compounds (Altemimi et al., 2017). Further, characterization can be done by hydrolyzing the molecules. The accurate identification of chemical compounds in medicinal plants is done with a combination of techniques of HPLC and MS (Halliwell et al., 1995a and 1995b).

The phytochemicals reported in family Lauraceae have a wide range of biological activities such as antioxidant, anti-inflammatory, antimicrobial, anti-feedant, analgesic, cytotoxic and antimalarial activities (Lin et al., 2007; Joshi and Mathela, 2012). HPLC with a diode array detector (DAD) and ESI-MS techniques were adopted to isolate flavonoid O-glycosides and catechin along with MS and 1D and 2D NMR techniques for elucidation of the isolated compounds in *Laurus nobilis* (Dall’Acqua et al., 2009).
Two flavonol glycosides were isolated (Ribiero et al., 2002) from Nectandra grandiflora and identified as 3-O-β-rhamnosykaempferol and 3-O-β-rhamnosylquercetine with their molecular structures elucidated by 1D, 2D NMR techniques. The constituents of essential oils of Ocotea quinox were identified by comparing their GC retention time with MS fragmentation pattern with known compounds and with those in the literature (Bruni et al., 2004). The constituents of essential oils of Lindera strychnofolia were identified by GC-MS analysis (Yan et al., 2009). The bioactive potential of genus Litsea is well established. Structural elucidation of the lactones isolated from L. japonica was done based on spectroscopic evidence (Tanaka et al., 1990). With the spectral analysis, structure of a novel phenanthrene alkaloid, isolated from the L. cubeba was elucidated as 3,7-dihydroxy-4,6-dimethoxy-N-methyl-tetrahydropyrido[4,3-a]phenanthrene (Wu et al., 1991). The structure of alkaloids isolated from L. cubeba (Lee et al., 1993) using centrifugal partition chromatography and ion-pair reversed phase, was elucidated by spectral analysis. Cheng et al. (2001) reported one nor-neolignan and five butanolides, from the leaves of L. acutineva and their structures were elucidated from spectral analysis.

Zhao et al. (2003) isolated a new compound, roundifolinol from the bark of L. rotundifolia with its structure characterized by spectroscopic methods such as GC-MS analysis. Three new sesquiterpenes isolitseans (A, B and C) and a novel butanolide (litseabutenolide) were isolated from the leaves of L. verticillata (Zhang et al., 2005), with their structural elucidation done using 1D - NMR analysis.

The structures of the six new butanolides isolated from L. akoensis were characterized in depth by NMR–spectroscopic and mass spectroscopic analysis (Wang et al., 2008a). The structure of a novel amide isolated from the leaves and twigs of L. auriculata was structurally elucidated using IR, UV, MS spectra along with Proton Nuclear Magnetic Resonance (1H-NMR) and Carbon-13 Nuclear Magnetic Resonance (13C-NMR) spectral analysis (Tanaka et al., 2009). The structure of C9 monoterpenoid acid viz. litseacubebic acid isolated from the fruits of L. cubeba was elucidated by various methods of spectral analysis (Yang et al., 2010a).

A new bis-benzyllisoquinoline, was isolated from the bark of L. lancifolia with its structure characterized with complete 13C-NMR data and other alkaloids structures elucidated by means of high field 1D and 2D NMR-IR, UV, and Liquid
Chromatography-Mass spectroscopy-Ion Trap-Time of Flight (LCMS-IT-TOF) spectral data (Sulaiman et al., 2011). The structural elucidation of the two new compounds isolated from L. costalis was done using 1D and 2D NMR spectral data (Hosseinzadeh et al., 2013). The chemical structures of aporphine alkaloids isolated from L. cubeba were confirmed using electrospray ionization-mass spectrometry, $^1$H-NMR and $^{13}$C-NMR (Sun et al., 2015). Totally 56 components were identified in the essential oil of fruit of L. cubeba using gas chromatography (GC) and GC-MS, of which 48 were detected by direct injection gas chromatography (DI/GC) and headspace-solid phase microextraction (HS-SPME/GC) method (Chen et al., 2016). The GC-MS analysis of the stem bark essential oil of L. glutinosa showed the presence of 37 compounds (Arunodaya et al., 2016). The structure of flavonoids was elucidated using GC-MS, 1D and 2D NMR-IR spectral techniques in L. coreana (Jia et al., 2017).

The detailed review of literature presented in this chapter reveals the ethnomedicinal value of Litsea species that are found distributed in the warm temperate and tropical regions of the world. The review presented highlights the biological activities, reported in Litsea species which mainly include antioxidant, antimicrobial, cytotoxic, anti-inflammatory, antimalarial, heptoprotective and analgesic activities and also the compounds isolated and identified from the genus Litsea mainly as alkaloids, flavonoids and terpenoids. There is no documentation of any work on L. floribunda selected in the current study. Hence, there is a need to study biological activities and to further identify the compounds responsible for the biological activity of L. floribunda. In order to achieve the same, the following objectives have been framed.

1. Evaluation of phytochemicals and antioxidant activity in the leaf and stem bark extracts of L. floribunda

2. In vivo antidepressant and anxiolytic potentials of L. floribunda extracts

3. Evaluation of nootropic and brain antioxidant activity of L. floribunda extracts

4. Characterization of compounds from leaf and stem bark extracts of L. floribunda