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Review Article

Traditional and Pharmacological Reports of The Genus Baccaurea. A Review

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Abstract

Baccaurea is a genus of flowering plant belongs to the family Phyllanthaceae categorically large genus with members of up to 100 species and few of which have been recognized as popular healing plants in South-East Asia. (*B. ramiflora*), (*B. angulata)*, (*B. courtallensis*), (*B. macrophylla*), (*B. macrocarpa*), (*B. lanceolata*), (*B. racemosa*) and (*B. motleyana*) are underutilized medicinal plants of the genus Baccaurea. The literature review revealed that Baccaurea species have been used traditionally in South-East Asian countries to treat various diseases. Baccaurea species have been believed to possess significant medicinal values like analgesic, anthelmintic, antioxidant, anti-diarrheal, antiatherosclerotic, anticancer, antidiabetic, neuropharmacological, thrombocytic, antimicrobial, etc. activities. Few species of the Baccaurea genus have demonstrated significant exposure to phytochemicals such as alkaloids, flavonoids, anthocyanins, carotenoids, tannins, phytosterols, saponins, phenolic compounds, steroids, rosmarinic acids, etc. Several bioactive constituents including 6′-O-vanilloylpicraquassioside D, 4′-O-(6-O-vanilloyl)-β-D-glucopyranosyl tachioside D, Icariside B5, picrotoximaesin, β-sitosterol, Sapidolide A, Daucosterol, methyl 2-hydroxy-3-methylbutanoate, quercetin, decanoic acid, etc. were also isolated and described from various species of Baccaurea. The purpose of this review is to evaluate the published article which is based on the medicinal values of different species of Baccaurea genus, provide updated information and knowledge on the ethnomedicinal, pharmacological and phytochemical properties and further phytochemical assessment opens a new prevalence, effectiveness in protection and clinical research.

Keywords: Baccaurea, Traditional, Pharmacological, Phytochemicals, Effectiveness, Alkaloids, Flavonoids, Anthocyanins, Carotenoids, Tannins, Phytosterols, Saponins, Phenolic Compounds, Steroids, Rosmarinic

Introduction

Plants and phytoproducts continue to play a vital role in the treatment of various diseases. From the beginning of human civilization, plants have beneficial activity in the treatment of human diseases. World Health Organization (WHO) survey reveals that about 80% of the world's inhabitant's problem is treated by medicinal herbal drug for their primary health care [1]. Nowadays, the use of medicinal plants for alleviating diseases is growing day by day around the world especially in Asia [2]. Drug discovery from plants is a multi-disciplinary approach and is interconnected with many disciplines like botanical, ethnobotanicals, phytochemical, biological, and various chemical separation processes along with combinatorial synthetic techniques [3]. Although pharmaceuticals derived from flowering plants still account for almost 30% of the prescribed items, modern orthodox. Western medicine over the last century has moved away from an obvious connection with plants [4]. In many other parts of the world herbalism flourishes as the standard method of treatment [5]. Among plants, the genus of Baccaurea have interesting biological activities. Baccaurea is a genus of flowering plant belonging to the family Phyllanthaceae. The genus comprises about 100 species, extensively distributed from Indo-Malaysia to the West Pacific [6].

Among them, few species of Baccaurea namely Baccaurea ramiflora Lour Baccaurea sapida Muell.Arg (*B. ramiflora*), Baccaurea angulata (*B. angulata*), Baccaurea courtallensis Muell. Arg. (*B.*

courtallensis), Baccaurea macrocarpa (*B. macrocarpa*), Baccaurea macrophylla Muell (*B. macrophylla*), Baccaurea lanceolata (*B. lanceolata*), Baccaurea racemosa Müll.Arg (*B. racemosa*), and Baccaurea motleyana (*B. motleyana*) are available in the south-east Asian region. According to ethanobotanical and traditional uses, these flowering plants are used for rheumatoid arthritis, cellulitis, abscesses, treat injuries, constipation, treatment of infectious diseases such as diarrhoea, dysentery, and skin infection, sore eyes etc. [7]. Plants of Baccaurea species have been shown to contain diverse phytochemical properties like phytosterols, saponins, flavonoids, steroids, phenolic compounds, tannins, volatile oils, etc. [7-8]. Different pharmacological studies including antioxidant, antimicrobial, cytotoxic, anti-inflammatory, anticancer, haemolytic, neuropharmacological, insecticidal, etc. on this Baccaurea species. Considering the secret potentialities of the underutilized Baccaurea species, so far, several research studies have been carried out to investigate their different medicinal uses, demand the isolation and detection of active concepts and comprehensive bioassay.

Baccaurea Species in Folklore Practice

Generally, the practice of herbal medicine is most widespread in developing countries and is often more affordable than expensive modern pharmaceutical drugs [9]. It has been revealed that 80% of the population in Asian countries are still using herbal medicines as their main medicinal source for their wellbeing [10].

B. ramiflora, the most well-known species, for the Southeast Asian region and found growing wild as well as under cultivation in Nepal, Bangladesh, India, Myanmar, South China, Indochina, Thailand, the Andaman Islands and Peninsular Malaysia. It grows in few districts of Bangladesh namely Narsingdi, Sylhet, Gazipur, Netrokona and Kishoregonj [11]. The folklore uses of *B. ramiflora* have attracted the attentions over time and thus various researchers documented different parts of species are used as ethnomedical for many purposes like as an anti-phlogistic and anodyne against rheumatoid arthritis, cellulitis, abscesses, indigestion, flavouring and colouring agent etc. by the inhabitants of different countries in Southeast Asia [Table 1]. *B. courtallensis* is another common species widely distributed in Western Ghats of India [12]. The plant is frequently used in India such as treatment of diarrhoea, dysentery, skin infection, controlling diabetes, piles, antidote, anti-inflammatory purposes etc. International Union for Conservation of Nature and Natural Recourses (IUCN) has enlisted it as threatened species [13].

Table 1: Folklore/Traditional uses of underutilized fruits of Baccaurea genus.

Species	Local Name	Used Part	Uses	References
B. ramiflora Lour. Muell-Arg	Latka/Latkan/lotko/ Notko/Anshfol.	Whole plant	An antiphlogistic and anodyne against rheumatoid arthritis, cellulitis, abscesses and to treat injuries in Chinese Dai medicine. Also used for stomach ulcer, stomachache and colic in Mizoram, India. Used against some ailments by hill-tribes in Northern Thailand.	[18-20]
		Fruit	Religious purpose as applied by Local people during the Holy Chariot Procession of Lord Jagannath. People pay their homage to God by throwing the latka fruit along with other rituals. The Fruit juice is considered as an Antidote for snake bite in Assam, India.	[21-22]
		Young leaves	Used as vegetable, flavoring agent with curries and minced meat in Bangladesh.	[23]
		Bark	In India, fresh bark is chewed or juice is used orally for constipation. Stem bark gives diuretic activity.	[24]
		Seed	Seeds are crushed to cure diarrhea. In Bangladesh, cultivated chiefly for production of valuable dye called annatto which is used for colouring silk, cotton, and other textile materials for orange colour.	[25-26]
B. courtallensis (Wight) Muell. Arg.	Mootapalam/ Muttithuri/ Kalikuki/ Muttathuri.	Root and leave	The paste of root and leaves are mixed with hot water and taken internally to treat piles and act as antidote.	[27]
		Fruit	Local tribal people such as kanikkar, Malampandarangal and Paniyar consume ripe fruit for its medicinal properties. Treatment for sterility, mouth, and stomach ulcers and for controlling serum cholesterol degree.	[12,28]
		Root	Used in the treatment of controlling diabetes and headache.	[12]
		Fruit rind	In Kerala, fruit rind is pickled for use in everyday life. The pericarp of tender fruit is consumed as antipyretic.	[27,29]
		Leave	In Kerala, boiled water of fruits, bark and leaves powder form is taken internally to take out poison traditionally. The fresh leaves paste is applied on swellings for anti-inflammatory purposes. Leaves are cooked like side dishes and consumed with rice or rice soup.	[30-31]
		Bark	The bark is used as a tonic in disorders of mucous membrane and to heal wounds and antibacterial recreation.	[32]

Baccaurea angulata Merr	Belimbing Dayak/ Belimbing hutan.	Skin	The red part (skin) is sour, and usually cooked by the rural communities.	[33]
		Whole fruit	Eaten fresh and used in cooking and as traditional medical practice. Aqueous juice of the whole fruit in daily meal also recommends.	[34-35]
		Berry	The soft whitish part of this fruit (berry) is edible.	[15]
		Extract gel	Good dental gel for wound healing in extracting a tooth.	[36]
Baccaurea lanceolata (Miq.) Muell. Arg	Lepeso/Limposu	Fruit	In Iban community, the solution obtained from the fruits as a component of an herbal formulation with other plant extracts, i.e., Etlingera elatior (fruits) and Begonia spp (leaves) applied on head when it was cooled to cure headaches. Fruits are potential to be used for the treatment of fever (due to infection), swellings on the body and topically on the skin to protect the skin from sunburn with natural skin care ingredients by the Bidayuh people.	[37–39]
		Leave	The decoction of leaves and water pounded in bamboo is used orally to treat stomach-ache for medicinal purpose in Sarawak, Bidayuh community.	[38]
		Bark	To prevent drunkenness, the Penan community pound the bark and drink the sap before consuming alcohol.	[39]
		Fruit shell	The shell of the fruit is eaten to cure diarrhea in the Kelabit community.	[10]
Baccaurea macrophylla Muell.	Langkha	Whole plant	Used in in local cuisine and herbal medicines in Thailand. Treatment of stomachache and sore eyes.	[17]
Baccaurea motleyana Müll. Arg.	Rambai	Bark	The bark has been used as an ingredient of a concoction of many ingredients and administered internally after childbirth in protective medicaments. Squeezed cambium and inner bark has been used as remedy for eye inflammation.	[40-41]
		Skin	Used for sore eyes. In the Malaysian and Indonesian traditional cosmetic industries, in medicated face powder preparation for treatment of acne and general skin complaints.	[42]
		Fruit	The fruits are turned into a jelly and used for cooking.	[42]
		Peel	Induce abdominal discomfort.	[43]

B. angulata, is also the popular plant that is native to Borneo Island of Malaysia and several other regions of Indonesia [14]. The high antioxidant levels of *B. angulata* had opened a new possibility of developing it as herbal preparations that has a high potential for producing nutraceutical benefits our wellbeing. In Borneo Island, the plant is considered as traditionally important by the rural communities [15]. *B. lanceolata*, another species is found in Thailand, Peninsular Malaysia, Sumatra, Borneo, and Philippines. In traditional contemplation the plant is used for stomach-ache, body swellings, diarrhoea, prevent drunkenness, skin care ingredients etc. in South Kalimantan region [16]. *B. motleyana* species is popular to Thailand, Peninsular Malaysia, Sumatra, Java, Borneo, and Moluccas regions, which is used to treat as eye inflammation, childbirth protective medicaments, abdominal discomfort, cosmetic industries etc. by the local people in the Malaysian and Indonesian countries [16]. *B. macrophylla* is a species of fruit tree, which is native to Southeast Asia, especially East Kalimantan, Indonesia. Various parts of plants are used in local cuisine and herbal medicines in Thailand for treatment of stomachache and sore eyes as well as used as antiulcer and anti-inflammatory [17-25] (Table 1).

Reported Pharmacological Activity

Antioxidant activity

Medicinal plants have always been recognized as a potential source of natural antioxidants which are preventive compounds that play an important role in protecting against oxidative damage induced by Reactive Oxygen Species (ROS) [26-44]. Among Baccaurea species, *B. ramiflora*, *B. angulata*, *B. courtallensis*, *B. macrocarpa*, *B. macrophylla*, *B. lanceolata*, *B. racemosa* are reported to have antioxidant property. *B. ramiflora* is claimed to possess moderate antioxidant activity. To make an overall calculation of *B. ramiflora*'s capacity for antioxidants several researchers have tried with the action of various solvents by using synthetic and natural antioxidants as standards. There are numerous studies for determining the antioxidant activity in terms of its aqueous, ethanolic, hydromethanol, methanolic and crude extracts of *B. ramiflora*, it can be suggested that the ethanolic extract of *B. ramiflora* leaf fractions presented better antioxidant potential (IC50 4.524µg/ml) determined by (DPPH) radical scavenging assay, compared to other extracts [44-52]. Recent study indicated that the antioxidant activity of ethanolic, aqueous and crude extracts of leaf, root, and peel of *B. courtallensis* were evaluated through DPPH, FRAP, Hydroxyl radical scavenging activity and Nitric oxide assay by several researchers. Among them, *B. courtallensis* root crude aqueous extract showed effective scavenging abilities against the free radicals by acting as hydrogen donors to scavenge DPPH free radicals with (IC50 1.0µg/ml) [27-31]. The comparative study of another two underutilized fruits of Baccaurea genus, *B. lanceolata* and *B. macrocarpa* were in-

vestigated for *in vitro* antioxidant properties, where it was found that *B. macrocarpa* (pericarp) showed the higher antioxidant activities than *B. lanceolata* in DPPH, ABTS and FRAP respectively [53].

The methanol extract of bark of *B. macrocarpa* has an antioxidant activity with (IC50 11.15ppm) [54]. Another investigation revealed that *B. macrophylla* dried leaf ethanolic extracts exhibited the highest antioxidant activities with (IC50 1.70µg/mL) [17]. Mining of literature showed a wide spectrum of antioxidant activities of different parts of *B. rasemosa* by using different solvents determined by (DPPH), (TEAC), (FRAP), and (ABTS) radical scavenging assays, whereas the methanolic leaf extract possessed highest activity (IC50 4.298µg/ml) in DPPH radical scavenging assays [55-57]. Both *in vitro* and *in vivo* assays were performed using many antioxidant methods in *B. angulata*. Among them, methanolic peel extracts displayed the higher DPPH (78.54±2.08 mg AA/100g), indicating antioxidant activity [58-59]. *B. angulata* fruits was also examined in vivo antioxidant effect in rabbits, where Plasma malondialdehyde levels greatest in peel juice treated group (671.04%), highest level of catalase activity (12.66 %) and total antioxidant capacity (309.08±35.59mM) [34-35].

Anti-microbial activity

Anti-bacterial activity: In antimicrobial study, it was observed that the ethanol extract of *B. angulata* fruit showed the highest levels of antimicrobial activity with maximum inhibition (37±1mm) using agar well diffusion against S. pneumonia [15]. Several researchers have been trying to make an overall antimicrobial estimate for potentiality of *B. ramiflora* (seed, stem bark, fruits) with the action of various solvents use against in many grams positive and gram-negative bacteria by disc diffusion method [46]. In this study, the methanolic extracts of *B. ramiflora* seed and fruits showed highest levels of antimicrobial activity with MIC 3.20mg/ml against Staphylococcus aureus, Sarcina lutea and Shigella boydii [2] and fruits displayed MIC values ranging between 2.50 to 5.00mg/ml against Staphylococcus aureus, *Staphylococcus epidermidis*, *Shigella fexneri*, *Bacillus subtilis*, *Bacillus cereus* and *E. coli* [60]. The stem bark (400µg/ml) was the most effective against Shigella boydii with 25mm zone of inhibition compared to the standard Ciprofloxacin 28mm at 30µg/disc [49]. The methanolic and benzene extracts *B. courtallensis* leaves exhibited significant antimicrobial activity in well diffusion method on Mueller-Hinton Agar (MHA) medium with MIC 1.6µg/ml against B. Subtilis and 2.36µg/ml, against S. Aureus where Amoxicillin (100µg/ml) disc isolates for comparison [61]. The comparative study of antimicrobial activity *B. lanceolata* fruit, leaves, and bark extracts was evaluated by using the disc diffusion method. Among them the fruits produced significant zones of inhibition in mm, 12.0 for B. cereus and M. catarrhalis, 10.29 for P. acnes, respectively [9,37]. The ethanolic peel extract of *B. motleyana* was also demonstrated highest zone of inhibition of 35mm against Proteus vulgaricus and Bacillus cereus and appeared to be as a good antimicrobial agent where streptomycin used as standard [40].

Anti-fungal activity: An experiment reported that, three compounds viz. sapidolide A, picrotoximaesin and ramifloside isolated from *B. ramiflora* berries showed antifungal activity against Colletotrichum gloeosporioides with MIC 12.50µg/ml, 50.00µg/ml, and 12.50µg/ml, respectively compared to the standard carbendazim (6.25µg/ml) [62]. The antifungal effect of B. sapida fruits due to presence of two isolated compounds, i.e., oleic acid and palmitic acid reveled activities against opportunistic plant pathogens Alternaria alternata and Alternaria tenuissima with IC50 197.75µg/ml and 154.22µg/ml, 116.89µg/ml and 168.22µg/ml respectively, for oleic acid and palmitic acid [63]. The stem bark of *B. ramiflora* revealed mild effectiveness with zone of inhibition of 10 mm against Candida arrizae in comparison to griseofulvin (13-18mm) [49].

Anti-inflammatory activity

B. ramiflora is known to be effective against inflammation, which is confirmed by investigating the anti-inflammatory effect using methanolic extract of their stem, leaves and fruit pulp by carrageenan induced paw oedema method in rodents. The result indicated that the extracts of *B. ramiflora* at the dose level of 100mg/kg and 200mg/kg exhibited significant anti-inflammatory activity that was strongly comparable with the (Ibuprofen, 10mg/kg) [64]. Another study reported the down-regulating the increased level of cytokine due to inflammation effect of Baccaurea leaf on the cytokine level IL-1β (4.4pg/mg protein) and TNF-α (0.21ng/µg protein). The proposed anti-inflammatory bioactivity of leaf might be due to the presence of rosmarinic acid [44] and β-sitesterol which are established anti-inflammatory compounds [65-66]. *B. courtallensis* leaf extract has also been reported to be effective against inflammation at doses of 150mg/kg and 450mg/kg bodyweight, demonstrated substantial inhibition of carrageenan-induced rat paw edema formation compared to the standard drug Indomethacin (10mg/kg) [30].

Anti-cancer activity

Cancer is a leading cause of death worldwide. According to the literature, the best anticancer activity was exhibited by hexane extract of *B. motleyana* peels that showed IC50 43.6µg/mL on colon cancer line (HT-29) compared to other extracts, measured by MTS assay [41]. *B. macrophylla* is also considered as the potential source for anticancer activities against human cervical cancer cell line (HeLa cells), human colon cancer cell lines (HT29 and HCT116 cells), human breast cancer cell line (MCF-7 cells), and a non-cancer cell line (African green monkey kidney epithelial cells; Vero cells) were determined using the MTT assay, where the dried leaf ethanolic extract of *B. macrophylla* exhibited significant toxicity to HeLa, HT29 and HCT116 cells growth [17].

Anti-hyperlipidemic activity

Methanolic extract (200 and 400mg/kg) of *B. courtallensis* produced impressive antihyperlipidemic activity in Triton WR-1339 and high fat diet–induced hyperlipidemic rats, altered the serum levels of total cholesterol, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol to near normal [32]. *B. ramiflora* is also known to be effective against hyperlipidemia, which is confirmed by investigating methanolic and ethanolic extracts of their leaf and seeds in alloxan-induced diabetic wistar rats. The result indicated that the extracts of *B. ramiflora* at the dose level of 150mg/kg, 200mg/kg, 250mg/kg and 500mg/kg bodyweight, extremely diminished levels of triglycerides, total cholesterol, (LDL)-cholesterol, and (HDL)-cholesterol and exhibited significant hypolipidimic activity that was strongly comparable with Metformin (100mg/kg/day) and Rosuvastatin (10mg/kg) [45-46].

Analgesic activity

Methanolic extract of fruit pulp and seeds of *B. ramiflora* were screened for analgesic activity by employing different animal models stating chemical (acetic acid induced writhing and formalin test), and physical (tail immersion) methods. Ibuprofen, morphine, and diclofenac sodium at the concentration of 10mg/ml were used as standard. The result indicated that the extracts of *B. ramiflora* at doses of 200mg/kg and 400mg/kg bodyweight, significantly inhibited induced pain. Due to these excellent pharmacologically active analgesics of *B. ramiflora* can manage both central and peripheral pain in used animal models [24,64].

Cytotoxic property

Almost entire plant has been accessed for cytotoxic activity of *B. ramiflora* [51,64,67,68]. Among them the stem bark of *B. ramiflora* was found to be the best cytotoxic activity, which was investigated by using brine shrimp lethality bioassay, where the result showed that aqueous soluble fraction of stem bark of *B. ramiflora* exhibited most toxicity with LC50 1.44µg/mL as compared to the standard vincristine sulphate (LC50 0.9258µg/mL) [51].

Hypoglycemic effect

A literature review revealed that methanolic extract of *B. ramiflora* leaves (200mg/kg) as a single dose per day to the alloxan induced (120mg/kg) diabetic rats for 14 days produced substantial hypoglycemia and reduced the elevated blood glucose level (50.06%). The result was comparable with the standard metformin (58.17%) [45]. The methanolic extract of the bark of *B. ramiflora* showed significant hypoglycemic activity with a significant 24.89% and 29.19% inhibition at 200mg/kg and 400mg/kg bodyweight, respectively [46].

Cytoprotective effect

Plant extracts having antioxidant activities also lead to the inhibition of oxidative damage to biological structures. Due to such antioxidant potential, the *in vitro* and in vivo cytoprotective effect of *B. angulata* juice was measured on plasma MDA levels in rabbits. They showed that *B. angulata* fruit significantly decreased the plasma level of MDA and increased the activities of superoxide dismutase, glutathione peroxidase and catalase in rabbits fed a high-cholesterol diet. Thus *B. angulata* protects Low-Density Lipoprotein (LDL) from oxidative modification may be attributed to phenolic compounds known to act as powerful chain-breaking antioxidants and free radical scavengers [14].

Anti-diarrhoeal activity

The protection and effectiveness of *B. ramiflora* fruit pulp and seeds were evaluated for in vivo castor oil induced anti-diarrheal activity against diarrhea. It is evident that the percentage inhibition of defecation by methanol extract (200mg/kg) of fruit pulp was close to that of loperamide (3mg/kg), while the seeds (200mg/kg) were marginally more effective. Thus, it demonstrated anti-diarrheal activity [64].

Sleep inducing property

Melatonin is involved in circadian rhythm and regulation of diverse body functions, including sleep [69]. Melatonin was extracted by using solid phase extraction and showed a modest amount of melatonin (43.2 ng/g of dry sample weight) in *B. ramiflora*. Melatonin content in the leaves is a promising result for future development of this overlooked part of *B. ramiflora* as a health food supplement [70].

Thrombolytic activity

To identify blood thinning medications from plant source different extractives (aqueous, methanolic, ethanolic, ethyl acetate, chloroform, and their cyclohexane soluble partitioning materials extracts) of *B. ramiflora* were studied for thrombolytic activity. The aqueous extract of *B. ramiflora* seeds showed the highest thrombolytic potential with promising clot disruption (88.21%) which was higher than the standard drug streptokinase (66.77%) [68]. Another thrombolytic evaluation of n-hexane extracts of *B. ramiflora* bark showed 17.00±1.31 % of clot lysis, whereas streptokinase exhibited 65.13±0.96% of clot lysis as standard [71]. From these experiments, it can be said that the *B. ramiflora* extracts can be used as thrombolytic agents with its best pharmaceutical possibilities.

Anti-atherosclerotic effect

Atherosclerotic diseases are still major causes of mortality globally. *B. angulata* is claimed to be plaque-reducing activity as a new anti-atherogenic plant which was investigated by using in vivo animal model, where the result showed that treatment with fruit juice of *B. angulata* reduced plaque formation in rabbits' entire aorta thus decrease serum IL-8 and IL-18 production of inflammatory biomarkers and thus could protect against oxidative stress linked atherosclerosis and decrease the atherogenic index [72-73].

Anthelmintic activity

B. ramiflora possess varying degree of *in vitro* anthelmintic activity conducted by solitary study. The acetone extract of leaf (100mg/ml) exhibited significant wormicidal activity against Pheretima posthuma in a dose-dependent manner, where the results were expressed in terms of time for paralysis and time for death of worms which was comparable to standard drug albendazole (10mg/ml) [68]. The anthelmintic effect of leaf might be attributed to the presence of β-sitosterol, which has proven antihelimintic property [74].

Insecticidal activity

Insecticidal activity of acetone fraction *B. ramiflora* leaf has been tested against adult Sitophilus oryzae. The fraction was effective in eliminating *S. Oryzae*, with a mortality rate of 80% and 100%, thus helping to manage the rice weevil field population, *S. Oryzae* [75].

Hepatoprotective activity

B. ramiflora exhibited a hepatoprotective effect against alcohol and paracetamol induced hepatotoxicity which was confirmed by histopathological examination of the liver tissue of control and treated animals. Treatment with ethanolic extracts of *B. ramiflora* leaves (100mg/kg and 200mg/kg) can alter the level of biochemical parameters to the near normal levels almost comparable to the silymarin. So that it can be concluded that *B. ramiflora* possess hepatoprotective effect against alcohol and paracetamol-induced liver damage in rats [76].

Haemolytic activity

A literature review analyzed that the haemolytic activity of fruit juice of *B. ramiflora* using human erythrocyte. Fruit juice (100µl/ml) was declared safe to human erythrocyte since it exhibited negligible haemolytic activity (% Haemolysis=5.69) compared to Triton X-100 (100µl/ml) where % Haemolysis is 60.28 as standard [52].

Neuropharmacological activity

Two different neuropharmacological models, named open field and whole cross test were used to study the CNS depressant activity of crude extaracts (100mg/kg and 200mg/kg) of *B. ramiflora* fruit pulp and seeds, respectively. Both the tests revealed that the extracts could reduce the locomotor activity which is a measure of Central Nervous System (CNS) depressant activity. The results were comparable to the standard diazepam [64,77].

Antidiabetic activity

A literature review revealed that *B. racemosa* leaf extract possesses mild to moderate antidiabetic property, which was experimented through *in vitro* antidiabetic assay, i.e., α-amylase inhibition method. It was observed that, methanol and ethanol leaf extracts of B. rasemosa exhibited similar potency of antidiabetic activity with IC_{50} values were 67.63±0.36 ppm, 67.46±0.23 ppm, respectively where Acarbose drug used as standard with IC50 23.48±0.35 ppm [57].

Phytochemical Investigation

Phytochemical screening

Preliminary phytochemical sampling of the genus Baccaurea disclosed the presence of many bioactive materials of terpenoids, glycosides, reducing sugar, phenols, flavonoids, alkaloids, phenols, tannins, steroids, flavonoids, volatile oils, quinones, coumarins, carbohydrates, anthraquinones, polyphenols, Ascorbic acids, phytosterols, gums and mucilage, saponins, proteins and fixed oils, phlobatannin, resins, organic acids, carotenoids from different crude alcohol and aqueous extracts of *B. courtallensis*, *B. ramiflora*, *B. motleyana*, *B. lanceolata*, *B. macrocarpa* and *B. angulata*. In *B. ramiflora*, the total polyphenilic content of the leaf extract was found 79.06±0.03mg (GAE)/g, 28.80±0.01mg (QE)/g flavonoid and 29.42±0.01µg cathechin equivalent/g proanthocyanidin respectively [44], similarly the total phenolic content was 51.4mg of GAE/g [78]. In *B. angulata*, the total phenolic content was 16.58mg GAE/g, flavonoid 31.05mg QE/g and anthocyanin 0.72(mgc-3-g/100g) [58]. *B. macrocarpa* pericarp contained the total phenolics, total flavonoid, total anthocyanin, and total carotenoid with the values of 60.04±0.53mg GAE/g, 44.68 ±0.67mg CE/g, 1.23±0.20mg c-3-gE/100g and 0.81±0.14mg BCE/g [53]. In B. rasemosa, pulp has the highest Total Phenolic Content (TPC) and Total Flavonoid Content (TFC) with values 42.975±1.978mg (mg GAE g-1 dry extract) and 122.813±1.604mg (mg RE g-1 dry extract), respectively [55].

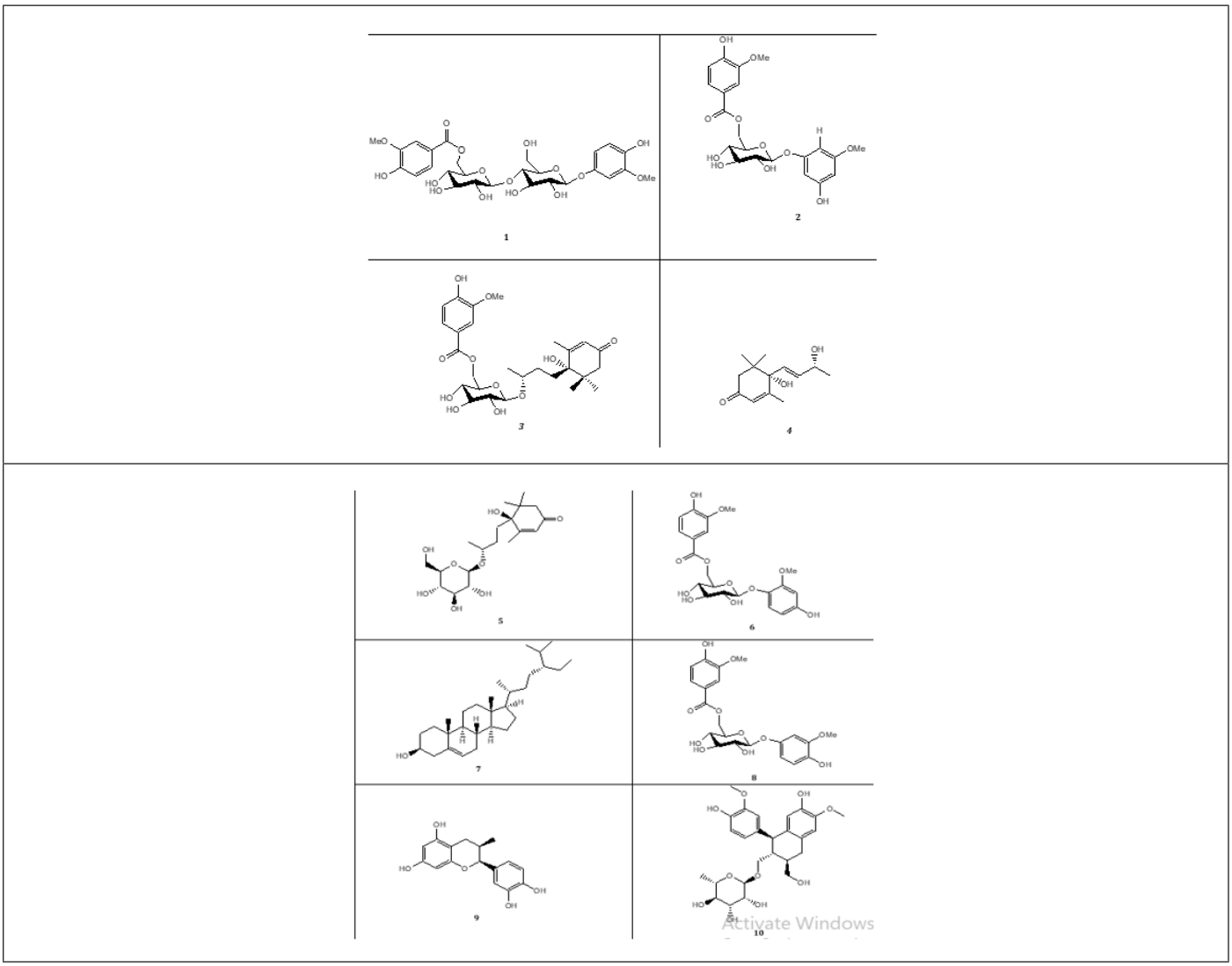
Identification and isolation of bioactive compound

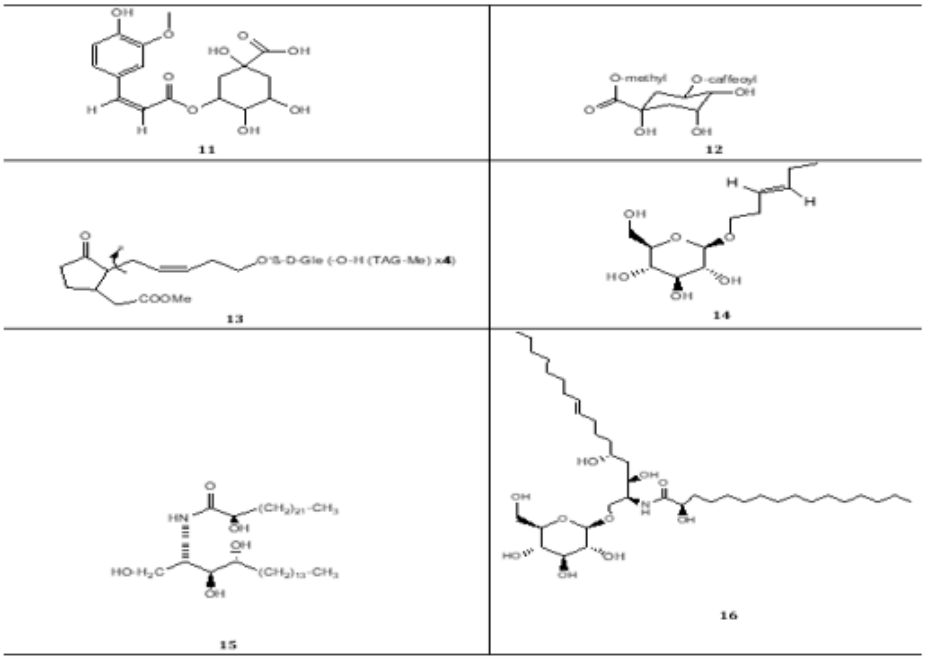
A variety of bioactive constituents are present in *B. ramiflora* contributed to the discovery and characterization of many secondary metabolites. Literature search showed that 4′-O-(6-O-vanilloyl)-β-D-glucopyranosyl tachioside D (1), 6′ ovanilloylpicraquassioside D (2), 6′-O-vanilloylicariside B5 (3) blumenol A (4), icariside B5 (5), 6′-O-vanilloylisotachioside (6), and β-sitosterol (7), 6′- O-vanilloyltachioside (8), (-)-epicatechin (9), bis(8-catechiny 1)methane (Structure not found), aviculin (10), 3-O-caffeoyl-4-O-methylquinic acid (11), 5-O-caffeoylquinic acid methyl ester (12), tuberonic acid glucoside methyl ester (13), erigeside B (14), (2S,3S,4R)-2-[(2R)-2-hydroxytetracosanoylamino]-1,3,4-octadecanetriol (15), aralia cerebroside (16), (24S)-24-ethylcholesta-3β,5α,6β-triol, stigmast-4-en-6β-ol-3-one (17), 7-oxo-β-sitosterol (18), 7α-methoxysigmast-5-en-3β-ol (structure not found), daucosterol (19), rosmarinic Acid (20), epidihydrotutin (21), ramifloside (22), sapidolide A (23), picrotoximaesin (24), phytol (25), betulinic acid (26), oleic acid (27), palmitic acid (28), 3 methoxy 4 hydroxy-cinnamaldehyde (coniferyl aldehyde) (29), 3, 4, 5 trimethoxy cinnamaldehyde (30),

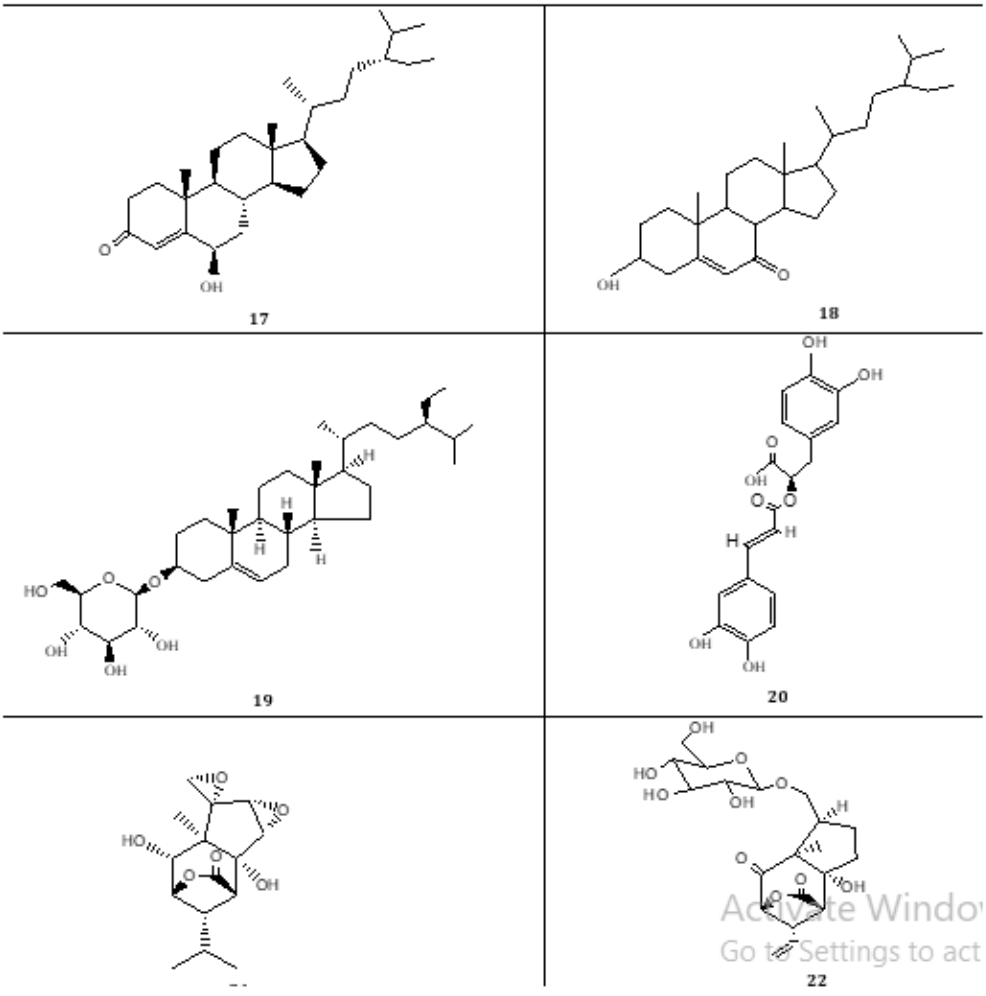
3, 4, 5 trimethoxy benzaldehyde (31), 3,4 dimethoxy benzaldehyde (veratraldehyde) (32) and melatonin (N-acetyl-5-methoxytryptamine) (33) from different parts like leaf, stem, root, seed kernel and fruits of *B. ramiflora* (Figure 1) through HPLC, 1H and 1D, 2D, 13C- NMR spectroscopic methods, Various chromatographic techniques and GS- MS analysis [20,44,49,51,62,63,70,79-82].

According to the literature, (E)- Hex-2-enal (1) considered as the major active ingredient in *B. motleyana* fruits also contained high levels of methyl 2-hydroxy-3-methylbutanoate (2), methyl 2-hydroxy-3-methylpentanoate (3) and methyl 2-hydroxy-4-methylpentanoate (4) as an antibacterial activity. Secondary metabolites contained in rambai; Decanoic acid (5), 1- Decene (6), Methyl salicylate (7) and Stearyl alcohol (8) (Figure 2) were analysed by capillary GC and GC-MS [83-84]. Literature search showed that, three greatest antimicrobial compounds (Figure 3) including Dimethyl 2, 3-bis [(trimethylsilyl)oxy] succinate (1), Arabino-hexos-2- ulose, 3, 4, 5, 6-tetrakis-o-(trimethylsilyl)-, bis (dimethyl acetal) (2) and Bis(trimethylsilyl) 2,3- bis [(trimethylsilyl)oxy] succinate (3) were identified from the crude extract of *B. lanceolata* based on derivatised GC-MS analysis of the Milli-Q water fractions [9]. β-sitosterol was also reported to be detected from the ethyl acetate (fr. EtOAc) extracts of Fruits of *B. lanceolata* [85].

In two different studies expand that a total of 17 phenolic compounds contained in the skin, pulp, and whole fruit of methanolic extract of *B. angulata* (Figure 4). Among them, five flavonoids (1-5), ten phenolic acids (6-15) and two phenolic diterpenes (16-17) were reported to be isolated and identified as quercetin (1), catechin (2), kaempferol (3), rutin (4), myricetin (5), caffeic acid (6), cinnamic acid (7), p-coumaric acid (8), ferulic acid (9), gallic acid (10), 4-hydroxybenzoic acid (11), protocatechuic acid (12), salicylic acid (13), sinapic acid (14), vanillic acid (15), carnosol (16) and carnosic acid (17) were performed on Chromatographic analyses of (LCMS/MS) (AB Sciex, Toronto, Canada) coupled to Perkin Elmer Flexar FX15 (UHPLC) system operated by AB Sciex analyst software for instrument control, data acquisition and data analysis [33-34,58](Table 2?).







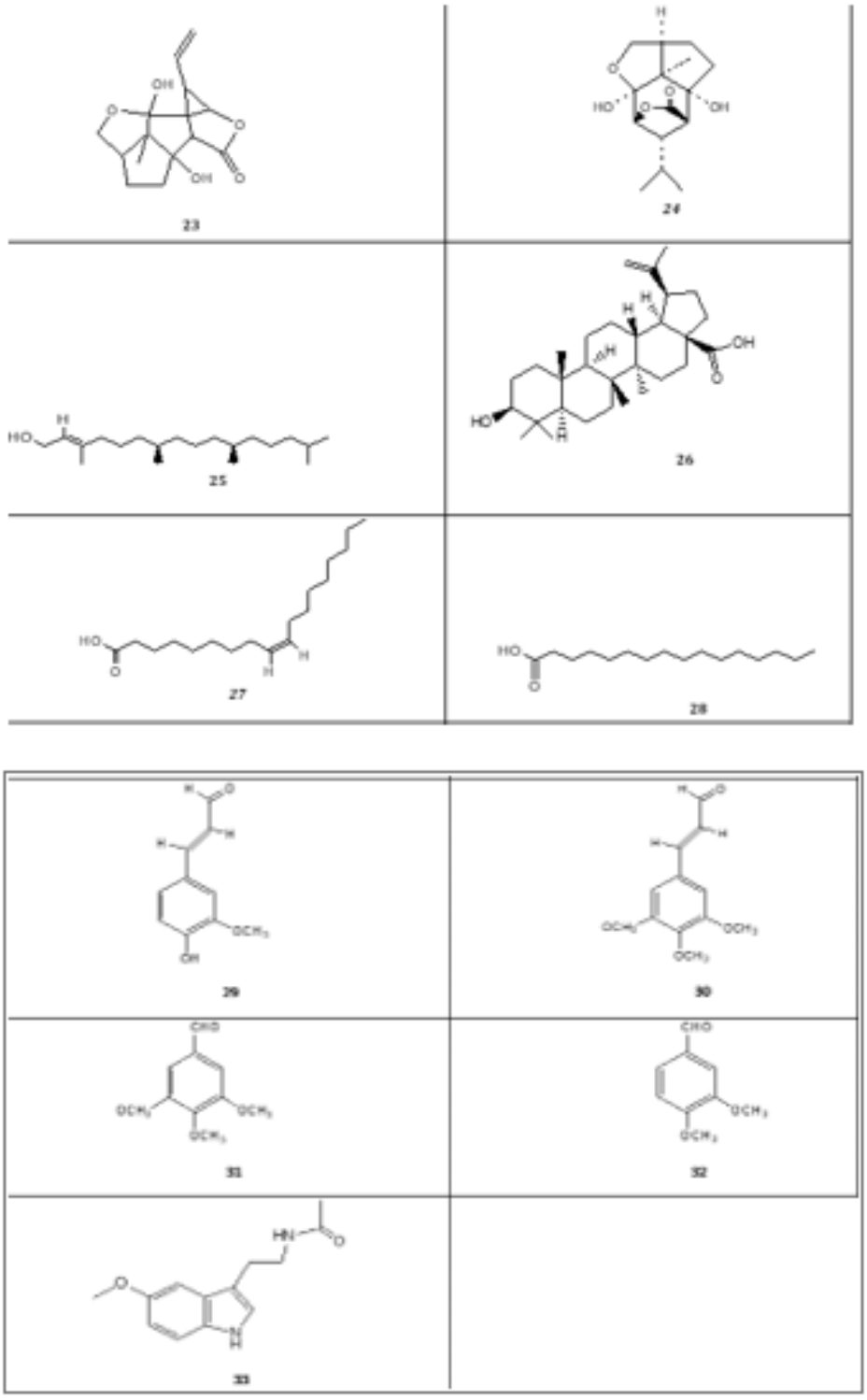


Figure 1: Isolated and identified bioactive constituents from B. ramiflora.
4′-O-(6-O-vanilloyl)-β-D-glucopyranosyl tachioside D (1), 6′ Ovanilloylpicraquassioside D (2), 6′-O-vanilloylicariside B5 (3) Blumenol A (4), Icariside B5 (5), 6′-O-vanilloylisotachioside (6), and β-sitosterol (7), 6'- O-vanilloyltachioside (8), (-)-Epicatechin (9), Aviculin (10), 3-O-Caffeoyl-4-O-methylquinic acid (11), 5-O-caffeoylquinic acid methyl ester (12), Tuberonic acid glucoside methyl ester (13), Erigeside B (14), (2S,3S,4R)-2-[(2R)-2-hydroxytetracosanoylamino]-1,3,4-octadecanetriol (15), Aralia cerebroside (16), stigmast-4-en-6β-ol-3-one (17), 7-oxo-β-sitosterol (18), daucosterol (19), rosmarinic Acid (20), epidihydrotutin (21), ramifloside (22), sapidolide A (23), picrotoximaesin (24), phytol (25), betulinic acid (26), oleic acid (27), palmitic acid (28), 3 methoxy 4 hydroxy-cinnamaldehyde (coniferyl aldehyde) (29), 3, 4, 5 trimethoxy cinnamaldehyde (30), 3, 4, 5 trimethoxy benzaldehyde (31), 3,4 dimethoxy benzaldehyde (veratraldehyde) (32) and Melatonin (33).

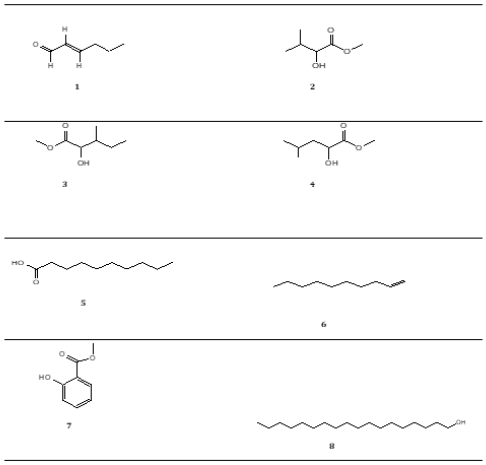


Figure 2: Isolated and identified secondary metabolites contained in B. motleyana fruits.
(E)-Hex-2-enal (1), methyl 2-hydroxy-3-methylbutanoate (2), methyl 2-hydroxy-3-methylpentanoate (3), methyl 2-hydroxy-4-methylpentanoate (4), Decanoic acid (5), 1-Decene (6), Methyl salicylate (7) and Stearyl alcohol (8).

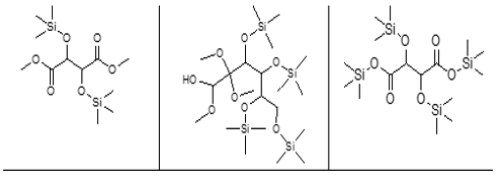


Figure 3: Antimicrobial compounds detected from B. lanceolata. Dimethyl2,3-bis[(trimethylsilyl)oxy] succinate (1), Arabino-hexos-2-ulose,3,4,5,6-tetrakis-o-trimethylsilyl)-, bis (dimethyl acetal) (2) and Bis(trimethylsilyl) 2,3- bis[(trimethylsilyl) oxy] succinate (3).

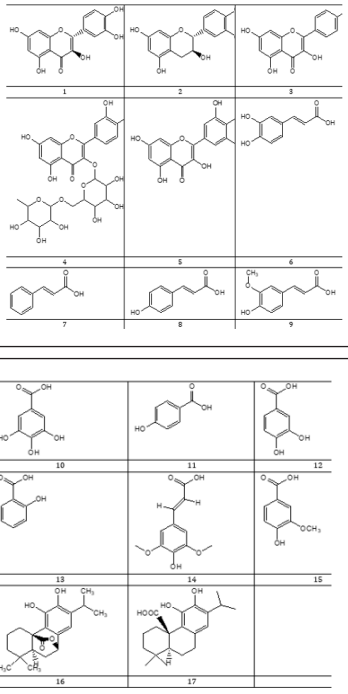


Figure 4: Isolated phenolic compounds from B. angulata. quercetin (1), catechin (2), kaempferol (3), rutin (4), myricetin (5), caffeic acid (6), cinnamic acid (7), p-coumaric acid (8), ferulic acid (9), gallic acid (10), 4-hydroxybenzoic acid (11), protocatechuic acid (12), salicylic acid (13), sinapic acid (14), vanillic acid (15), carnosol (16) and carnosic acid (17).

Table 2: Bioactive compounds isolated from Baccaurea genus along with their activity.

Species	Compound Isolated Plant Parts	Bioactive Compound	Activity	References
B. ramiflora Lour. Muell. Arg	Stem	4′-O-(6-O-vanilloyl)-β-D-glucopyranosyl tachioside D	Antioxidant activity, Antili-poxygenase activity	[80,86]
	Leaves	6′-O vanilloylisotachioside	Antioxidant activity	[20]
		6′-O-vanilloylitachioside		
		3-O-cafeoyl-4-O-methylquinic acid		
	Stem	Blumenol A	Cytotoxic activity	[80,87]
	Leaves, Stem	Icariside B5	Antioxidant activity	[20,80,88]
	Stem	6′-O-vanilloylpicraquassioside D	Antioxidant activity, antili-poxygenase activity	[80,86]
	Leaves	Aviculin	Induces apoptosis, Antioxidant activity	[20,89]
	Leaves	5-O-cafeoylquinic acid methyl ester	Antioxidant activity, Anti-radical	[20,90]
	Leaves	Erigeside B	Peroxyl scavenging activity	[20,91]
	Leaves	Melatonin (N-acetyl-5-methoxytryptamine)	Sleep inducing activity	[70]
	Leaves	(−)-Epicatechin	Anti-hyperlipidemia, Reduce high pressure, Antioxidant activity.	[20,92-93]
	Stem and leaves	Daucosterol	Anti-cancerous, Neuroprotective, Apoptosis	[94–98]
	Leaves	Rosamaric acid	Anti-Inflammatory activity	[44]
	Seed kernel, Fruits	Sapidolide A	Anti-fungal activity.	[62,79]
	Berries	Ramifoside	Anti-fungal activity.	[62]
		Picrotoximaesin		
	Fruits	Palmitic acid	Anti-fungal activity.	[63]
		Oleic acid		
	Stem bark	Phytol	Antidepressant, Anti-inflammatory, Antimicrobial, Cytotoxic, Antioxidant activity	[20,49-50,64,99-100]
	Stem bark	Betulinic acid	Anti-bacterial activity	[49]
B. ramiflora Lour. Muell. -Arg, Baccaurea lanceolata	Stem and leave; Leaves; Stem; Fruits.	β-sitosterol	Antioxidant, Anti-inflammatory, Analgesic, Anthelmintic.	[20,74,78,80, 85,98,101-102]
Baccaurea motleyana (Muell. Arg.) Muell.	Fruits	Methyl 2-hydroxy-3-methylbutanoate,	Antibacterial activity	[83]
		Methyl 2-hydroxy-3-methylpentanoate,		
		Methyl 2-hydroxy-4-methylpentanoate		

Baccaurea lanceolata.	Fruits	Dimethyl 2, 3-bis[(trimethylsilyl) oxy] succinate	Antimicrobial activity	[9]
		Arabino-hexos-2- ulose, 3, 4, 5, 6-tetrakis-o-(trimethylsilyl)-, bis (dimethyl acetal)		
		Bis(trimethylsilyl) 2,3-bis[(trimethylsilyl)oxy] succinate		

Conclusion

Medicinal Plants are the gift of nature to human beings to have a healthy life free of disease. In Southeast Asia, phytomedicine for local healers is very common with Baccaurea species. The numerous ethnomedicinal practices, phytochemical properties, pharmacological activities, and pharmaceutical applications of Baccaurea species have been demonstrated in this study. Phytochemical and pharmacological screening records of the various species of Baccaureas indicated the presence of important bioactive substances. A review is worthwhile due to the significance of the underutilized plants as a source of new medicinal agents. Therefore, for the production and creation of new drugs, more research and activities relating to the inventory, conservation, characterization, and isolation of the compound from the medicinally conspicuous Baccaurea plant species are required [86-106].

Conflict of Interest Statement

Authors announce that no conflict of interest occurs.

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