Ethnobotanical review and pharmacological properties of selected medicinal plants in Brunei Darussalam: *Litsea elliptica*, *Dillenia suffruticosa*, *Dillenia excelsa*, *Aidia racemosa*, *Vitex pinnata* and *Senna alata*

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ABSTRACT

The aim of the current study is to review the medicinal properties of the plants found in Brunei Darussalam namely *Litsea elliptica*, *Dillenia suffruticosa*, *Dillenia excelsa*, *Aidia racemosa*, *Vitex pinnata* and *Senna alata*. The known phytochemical constituents of these plants and their ability to bring about a range of biological activities are included in this review. These plants have been used traditionally for a multitude of diseases and illnesses. There is a lot of untapped potential in these medicinal plants which could cure multiple diseases.

1. Introduction

Brunei Darussalam, also known as the Kingdom of Unexpected Treasures, is a country that is prosperous, not only in oil and natural gas, but also in many other resources. Located in the Island of Borneo, the country is also rich in natural flora that covers a large portion of its land. This natural flora is well-preserved as a good proportion which is still left untouched. Needless to say, the floral species that make up this abundant vegetation can be exceptionally wide-ranging. Many of these species are of great medical importance as they could potentially treat many modern day diseases following proper identification and extensive research work. Nevertheless, there are several species that have already been identified for their use in local traditional remedies. They are either taken raw, cooked, or taken in the form of decoction, poultices, infusions or pounded pastes that are then consumed orally, applied topically or used in herbal baths. Today, some of these practices are still considerably active within the local community where they are used to treat known and unknown diseases as an alternative to modern medicine.

With the trend in emerging diseases, there is an increased interest to revert back to knowledge of traditional medicine, with hopes to discover novel biological activities within these plants. Thus, this article reviews the traditional uses and scientific findings of some of the species used in traditional remedies in Brunei Darussalam, including *Litsea elliptica* Blume (*L. elliptica*), *Dillenia suffruticosa* (Griff.) Mart. (*D. suffruticosa*), *Dillenia excelsa* (Jack) Martelli (*D. excelsa*), *Aidia racemosa* (Cav.) Tirveng. (*A. racemosa*), *Vitex pinnata* L. (*V. pinnata*) and *Senna alata* (L.) Roxb. (*S. alata*).
2. *L. elliptica*

*L. elliptica*, found widely in the forests of South East Asia, is a tropical tree from the Lauraceae family [1] (Figure 1). It is locally known as “Pawas” in Brunei Darussalam. The leaf extract of this plant species have been used to treat different illnesses such as stomach ulcers, fevers and headaches [1,2]. The methanolic extract of its leaf was shown to inhibit the growth of *Helicobacter pylori* (*H. pylori*), a bacterium that is responsible for the multiple forms of gastric complications such as gastritis, dyspepsia, peptic ulcer disease and gastric cancer [3]. This demonstrates their potential chemo-preventive properties [3]. The leaf of *L. elliptica*, similar to the leaves of *Pouzolzia pentandra*, *Cycas siamensis* and *Melaleuca quinquenervia*, was found to have a minimum inhibitory concentration (MIC) of 100 mg/mL against *H. pylori* [3]. This inhibitory activity was lower when compared to the extracts of other plant species in the study, such as the aril of *Fusarium* that had a MIC of 12.5 mg/mL, the leaf of *Barringtonia acutangula* and rhizome of *Kaempferia galanga*, that exhibited an MIC of 25 mg/mL, and the leaves of *Cassia grandis*, *Cleome viscosa*, *Myristica fragrans* and *Syzygium aromaticum* with an MIC of 50 mg/mL [3]. Nonetheless, the apparent inhibitory activity against *H. pylori* justifies how *L. elliptica* was a useful traditional remedial plant for the treatment of stomach ulcer.

![Figure 1. Leaves of *L. elliptica*.](image1)

In more recent studies, the methanolic extracts from the stems, roots and leaves of *L. elliptica* showed significant antioxidant activities that were higher than those of synthetic antioxidant, butylated hydroxytoluene, and antioxidant standards, vitamin C and trolox [4,5]. Wong *et al.* has also shown that the stems of the plant have significantly higher inhibition against bacterial growth, as compared to its roots and inner bark [5]. This is especially shown by dichloromethane and chloroform extracted stems that showed reactivity against skin pathogen *Pseudomonas aeruginosa* (*P. aeruginosa*) and food-borne pathogens *Escherichia coli* (*E. coli*) and *Bacillus subtilis* (*B. subtilis*) [5]. Additionally, the essential oils extracted from the roots have also displayed antifungal properties, where they were able to inhibit about 67% of mycelial growth of *Fusarium oxysporum* [5].

Previous reports also have indicated that *L. elliptica* possesses remarkable insecticidal properties especially towards mosquitoes [6-10]. Its median lethal concentration (LC50) against adult *Aedes aegypti* was found to be < 20 mg/cm² (i.e. 0.11 mg/cm²) which is more effective than the well-known insecticidal plant *Azadirachta indica* and *Asimina triloba* [8]. It was also found that a high concentration of 12.42 mg/cm² was able to cause 50% mortality in the *Aedes aegypti* population within 10 min [8]. This is a relatively short period of time when compared to the other plant species studied which required more than 20 min to achieve the same percentage mortality [8]. Moreover, the essential oil of the leaf also displayed 100% repellency against the same species of mosquito at 0.00379 mg/cm² [9]. Due to this profound property, several studies were carried out to determine its potential safety/health hazard on red blood cells and other parts of the body. These studies focused on acute and subacute toxicities, morphological, hematological and biochemical parameters of mice that were administered orally with the essential oils. They have demonstrated that the essential oil of this plant species is likely to be non-toxic in all aspects under normal usage following the World Health Organization guidelines [1,10].

3. *D. suffruticosa*

Locally known as “Simpor bini”, *D. suffruticosa* is a medium sized tree characterized by its large bright flowers with five thin yellow petals around its white stamen, and dark-pink star-shaped fruits all of which are surrounded by large oval leaves (Figure 2). This plant species typically grows in wastelands, swamps, poor soil, white sands, secondary forests, along roadsides or the edge of forests [11-13]. Its leaves have been traditionally used for different treatments such as to promote wound healing, relieve rheumatism and treat fever while the fruit was claimed to be able to treat cancerous growths [12-16].

![Figure 2. Flowers and leaves of *D. suffruticosa*.](image2)

The methanolic extract of the roots of this plant have displayed significant antioxidant and cytotoxic activities particularly towards the *HeLa* cervical cancer cell line [17]. Studies conducted by Armania *et al.* have indicated that the phenolic content was an important contributor to the high antioxidant activity observed in the methanolic root extract of this plant species [17,18]. Although this extract showed the highest antioxidant and cytotoxic activities in the *HeLa* cell line, it was found that the dichloromethane and ethyl acetate extracts exhibited higher cytotoxicity in the breast cancer cell lines, MCF7, MDA-MB-231, the A549 lung cancer cell line and the HT29 colon cancer cell line [17]. Further mechanistic investigation demonstrated that the plant extract inhibited the proliferation of the *HeLa* cervical cancer cell line as well as...
the MCF7 and MDA-MD-231 breast cancer cell lines via the induction of apoptosis and the G2/M cell cycle arrest [17,18]. An in vivo study conducted by Yazan et al. showed that oral intake of aqueous root extracts have successfully reduced breast cancer induced in rats and also inhibited metastasis of the cancer to the heart [19]. The study further demonstrated that the extract was not toxic at the acute toxicity level up to a high dose of 500 mg/kg, however, mild focal hemorrhage was observed when a dose of 1000 mg/kg of the extract was used for treatment [19]. The cytotoxic activities of this plant species could be attributed to the presence of phytochemicals such as saponins, triterpenes, sterols, and polyphenolic compounds [17,20–26].

Saponins is a collective term for triterpenoid and steroidal glycosides [27], which consists of at least 150 kinds of natural saponins that have displayed significant anti-cancer properties [28]. Moreover, they have been recognized for their ability to reduce cholesterol level in the blood [29]. Dietary and endogenous sterols pass through the bile or desquamated-intestinal cells and reach the intestine before they are absorbed into the blood stream [29]. Saponins, being poorly absorbable from the intestine into the blood stream, interact with sterols and other sterols, and thus interfere and prevent them from being absorbed into the blood stream [29]. Additionally, saponins have the ability to stimulate the immune system and enhance antibody production [30]. Interestingly, multiple studies have reported reduction in bone loss with diets that are high in saponins [31,32]. One of the many saponins in particular, called asperosaponin VI, was able to induce the differentiation and maturation of osteoblasts and thus increase bone formation via the bone morphogenetic protein-2/p38 synthesis, and activation of the extracellular signal-regulated kinase 1/2 pathway [32].

On the other hand, polyphenols, which include phenolic acids, flavonoids, stilbenes and lignans, have been recognized for their multiple health-benefitting properties [33]. Polyphenols such as resveratrol and quercetin were found to exhibit significant cardio-protective effects by preventing platelet aggregation, disrupting atherosclerotic plaques and inhibiting protein expressions [33]. Other than that, anti-cancer, anti-viral, anti-diabetic, anti-aging and neuro-protective effects were also noted for the phytochemicals in the polyphenol group. They also showed beneficial effects towards asthma, osteoporosis, bone loss, skin damage and mineral absorption in intestines [33].

The phytochemical contents within D. suffruticosa play a significant role in relieving and alleviating illnesses. Perhaps it is a combination of their effects that promote wound healing, relieve rheumatism, and treat fever and cancerous growth traditionally. However, more studies should be performed to fully validate their traditional uses for such diseases.

4. D. excelsa

Another species in the Dillenia genus is D. excelsa, which is also known as “Simpur laki” by locals in Brunei (Figure 3). This particular species of Dillenia is well represented by its distinct purple stamen in the middle of its flower with five pale yellow petals and white star-shaped fruits [12]. It has been noted to grow in dry to swampy soils, often along streams within forests [34].

Figure 3. Flower of D. excelsa.

Not much has been reported on the remedial use of this plant, except that its bark and fruits may possess medicinal values, one of which is to treat diarrhoea [12]. Similarly, scientific studies of this species also seem to be lacking, possibly due to its rare occurrence.

5. A. racemosa

A. racemosa or locally referred to as “Sambil/Sambah Bagangan”, is a plant that belongs to the Rubiaceae family [13]. It is a small tree with pinkish-red young leaves, and mature green leaves [13]. The leaves are glossy on the upper surface (Figure 4). This plant was brought into light recently due to the ability of its roots and leaves to relieve body aches and tiredness. It is now being marketed locally as a tea or tonic for energy and overall body strength [35]. In addition to this, it was also traditionally known to be able to cure gastric pains [13,35].

Although having a good marketable value, the scientific investigations and information on this plant are still very limited. The medicinal property of this plant remains understudied.
6. *V. pinnata*

*V. pinnata* is a small tree from the Lamiaceae family (Figure 5), and is commonly known as “Kulimpapa” in Brunei [13]. It has whitish blue flowers with purplish black berries [13]. Traditionally, the whole plant has been used to treat jaundice [36], while the bark has been used in post-natal herbal baths and for the treatment of stomachaches [13]. Along with the leaves, the bark has also been used for treating wounds, dysentery and stomach diseases [13,37] while the leaves alone were used to treat fever and hypertension [13,38]. Additionally, the roots of the plant species have also been taken as a tea for relieving tiredness, body aches and backaches [13,38].

With an IC50 value of 17.38 mg/mL, the methanolic extract of this plant species was found to be a less potent anti-proliferation agent when compared to that of *Syzygium polyanthum* and *Barringtonia racemosa*, with IC50 values of 5.50 mg/mL and 3.47 mg/mL respectively [39]. However, it was found to be more potent compared to *Oroxylum indicum* which did not show any IC50 value [39]. Moreover, since the IC50 value of the extract of this plant species was less than 20 mg/mL, it can thus be considered as being an active anti-proliferative agent [39–41].

A study by Ramesh *et al*. has indicated that the petroleum ether, ethyl acetate, methanol and aqueous leaf extracts of *V. pinnata* contain varying amounts of the alkaloid, anthocyanidins, aucubins, coumarins, flavonoids, flavanols, gallic tannins, iridoids, proteins, reducing compounds, steroids, triterpenoids and glycoside compounds where flavonoids appeared to have the highest frequency in all the four different extracts [42]. Additionally, a new compound, pinnatoside iridoid glucoside, along with other known flavonoids, namely viscoside, apigenin and luteolin were isolated by Ata *et al*. from the bark of this plant species and their structures were determined by nuclear magnetic resonance spectroscopy [36]. Interestingly, the pinnatoside iridoid glucoside compound was found to have modest inhibition against the fungus *Candida albicans* [36].

The identification of the phytochemical compounds from the most commonly used parts of this plant species can definitely provide clues for further scientific investigations.

7. *S. alata*

*S. alata*, locally known as “Daun Kurap”, or commonly known as “Candlestick”, is a perennial shrub with only few branches (Figure 6) [13]. It is recognizable by its bright orange-yellow flowers that are arranged spirally on its rachides [13]. This plant species was found to have abortifacient properties [43]. *S. alata* has been considered of high value due to its ethnomedicinal uses in multiple health disorders traditionally. These disorders include gastroenteritis, asthma, hypertensions, sickle-cell anemia, diabetes, hepatitis, skin diseases, jaundice, eczema and ringworm, constipation and food poisoning, burns, wounds, skin infection, diarrhea and upper respiratory tract infection [16,44,45].

Consequently, there has been a considerable amount of literature reporting on this plant species. Some of these studies revealed that the plant species displayed significant cytotoxic activities, apoptotic induction and proliferation inhibition in selected breast cancer cell lines and leukemia cells [46–48]. A study carried out by Essien *et al*. revealed that the essential oils of the Nigerian origin of this plant species contained mainly ar-turmerone (13.5%), β-caryophyllene (7.3%), (E)-phytol (7.0%) and 6,10,14-trimethyl-2-pentadecanone (6.8%) [46]. In addition, the essential oils of *S. alata* were found to be cytotoxic against the Hs 578T human tumor breast cell line [46]. Jaabir *et al*. has also showed that the methanolic extracts of the leaves of this plant species were cytotoxic towards...
inhibitory effect against a MCF-7 breast cancer cell line at 1 mg/mL [47]. Further investigation indicated that the extract caused cell death in the selected cell line via apoptosis [47]. On the other hand, it was found that, the inhibition of proliferation of the L1210 leukemia cells after 72 h increased with the concentration of ethanolic extract of the S. alata leaves [48]. The plant extract was also able to significantly decrease protein synthesis of leukemia cells [48]. Moreover, the study showed that, the addition of α-difluoromethylornithine to the plant extract decreased the production of polyamines that were produced from the proliferation of leukemia cells, such as putrescine, spermidine and spermine [48]. This signifies that more effective inhibition of leukemia cell proliferation is achieved via the α-difluoromethylornithine plant extract complex [48].

Apart from that, the crude methanolic extract of the leaves of this plant species also displayed more effective anti-diabetic property when compared to the standard clinical drug, acarbose, via the inhibition of α-glucosidase [49]. Subsequently, the crude plant extract was fractionated in different solvents, namely petroleum ether, chloroform, ethyl acetate, n-butanol and water, in order to further determine the chemical constituents responsible for the finding [49]. The results showed that the ethyl acetate and n-butanol fractions exhibit the highest inhibitory effect against α-glucosidase [49]. Following that, these two fractions were found to contain mainly kaempferol and kaempferol 3-O-gentiobioside [49]. Thus, these suggest that these two compounds found in the S. alata leaves could be the major contributors to the anti-diabetic effect observed [49]. This also allows justification for the traditional use of this plant species to treat diabetes [45].

Antibacterial and antifungal properties have also been reported for this plant species [46,50], According to Essien et al., the volatile oil from this plant species demonstrated antimicrobial activities when tested against standard strains of Bacillus cereus, P. aeruginosa, E. coli, Staphylococcus aureus (S. aureus), Candida albicans and Aspergillus niger although only moderately [46]. Contrastingly, Alalor et al. found that the crude methanolic and aqueous extracts of the leaves and barks were able to inhibit S. aureus and B. subtilis in a concentration-dependent manner, however, no activity was shown on the Gram-negative bacteria, E. coli and P. aeruginosa [50]. The aqueous extracts had higher inhibitory activity against the two susceptible bacteria when compared to the methanolic extracts [50]. Additionally, B. subtilis was found to be more susceptible to the extract than S. aureus [50]. Another study has shown that the crude ethanolic extract of the stem bark of S. alata inhibits the growth of clinical dermatophytes in a concentration-dependant manner [51]. The strain with the lowest susceptibility was the Microsporum canis, followed by Trichophyton mentagrophytes, Epidermophyton floccosum and Trichophyton verrucosum [51]. Furthermore, it was also demonstrated that the MIC and minimum fungicidal concentration of the extract were 5.0 mg/mL against all four of the dermatophytes except for Epidermophyton floccosum (as it appears to be only fungistatic at that concentration) [51]. Nonetheless, these findings provide justification for its traditional use in treating many diseases such as skin diseases, gastroenteritis, ringworm, food poisoning, skin infection and upper respiratory tract infection.

According to Singh et al., the leaves of S. alata also possess anti-allergic properties [44]. In this study, the hydroalcoholic extract of the leaves and two of its constituents, rhein and kaempferol were evaluated for its anti-mast cell degranulation activity [44]. Additionally, in vitro studies were also carried out to evaluate the inhibitory effects they have on the lipoxigenase (LOX) enzyme as the increased expressions of the enzyme have been linked with increased allergic reactions [44,52]. It was found that both the extract and the active constituents were able to significantly inhibit the mast cell degranulation at doses of 200 mg/kg and 5 mg/kg respectively [44]. However, only the extract and rhein was able to inhibit the LOX enzyme, while kaempferol appeared inactive against the enzyme [44]. According to Morris, rhein was also noted to have anti-carcinomic, anti-tumor and antiseptic properties [53]. Nevertheless, Singh et al. suggested that the anti-allergic properties of the leaves of this plant species were via the stabilization of mast cells and inhibition of the LOX enzyme [44]. These findings justify the traditional uses of the plant species for treating complications such as asthma and eczema.

Antioxidant compounds and activities of this plant species have also been reported in several other studies [54,55]. In a study by Panichayupakaranant and Kaewsuwan, the methanolic extract of the leaves of S. alata was determined to have the highest antioxidant activity when compared to the methanolic extracts of its flowers and pods [54]. It was also found that methanolic extract of the leaves has stronger antioxidant...
activity when compared to the n-hexane extract and therefore, the methanolic extract of the leaves was subsequently purified to determine which compound contributed to the highest antioxidant activity [54]. The compound that produced the highest activity was determined to be kaempferol [54]. The antioxidant activity of the flavanol compound was found to be six times more active than that of butylated hydroxytoluene, and 58 times more active than that of emodin suggesting that kaempferols are the significantly active antioxidant compound in S. alata leaves [54]. Emodin is a major compound in the active fraction of the Cassia tora extract, however it was noted that since the pure isolated emodin did not exhibit a strong antioxidant activity as in the active fraction, the significant antioxidant activity could possibly be a minor component in the active fraction of Cassia tora [54]. Nevertheless, emodin was also noted to be one of the phytochemicals in S. alata and it was noted to have antiaggregant, anti-inflammatory, antimutagenic, antiseptic, antitumor (breast), antiulcer and spasmylocytic properties [53]. In another study by Chatterjee et al., it was suggested that the good amount of phenols, vitamin C, vitamin A, flavonoids, carotenoids and anthraquinone in the extract also contributes to the strong antioxidant activity noted for the alcoholic extracts of the leaves of this plant species [55]. In addition to this, the study also showed that rabbits that have been administered with the extract displayed significant increase in blood hemoglobin and red blood cell count, leukocytes, peritoneal macrophages and the granulocyte/agranulocyte ratio [55]. This showed the strong immune-modulating or immune-stimulating potency of the aqueous leaf extract of the plant species, which can also be attributed to the phenols, vitamins, carotenoids and anthraquinone found in the plant [55]. In summary, this study also demonstrated apparent antioxidant activities and additional immune system stimulating properties of the S. alata leaves.

Additionally, Morris suggested that this plant species possesses anti-leukemic, antiseptic, anti-tubercular and anti-tumor properties as it contains the phytochemical, aloe-emodin that is known for these activities [53]. In addition, the plant species is also said to contain chrysophanol that is known to be antiaggregant and haemostatic [53]. Moreover, the flavonoids, quercetin and kaempferols, found in the plant species have exhibited anti-pancreatic cancer properties [56]. Therefore, it is likely that the activity of this species is attributed to the presence of the combination of the phytochemicals of the plant species.

Scientific links to the treatments of the other notable complications by S. alata such as in sickle-cell anemia, hypertension and constipation are yet to be discovered. Nevertheless, it seems that these wide-ranging properties have contributed significantly to its effectiveness in treating the complications such as diabetes, hepatitis, skin diseases, gastroenteritis, eczema, ringworm, food poisoning, skin infection and upper respiratory tract infection traditionally.

8. Conclusion

This review summarizes the known literature in relation to some of the medicinal plant species found in Brunei Darussalam. All six plant species have been used varying for treatments and reliefs of different illnesses traditionally. It is evident that these plants possess great potential to become useful natural treatments for many modern day diseases. However, it is inevitable that further scientific exploration is required. Certain species such as S. alata have been reputed to have wide medicinal applications. However, their exact mechanisms are still uncertain. Thus, much more comprehensive studies need to be carried out to reveal the full potential of these plants for novel drug discovery.

Conflict of interest statement

We declare that we have no conflict of interest.

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References


