Https://Doi.Org/10.48047/Afjbs.6.Si4.2024.5853-5866

African Journal of Biological Sciences

Schefflera J.R.Forst. & G.Forst. – A Hidden Genus of the Family Araliaceae

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Article History
Volume 6, Issue Si4, Aug 2024
Received: 25/07/2024
Accepted: 08/08/2024
Published: 29-08-2024
doi: 10.48047/AFJBS.6.Si4.2024.5853-5866

Abstract
Schefflera, the largest and an important genus belonging to the family Araliaceae has a wide range of ethnic medicinal importance among various cultures of the world. The genus has been studied for its ethnomedicinal uses, which mainly includes its use in the treatment of asthma and liver diseases. The major phytochemicals identified from Schefflera species are saponins and triterpenoid glycosides. Extensive work has been carried out on the isolation and identification of compounds present in the genus, but, their role in biological activities has not been much reported. This review highlights the distribution of the genus the ethno-medicinal uses, major phytochemicals identified, reported biological activities and compounds isolated and identified from *Schefflera* species and from some major species of Araliaceae.
Key words: *Schefflera,* Araliaceae, ethnomedicinal

Introduction

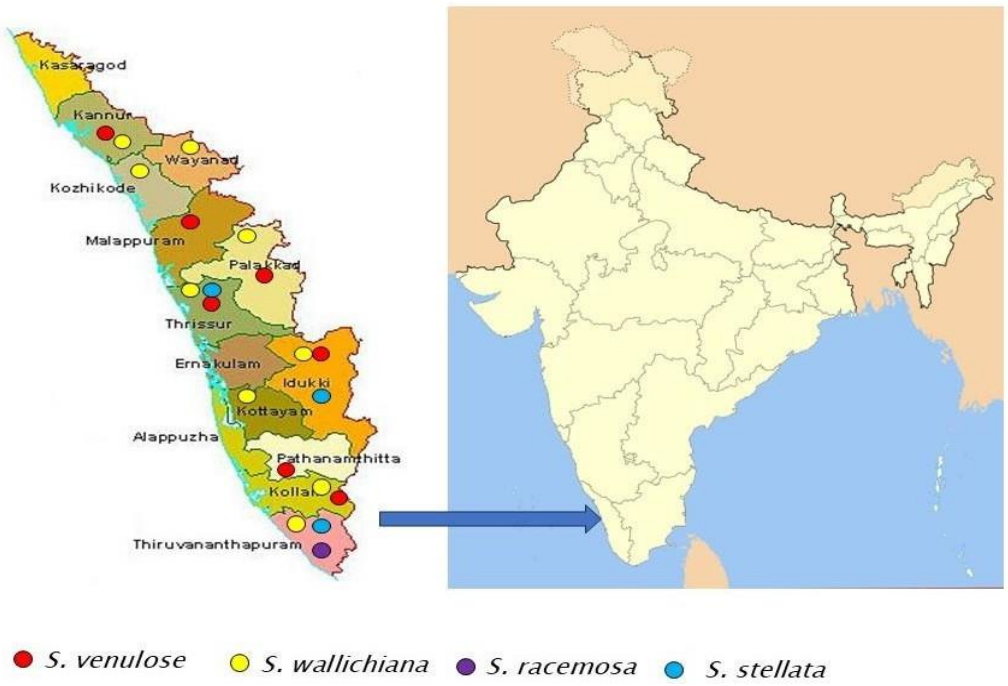
The Araliaceae, known as the ginseng family comprise 55 genera and 1,500 species (Plunkett et al., 2005). The family is broadly distributed in the tropics and sub-tropics (especially in southern Asia and the Pacific islands), but several genera from the temperate zones are documented as well (viz., Aralia, Hedera, Oplopanax and Panax). The family includes a number of medicinally important plants, such as Panax (ginseng) and Eleutherococcus (Siberian ginseng) and several well-known ornamentals, including Hedera (English ivy), *Schefflera* (the umbrella trees), and Polyscias.

Distribution of *Schefflera* species

The plant species are not found to be uniformly distributed around the world. Similarly, no particular region in the world has been reported to harbor all the plants of the plant kingdom. This disparity in plant distribution depends on the interaction of plants with the surroundings (Dwivedi and Tripathi, 2007). The distribution of a particular plant species, mainly depends on the geographical area, climatic conditions and type of soil required for their growth. The family Araliaceae, comprising about 55 genera, is native to Asia, the Malayan Peninsula, Polynesia, Europe, North Africa and the Americas (Davydov and Krikorian, 2000; Wen et al., 2001). The genus *Schefflera* consists of 1100 species, and 35 of them are found in China. The genus is widespread in the tropical and the

subtropical regions of both the hemispheres (Wang et al., 2013). Phylogenetic studies by Plunkett et al. (2005) suggests, *Schefflera* as the largest genus which includes more than half the species of Araliaceae. The polyphyletic nature of *Schefflera* was ascertained based on nuclear (ITS) and plastid (trnl-trnf) DNA sequences which comprised not more than five major clades distributed across the phylogenetic tree of Araliaceae. Comparison with the molecular cladograms showed only one out of all its infrageneric groupings to be monophyletic. Geographic distribution of these five clades revealed two morphologically distinct clades to be centered in the southwest Pacific and remaining three clades to be centered in the Neotropics, Asia/Malaysia and Africa/Madagascar.In India, *Schefflera* species are mainly reported from the Western ghats (Selvi et al., 2015). *S. arboricola* (Hayata) Merr., is a popular ornamental plant in Europe (Hansen and Boll, 1985) and Japan (Melek et al., 2003). *S. impressa* (C. B. Clarke) Harms., has been reported from Darjeeling, India (Srivastava, 1992). *S. taiwaniana* (Nakai) Kaneh., is said to be indigenous to Taiwan (Kuo et al., 2002). Mohanan and Sivadasan (2002) reported the occurrence of *S. stellata* (Gaertn.) Harms., from the Peninsular India and Sri Lanka. Li et al. (2005) reported *S. heptaphylla* (L.) Frodin, one of the popular medicinal plants from southern China. *S. abyssinica* (Hochst. Ex A. Rich.) Harms, a tall tree, is widely distributed in sub-Saharan Africa (Tapondjou et al., 2006). *S. umbellifera* (Sond.) Baill., a semi-deciduous tree, has been reported from Malawi, Mozambique, Zimbabwe, and South Africa (Mthembu, 2010). *S. venulosa* (W. & A.) Harms, also known as *Schefflera* vine is often an epiphyte and is said to be distributed in China, Indo-China, and Myanmar and in tropical and subtropical climates of India usually in the Western Ghats (Pullaiah, 2006). Later, Sabulal et al. (2008) reported the distribution of *S. stellata* (Gaertn.) Harms., from the Silent Valley of Kerala state and Agasthyamalai hills as well. Matsui et al. (2010) reported the occurrence of *S. leucantha* (Viguier), which is a shrub, from Thailand and China. *S. wallichiana* (W. & A.) Harms., has been reported from the southern India and Sri Lanka. In India, it is mainly distributed in the Western Ghats, Tamil Nadu (http://www.Indiabiodiversity.org) and Meghalaya (Baiswar et al., 2014). S. racemosa (Wight) Harms., is endemic to the Western Ghats (Selvi et al., 2015). The distribution of *Schefflera* species considered in the present study (*S. venulosa, S. wallichiana, S. racemosa* and *S. stellata*) are shown in Figures 1-2.

Figure 1: Distribution of *Schefflera* species across the world



(Source: http://www.discoverlife.org/mp/20lid=GBIF543272421)

Figure 2: Distribution of *Schefflera* species in India

Ethno-medicinal uses of Schefflera species

Traditional medicine has been practiced for many centuries in many parts of the world, to treat human diseases at low costs. Traditional medical treatments in daily life are now being used with empirical methods. Nature has provided a source of medicinal agents for thousands of years and several modern drugs have been isolated from natural sources, on the basis of their use in traditional medicine (Criag, 2004). The science of the application of the indigenous or local medicinal remedies, including plants for the treatment of diseases is called ethnopharmacology. Ethnopharmacology has been the mainstay of traditional medicines and is currently being integrated into mainstream medicine. According to the concept of traditional Chinese medicine, the genus *Schefflera* has a bitter and sweet taste. Its main function is to promote the circulation of blood and to relieve pain. The extracts of *Schefflera* species have importance in the treatment of liver, rheumatic heart diseases and asthma (Purohit et al., 1991). *Schefflera* extracts contain a variety of chemicals including fumaric acid and gamma-hydroxybutyric acid. Modern uses of *Schefflera* include the treatment of rheumatoid arthritis, numbness in limbs, abdominal pain, headaches, arthralgia and sore or swollen throat. It also helps to relieve asthma. Externally, it is ground into a paste to treat injuries and has haemostatic effect (http://www.acupuncture.com/herbcentral/Schefflera.php.). A detailed report on the medicinal plants used by the Apatani tribe of Arunachal Pradesh has been reviewed by Kala (2005). Apatani have traditionally settled in seven villages and in the Ziro valley of lower Subansiri district of Arunachal Pradesh in the Eastern Himalayan region of India. The author has documented 158 medicinal plant species used by the tribes. These medicinal plant species were distributed across 73 families and 124 genera. Among the medicinal plants used by the tribes, the fruits of S. glomerata of Araliaceae have been used for cough and indigestion respectively. The study revealed that, about 52 types of ailments were cured by using 158 medicinal plant species. S. stellata has been included in the mediflora of Penusila Narasimha Sacred grove used by the local tribes. 160 species of probable medicinal potential belonging to 138 genera and 71 families have been studied by Basha et al. (2012). The study conveys the usage of mediflora by the tribal and local people, residents near and around the sacred grove for various ailments.

The following list includes the medicinal uses of *Schefflera* species:

1. ***S. arboricola*** (Hayata) Merr.: The ethanolic leaf extracts possess sedative, hypnotic, analgesic, anticonvulsant and smooth muscle relaxant effects (Melek et al., 2002). The roots are found to be effective for abdominal diseases, arthritis, external bleeding, fracture, gall stones, headache, internal injury and kidney stones. It is best used for asthma (http://www.herbpathy.com/uses and benefits-of-schefflera-arboricola-id4994).
2. ***S. caudata* = *S. vidal*** (Merr. & Rolfe): Decoction is given as tonic to women after child birth (Batugal et al., 2004).
3. ***S. cumigii*** (Seem.) Harms.: The plant helps to cure stomach trouble (Batugal et al., 2004).
4. ***S. digitata*** (J. R. Forst & G. Forst): The sap is used to cure ringworm and scrofulous sores (Pullaiah, 2006).
5. ***S. elliptica*** (Blume) Harms.: The bark is employed to relieve cough. The decoction of leaves is an effective antiscorbutic and wood relieves toothache (Batugal et al., 2004).
6. ***S. elliptifolia*** (Merr.): The decoction of leaves is used as a tonic by women after child birth (Batugal et al., 2004).
7. ***S. fagueti*** (Baill.): Saponins, isolated from the plant are said to be cytotoxic (Cioffi et al., 2003; Pullaiah, 2006).
8. ***S. heptaphylla*** (L.) Frodin: The plant is mainly used as anti-pyretic, anti-inflammatory and antirheumatic in southern China (Li et al., 2005). The bark is widely used in folk medicine for its diuretic properties and as a tonic. The ash is sometimes used to treat dropsy. In Hong Kong, the fresh branchlets are used as a wash to soothe itching of the skin (Orwa et al., 2009).
9. ***S. insularum*** (Seem.) Harms.: The juice of powdered fresh leaves is used as purgative and to treat cancer (Batugal et al., 2004).
10. ***S. leucantha*** (Viguier): The leaves of this plant have been traditionally used in Thailand and China to relieve cough and asthma (Matsui et al., 2010).
11. ***S. longipedicellata*** (Lecomte): The plant is used to cure epilepsy, cold and gonorrhea (Razafindraibe et al., 2013).
12. ***S. octophylla*** (Lour.) Harms.: The plant is used in Chinese and Vietnamese folk medicine as an anti-rheumatic agent and as tonic (Sung et al., 1991). The wood of this plant is used to treat cancer locally in Taiwan (Kuo et al., 2002). The root bark and stem bark possess anti-inflammatory and diuretic properties and are used in treating rheumatism, lumbago, ostedynia paresis, amnesia, vulval prunitis, impotence, dyspepsia, infantile rickets, edema, dysuria and impetigo (Pullaiah, 2006).
13. ***S. stellata*** (Gaertn.) Harms.: The plant is used to cure neurological weakness (Rao et al., 2011). There is a belief that the bark ash is used to control evil spirits (Kadavul and Dixit, 2009).
14. ***S. trifoliata*** (Merr. & Rolfe): The crushed leaves are applied externally against tympanites of children and is given as tonic for women after child birth and in treating irregular menstruation (Batugal et al., 2004).
15. ***S. umbellifera*** (Sond.) Baill.: The root bark decoctions are administered for mental illness. The bark is used for stomach ulcers and magical purposes (Watt and Breyer-Brandwijk, 1962). The leaves are traditionally used to cure rheumatism and for malaria. Vhavenda people use the roots as a diuretic and laxative, for bathing, for weaning infants, venereal diseases and nausea (Hutchings et al., 1996).
16. ***S. venulosa*** (W. & A.) Harms.: Roots mixed with rice are eaten by Munda tribes to cure dropsy. The ethanolic extract (2%) of the leaves caused 100% immobilization of human spermatozoa (Pullaiah, 2006).

Phytochemicals of *Schefflera* species

The major phytochemicals isolated from species of *Schefflera* are mainly saponins and triterpenoid glycosides. In the early years, the phytoconstituents from *Schefflera* species were mainly isolated and identified by the chromatographic techniques and spectral analysis. Hansen and Boll (1986) first reported an allergen, falcarindol, from the ether leaf extract of *S. arboricola*. The plants were obtained from a nursery in Denmark and were subjected to column chromatography and spectral analysis, which described the presence and structure of falcarindol, phytol and poriferasterol. Similarly, Srivastava (1989) reported the presence of saponins and later triterpenic acid (Srivatsava, 1992) from the stem and bark of *S. impressa* collected from Darjeeling, India. The stem and bark of *S. impressa* were extracted with methanol and chromatographic separation method was followed for the identification and isolation of the saponin and triterpenic acid. Later, Purohit et al. (1991) reported betulinic acid, a triterpenic glycoside, from the ethanolic leaf extract of S. venulosa by using chromatographic and spectroscopic techniques. Similarly, a sulphated triterpenoid saponin (Sung and Adam, 1992) and a bidesmosidic triterpenoid saponin was isolated from the leaves of *S. octophylla* (Sung et al., 1991). *S. leucantha*, commonly called Hanuman Prasanki in Thailand, was studied for its phytoconstituents, which revealed the presence of triterpenoid glycosides (Pancharoen et al., 1994). The roots and leaves of *S. bodinieri* collected from Jinfo Mountain, China, during November 1990 was studied for their phytochemicals by Zhu et al. (1996a). The ethanol extract mainly showed the presence of triterpene glycosides in roots, whereas both triterpenoids and triterpene glycosides were identified from the leaves by using Sephadex coloumn chromatography. Triterpenoid saponins were identified by De Tommasi et al. (1997) from the aerial parts of *S. divaricata*. The phytochemical studies on *S. octophylla* and *S. arboricola* revealed the presence of steroids, steroid glycosides, sesquiterpenes, diterpenes, triterpenes, triterpene glycosides and sugars. Special components of *S. octophylla* were identified by spectroscopic analysis as 3α-and 3β-betulinic acid sulfate (Kuo et al., 2002). The leaves and stem of *S. arboricola* (Melek et al., 2003), aerial parts of *S. fagueti* (Cioffi et al., 2003), aerial parts of S. rotundifolia (Braca et al., 2004) were considered as a rich source of saponins which possessed oleanane-type and/or lupane-type aglycones. The phytochemical studies from the leaves of *S. heptaphylla* contained triterpenoids and their glycosides (saponins) as the major chemical constituents. The special components were found to be sulfated triterpenoids and their glycosides (Li et al., 2005). The leaves of *S. abyssinica*, collected from the village of Baleveng, near the city of Dschang, Cameroon, during June 2003 was studied for its phytoconstituents (Tapondjou et al., 2006), using chromatographic techniques. The major phytoconstituents were found to be saponins and by further analysis were identified as oleanolic acid and hederagenin. Aman et al. (2010) studied the qualitative phytochemical analysis of S. stellata, collected from Chamundi hills, Mysore. Standard protocols (Trease and Evans, 1989; Sofowora, 1993; Harborne, 1993) were followed for the phytochemical investigations, which revealed the presence of alkaloids, flavonoids and saponins. Similarly, new triterpenoid glycosides, Schefflerins A-G were isolated from *S. arboricola* (Zhao et al., 2010) and *S. actinophylla* (Wanas et al., 2010). Later, triterpenoid saponins, schekwangsiensides, have been identified and isolated from the aerial parts of *S. kwangsiensis* (Wang et al., 2014). Recently, the methanolic extract of *S. racemosa* has been studied for its phytoconstituents by Selvi et al. (2015) using standard procedures (Trease and Evans, 1989; Sofowora, 1993; Harborne, 1993). The investigation revealed the presence of alkaloids, saponins, tannins, steroids, flavonoids, terpenoids, phenols and coumarins. Phytochemical analysis from Schefflera species has been extensively studied, but the compounds responsible for the biological activity have not been isolated and identified.

Biological activities of Schefflera species

Biological activity is defined as any entity which can effect a change in a biological process (Jackson et al., 2007). The plant derived secondary metabolites have, over the years, greatly contributed to various biological activities like antioxidant, antimicrobial, anticancer, anti-inflammatory, antimalarial, cytotoxic etc. The following are some of the biological activities that are reported from Schefflera species.

Antioxidant activities

All organisms are protected from the free radical attack by defense mechanisms such as a preventive antioxidant system that reduces the rate of free radical formation, and another is a system to produce chain-breaking antioxidants that scavenge and stabilize free radicals. Whenever the free radical production rate exceeds the capacity of the antioxidant defense mechanisms, substantial tissue injury results (Halliwell, 1997). Therefore, antioxidants with free radical scavenging activities may have great relevance in the prevention and therapeutics of free radical mediated diseases. Many herbs and spices, usually used to flavour dishes, are excellent source of phenolic compounds which have been reported to show good antioxidant activity (Rice-Evans et al., 1996; Zheng and Wang, 2001). Antioxidant activity from the plant species of Araliaceae have been reported, but this activity has not been reported much from *Schefflera* species. The antioxidant activity has not been much documented from the species of Schefflera. Only few species have been studied for their antioxidant potential. Antioxidant activity was reported in *S. leucantha* by Potduang et al. (2007). The ethanolic extract of leaves was used for DPPH assay which showed significant activity with IC_{50} value of 71.90 mg/ml. Later, Moussa et al. (2011) studied the antioxidant potential of *S. actinophylla* by DPPH assay along with 124 Egyptian plants. The study showed that *S. actinophylla* possessed potent antioxidant activity with IC_{50} value of 19.23 µg/ml in comparison with the standard ascorbic acid (IC_{50} value of 11.50 µg/ml). The antioxidant activity is one of the important biological activities which has been concentrated much in recent years. There are very few reports on the antioxidant activity of Schefflera species which gives scope for its study.

Hepatoprotective activity

Liver diseases represent a major health burden worldwide, with liver cirrhosis being the ninth leading cause of death in western countries (Kim et al., 2002). Chronic viral hepatitis B and C, alcoholic liver disease, non-alcoholic fatty liver disease and hepatocellular carcinoma are the major entities and many problems remain unresolved. Treating liver diseases with plant-derived products which are accessible and that do not require laborious pharmaceutical synthesis seems highly attractive. Seven new triterpenoid saponins, schekwangsiensides A-G (1-7), and a new triterpenoid schekwangsienin (8), together with nine known triterpenoids and saponins (9-17), were isolated from *S. kwangsiensis* by Wang et al. (2014), wherein, compounds 4, 8, 9 and 15 exhibited moderate hepatoprotective activities in vitro against D-galactosamine-induced HL-7702 cell damage. Hepatoprotective activity, being one of the emerging and important fields in life sciences is being studied by many researchers. Many plant species need to be evaluated for the hepatoprotective potentials. Hepatoprotective activity from the family Araliaceae and from *Schefflera* species have not been much reported.

Antiviral activity

A number of phytochemials extracted from species of plants have shown antiviral activity, which include tannins, flavones and alkaloids that display in vitro activity against numerous viruses (Vijayan

et al., 2004). Antiviral drugs for diseases caused by herpes, retro, orthomyxo, hepatitis B and hepatitis C viruses (HCV) are currently available (Clercq and Field, 2006). However, due to the prevalence of viral infections and the constant appearance of new resistant viral strains coupled with the problem of viral latency and conflicting efficacy in recurrent infections in immunocompromised patients, the development of novel antiviral agents is necessary (Jaime et al., 2013). *S. heptaphylla*, the active ingredient of herbal tea formulations, most commonly used in southern China for the treatment of common cold showed potent antiviral activity against Human respiratory syncytial virus (RSV) (Li et al., 2005). Of the three caffeoylquinic acid derivatives isolated, 3, 4-Di-O- caffeoylquinic acid and 3, 5-di-O- caffeoylquinic acid possessed potent anti-RSV activity. The caffeoylquinic acids isolated exerted their anti-RSV effects via the inhibition of virus-cell fusion in the early stage, and the cell-cell fusion at the end of the RSV replication cycle. Li et al. (2007), further isolated two triterpenoids, namely, 3 alpha-hydroxylup-20(29)-ene-23,28-dioic acid and 3-epi-betulinic acid 3-o-sulfate, which showed potent antiviral activity against RSV, influenza A (H1N1) virus, Coxsackie B3 (Cox B3) virus and herpes simplex virus type 1 (HSV-1) at concentrations of 6.25 µg/ml, 31.3 µg/ml, 20.0 µg/ml and 25.0 µg/ml respectively. Since viral diseases are rapidly emerging and are spreading at a faster rate, an accelerated search for new agents is extremely essential.

Schistosomicidal activity

Schistosomiasis is a snail-borne trematode infections of humans, domestic and wild animals in different parts of Asia, Africa, the Middle East, South America and Carribbean (Bakry and Mohamed, 2011). This infection is said to be endemic in 76 countries, and the control of snails as vectors seems be a suitable measure to control the parasitic disease (Abdel-Gawad et al., 2004). This disease affects more than 200 million people worldwide, resulting in 2,80,000 deaths each year with over 779 million people at risk of infection (Zhang et al., 2010). The use of plants with molluscicidal properties is an inexpensive, simple, and appropriate technology for the snail control and so far, more than 1,500 plant species have been screened for molluscicidal properties (Abdel-Gawad et al., 2004; Bakry and Mohamed, 2011). Crude extracts, n-hexane and the ethyl acetate fractions of *S. vinosa* (Cham. and Schltdl.) Frodin from Brazilian Cerrado were studied for the schistosomicidal activity by Cunha et al. (2012). Betulin, the isolated compound from *S. vinosa* caused the death of *S. mansoni* adult worms at percentage values of 25 after 120 h (at 100 µM), and 25 and 50 after 24 and 120 h (at 200 µM), respectively. This activity displays significant values of prevalence and morbity. No other plant species from Araliaceae have been studied for the schistosomicidal activity.

Antimalarial activity

Malaria is one of the major global public health problems with its ravaging effects seen across the world. About 36% of the world population is at the risk of malaria. Around 2.5 million malaria cases are reported annually from South East Asia and 76% of it is in India (Qayum et al., 2014). The infection is caused by a protozoan species, Plasmodium falciparum, a parasite (in humans) and transmitted by the female anopheles' mosquitoes (DeVilliers et al., 2010). Malaria can be treated with quinine, chloroquine, mefloquine and artemisinin. However, the protozoans have developed resistance against many of the current regimens (White, 2004), and due to this, a general call for the use of natural products as drugs for malaria or for the development of novel antimicrobials in order to avoid problems related to drug resistance are being developed (Anthony et al., 2012). The dichloromethane extract of *S. umbellifera* yielded an active compound, Betulin, which exhibited significant antimalarial activity (IC_{50} = 3.2 µg/ml) against P. falciparum chloroquine-susceptible strain (D10) (Mthembu et al., 2010). Quantitative assessment of in vitro antiplasmodial activity was

determined via a parasite lactate dehydrogenase (pLDH) assay. It was observed that, betulin did not show significant antimalarial activity unless converted to betulinic acid. The results from the study confirmed the traditional use of *S. umbellifera* and the derived compound to poses good antimalarial activity. *Cussonia* and *Schefflera* are the only two genera considered for the antimalarial studies. Focus in this regard is essential, so that many more plant derived products can be used as antimalarial compounds.

Antimicrobial activity

Plants are being used as medicinal source since ages. They have been the largest natural drugs, though only less than 5% of known plants have been chemically characterized. Scientific validation of antimicrobial potential of these medicinal plants would justify the folklore claims (Uniyal et al., 2003). Plant and plant-derived agents have long history of clinical relevance as a source of potential chemotherapeutic agents (Tim-Cushnie and Lamb, 2005). Members of Araliaceae have been much exploited for their antimicrobial potentials. Sabulal et al. (2008) isolated volatile oils from the roots, stems and leaves of *S. stellata* by hydro distillation method. The major constituents of these oils were found to be β-caryollene (11.1-19.2%), α-humulene (7.3-15.4%), germacrene D (3.3-14.4%), germacrene B (8.3-21.7%) and epi-α-cadinol (5.6-15.0%). Disc diffusion technique was employed to test the antimicrobial activity which ensured that the leaf oil was a good antifungal agent against *C. albicans* and *C. glabrata*. But it had a very low antibacterial activity. The antimicrobial activity of *S. leucantha* was studied against organisms responsible for nosocomial infections like respiratory tract and urinary tract infections (Sittiwet et al., 2009). The aqueous extract from the aerial parts of the plant was tested for their antibacterial activity against both Gram-positive (*S. aureus, S. epidermis*, *M. luteus, B. subtilis, L. plantarum*) and Gram-negative bacteria (*E. coli, S. typhimurium*, *K. pneumoniae*, *P. vulgaris, P. aeruginosa*) using agar diffusion method. The extracts showed inhibitory effect on the growth of *L. plantarum, E. coli, K. pneumoniae, P. vulgaris*. The MICs of the extract ranged between 8-16 g/L while that of MBC between 16-32 g/L. The results indicated the inhibitory effect of *S. leucantha* aqueous extract on respiratory tract and urinary tract-infecting bacteria at low concentrations. The methanolic leaf extracts of *S. stellata* was studied by Aman et al. (2010), against many microorganisms by disc diffusion method. *E. aerogenes* showed a greater zone of inhibition (11 mm) when compared to all the tested organisms, followed by *X. axonopodis* pv. *malvacearum* with a zone of 9 mm. An inhibition zone of 7 mm was observed in *S. aureus, X. oryzae* pv. *oryzae* and *S. typhi* strains. In recent years, Estari and Supriya (2012) studied the antibacterial activity of *S. stellata* leaf extracts against six pathogenic bacteria using disc diffusion assay. Different solvent extracts were used for the study, among which the petroleum ether, chloroform and aqueous extract showed potent antibacterial activity against *E. coli* (3.5 mm zone of inhibition), *L. bacillus* (6.0 mm zone of inhibition) and *B. subtilis* (4.0 mm zone of inhibition) respectively. Since, antibacterial resistance to commonly used antibiotics along with the emergence of new and re-emerging diseases has become a serious problem; an urgent need exists to discover novel plant compounds with antimicrobial activity. *Schefflera* species have not been worked much for their antimicrobial properties and there is scope for such studies since saponins are the major phytocomponents of the genus and are responsible for the antimicrobial properties.

Cytotoxic activity

Plant secondary metabolites and their semi-synthetic derivatives continue to play an important role in anticancer drug therapy. These include vinblastine, vincristine, the camptothecin derivatives,

topotecan and irinotecan, etoposide, derived from epipodophyllotoxin and paclitaxel (taxol) (Jain and Jain, 2011). Sixty percent of currently used anticancer agents are derived in one way or another from natural sources (Cragg et al., 2009). Uncontrolled proliferation is a universal property of tumor cells. Investigation of cellular growth control mechanism has contributed to the understanding of carcinogenesis and to the identification of compounds with specific antitumoral activity (Ruffa et al., 2002). Kuo et al. (2002) studied the cytotoxic activity of *S. taiwaniana* leaves, an unique and indigenous species to Taiwan. The compounds falcarindiol and C_{18}-acetylenverbindung from the ethyl acetate fraction of the methanol extract, tested against HONE1 (nasopharyngeal carcinoma) showed potent cytotoxic activity at a concentration of 50 µg/ml. Similarly, Cioffi et al. (2003) reported six new lupane (1-4) and oleanane (5&6) cytotoxic saponins from the aerial parts of S. fagueti. Three continuous murine and human culture cell lines J774, HEK-293, WEHI-164 were used for the evaluation, which revealed oleanane saponins 5 and 6 to be most active and showed significant inhibitory effects on all cell lines, while their prosapogenins 5a and 6a demonstrated minor activity. Later, Braca et al. (2004) isolated eight new oleanane and lupine saponins (1-8) as well as two new benzyl glycosides, which acted as cytotoxic saponins, from the aerial parts of S. rotundifolia. Three continuous murine and human culture cell lines J774, HEK-293, WEHI-164 were used to evaluate the antiproliferative activity of all compounds. Compounds 7 and 8, having betulinic acid as aglycone turned up to be the most active constituent. Since cytotoxic effects from Schefflera species has been reported, a novel drug from the genus can be expected in the coming years.

Isolation and identification of compounds from Schefflera

Due to the fact that plant extracts usually occur as a combination of various types of bioactive compounds or phytochemicals with different polarities, their separation still remains a big challenge for the process of identification and characterization of bioactive compounds. It is a common practice in the isolation of bioactive compounds that a number of different separation techniques such as TLC, column chromatography, flash chromatography, gel filtration technique, HPLC, GC-MS, LC-MS and NMR should be used to obtain pure compounds. The pure compounds are then used for the determination of structure and biological activity. Besides that, non-chromatographic techniques such as immunoassays, phytochemical screening assay, Fourier-transform infrared spectroscopy (FTIR), can also be used to obtain and facilitate the identification of the bioactive compounds (Sasidharan et al., 2011). A number of compounds with distinct biological activity have been isolated and identified from the genus Schefflera. *S. arboricola*, the only *Schefflera* species is known to cause allergic contact dermatitis. Hansen and Boll (1985) isolated and identified a major allergen, falcarindol, heptadeca-1,9(Z)-dien-4,6-diyn-3-ol, from the ethanolic leaf and stem extracts of *S. arboricola*. They also isolated (E)-β-farnesene, phytol and 24β-ethylcholesta-5,22(E)-diene-3β-ol (poriferasterol) using HPLC, UV, IR, mass, ^{1}H and ^{13}C NMR spectroscopy. The methanolic leaf extract of *S. octophylla* revealed the presence of a sulphated triterpene glycoside, 3-epi-betulinic acid 3- O-sulphate 28-O-[α-L-rhamnopyranosyl (1→ 4)-O-β-D-glucopyranosyl (1→6)]- β-D- glucopyranoside and also 3,28-bidesmosidic triterpenoid saponin, 3-epi-betulinic acid 3-O-β-D- glucopyranoside 28-O-[α-L-rhamnopyranosyl(1→4)-O-β-D-glucopyranosyl(1→6)]-β-D- glucopyranoside and α-L-rhamnopyranosyl (1→4)-O-β-D-glucopyranosyl (1→6)] -β-D- glucopyranosyl (1→6)-β-D-glucopyranose based on ^{1}HMR and ^{13}C NMR spectroscopic analysis (Sung and Adam, 1990 and 1991). Similarly, a new betulinic acid glycoside, lup-20 (29)-en-28-oic- 3-o-β-d-glucopyranosyl (2→1)-o-β-d-glucopyranoside was isolated from the leaves of *S. venulosa* (Purohit et al., 1991). An acetylated saponin, hederagenin-3-O-β-D-6'-acetylglucopyranoside and a triterpenoid saponin, 3α, 11α-dihydroxylup-20(29)-en-28-oic acid 28-O-β-D-glucopyranoside

has been isolated from the bark and stem of *S. impressa* (Srivastava, 1989 and 1992). Its structure has been elucidated from spectroscopic data and by chemical correlation with compounds of established structures. Two triterpenoids, 3-oxo-20-demethylisoaleuritolic-14(15)-ene-28, 29-dioic acid, 28-O-[α-L-rhamnopyranosyl(1→4)-O-β-D-glucopyranosyl(1→6-]-O-β-D-glucopyranoside of 3-oxo-20-demethylisoaleuritolic-14(15)-ene-28, 29-dioic acid and a triterpene glycoside 3α-hydroxyl-20-demethylisoaleuritolic-14(15)-ene-28, 30-dioic acid was isolated from the ethanolic leaf extracts and four triterpene glycosides 28-O-[α-L- rhamnopyranosyl (1→4)-O-β-D-glucopyranosyl-(1→6-]-O-β-D-glucopyranoside of 3β-hydroxy-isopolygalic-13(14)-ene-28-acid, 28-O-[α-L-rhamnopyranosyl(1→4)-O-β-D-glucopyranosyl-(1→6-]-β-D-glucopyranoside of 3-oxo-isopolygalic-13(14)-ene-28-acid, 28-O-β-D-glucopyranosyl(1→6)-β-D- glucopyranoside of 3β-hydroxy-isopolygalic-13(14)-ene-28-acid and 28-O[α-L- rhamnopyranosyl (1→4)-O-β-D-glucopyranosyl-(1→6-]-O-β-D-glucopyranoside of 3β-hydroxy-18-methyl-polygalic-13(14)-ene-28-acid were isolated from the ethanolic root extracts of *S. bodinieri* using spectroscopic analysis, including ^{1}H-^{1}H COSY and ^{13}C-^{1}H COSY NMR by Zhu et al. (1996a and 1996b). In the later years, Melek et al. (2002) isolated nine triterpenoid saponins from the ethanolic leaf extracts of *S. arboricola* based on chemical and spectral evidence. Eighteen compounds, falcarindiol, C_{18}-acetylenverbindung, loliolide, oplodiol, oplopanone, T-murrolol, phytol, 3α,23-dihydroxyolean-12-en-23,28-dioic acid, 3α,11α-dihydroxylup-20(29)-en-28-oic acid, 3α-hydroxyolean-12,28-dioic acid, 3α-hydroxylup-20(29)-ene-23,28-dioic acid, γ-tocopherol, δ-tocopherol, a mixture of docosyl and tetracosyl 4-hydroxy-trans-cinnamate, a mixture of docosyl, tetracosyl, and hexacosyl 4-hydroxy-cis-cinnamate were isolated from the methanol leaf extract (ethyl acetate fraction) of S. taiwaniana by Kuo et al. (2002). Three triterpene glycosides namely 28-o-[α-1-rhamnopyranosyl (1→ 4)-o-β-d-glucopyranosyl (1→6)-]-β-d-glucopyranosides of 3α-hydroxy-lup-20 (29)-ene-23, 28-dioic acid, 3α, 11α-dihydroxy-lup-20 (29)-ene-23, 28-dioic acid and 3 epi-betulinic acid were isolated from the leaves of *S. octophylla* (Sung et al., 1991). Similarly, oleanolic acid, lutein, fatty alcohols and hydrocarbons were isolated from the leaves of S. odorata by Ragasa and Kim (2005). 1D and 2D NMR were used to elucidate the structure of oleanolic acid. The structure of lutein was deduced by comparison of its 'H NMR spectral data with those of lutein. 12α, 13-Dihydroxyolean-3-oxo-28-oicacid (1), a new pentacyclic triterpene, was isolated from *S. venulosa* (W. & A.) Harms., by Rui et al. (2005) through a bioassay-guided fractionation procedure together with the known oleanonic acid (2) which is known to be a new cell cycle inhibitor. Structures were established by spectroscopy. Oleanonic acid inhibited the proliferation of K562 cells with the IC_{50} value of 0.13 μmol/ml by the SRB method and inhibited the cell cycle of tsFT210 cells at the G_0/G_1 phase at the concentration higher than 10 μg/ml. Oleanolic acid hederagenin were isolated from the methanolic leaf extracts of *S. abyssinica* by Tapondjou et al. (2006). Triterpenoids were isolated by Li et al. (2007) from *S. heptaphylla* which acts as an active ingredient of herbal tea formulations most commonly used in China for the treatment of common cold. The two highly active pure triterpenoids namely 3alpha-hydroxylup-20(29)-ene-23, 28-dioic acid and 3-epi-betulinic acid 3-o-sulfate, together with an inactive saponin, 3alpha-hydroxylup-20(29)-ene-23, 28-dioic acid and 28-o-alpha-1-rhamnopyranosyl-(1→4)-o-beta-d-glucopyranosyl-(1→6) beta-d-glucopyranoside, were isolated. Sabulal et al. (2008) isolated volatile oils from roots, stems and leaves of *S. stellata* by hydrodistillation method. The characterization by analytical gas chromatography and GC-MS revealed the presence of sesquiterpenes hydrocarbons in abundance, followed by oxygenated sesquiterpenes, monoterpenes hydrocarbons and oxygenated monoterpenes. The major constituents of these oils were found to be β-caryollene (11.1-19.2%), α-humulene (7.3-15.4%), germacrene D (3.3-14.4%), germacrene B (8.3-21.7%) and epi-α-cadinol (5.6-15.0%). Recently,

Wang et al. (2014) isolated seven new triterpenoid saponins, schekwangsiensides A–G (1–7) and a new triterpenoid, schekwangsienin (8), together with nine known triterpenoids from the aerial parts of *S. kwangsiensis*. The structures of these compounds were elucidated using spectroscopic and chemical data analysis. Selvi et al. (2015) employed HPLC and GC–MS to identify the number of secondary metabolites present in the methanolic extract of S. racemosa. The results from the HPLC analysis revealed the presence of eight non-volatile compounds at 272 nm, whereas GC–MS analysis showed twenty-one peaks indicating the presence of twenty-one phytochemical constituents. Most of the compounds analyzed from GC–MS possess medicinal properties like antioxidant, antimicrobial and anti-inflammatory activities.

Conclusion

The detailed review presented in this article reveals the ethnomedicinal value of sixteen *Schefflera* species which are mainly distributed in the tropical and the subtropical regions of the world. This review highlights the biological activities, reported in *Schefflera* species which mainly includes, antioxidant, hepatoprotective, antimicrobial, antiviral, antimalarial, schistosomicidal and cytotoxic activities and also the compounds isolated and identified from the genus, which mainly includes saponins and triterpene glycosides. Since, *Schefflera* is popularly grown as an ornamental plant, not much work has been documented from the genus. Hence, there is a need to further study, identify and isolate the compounds responsible for the biological activity, so that a novel drug from the Schefflera species can be developed and used for therapeutic benefits.

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