Borreria and *Spermacoce* species (Rubiaceae): A review of their ethnomedicinal properties, chemical constituents, and biological activities

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ABSTRACT

Borreira and *Spermacoce* are genera of Rubiaceae widespread in tropical and subtropical America, Africa, Asia, and Europe. Based on its fruits morphology they are considered by many authors to be distinct genera and most others, however, prefer to combine the two taxa under the generic name *Spermacoce*. Whereas the discussion is still unclear, in this work they were considered as synonyms. Some species of these genera play an important role in traditional medicine in Africa, Asia, Europe, and South America. Some of these uses include the treatment of malaria, diarrheal and other digestive problems, skin diseases, fever, hemorrhage, urinary and respiratory infections, headache, inflammation of eye, and gums. To date, more than 60 compounds have been reported from *Borreria* and *Spermacoce* species including alkaloids, iridoids, flavonoids, terpenoids, and other compounds. Studies have confirmed that extracts from *Borreria* and *Spermacoce* species as well as their isolated compounds possess diverse biological activities, including anti-inflammatory, antitumor, antimicrobial, larvicidal, antioxidant, gastrointestinal, anti-ulcer, and hepatoprotective, with alkaloids and iridoids as the major active principles. This paper briefly reviews the ethnomedicinal uses, phytochemistry, and biological activities of some isolated compounds and extracts of both genera.

Key words: Alkaloids, *borreria*, flavonoids, iridoids, rubiaceae, *spermacoce*, terpenoids

INTRODUCTION

The Rubiaceae family comprises one of the largest angiosperm families, with 650 genera[1] and approximately 13,000 species,[2] distributed mainly not only in tropical and subtropical regions, but also reaching the temperate and cold regions of Europe and Northern Canada.[3] In Brazil, this family comprises about 130 genera and 1500 species distributed across different vegetation formations, with a great occurrence in the Atlantic Forest.[3-5] This family is currently classified in three subfamilies and over 43 tribes.[2] The tribe Spermacoceae (subfamily Rubioideae), which belongs to the genera *Borreria* G.F.W. Mey. and *Spermacoce* L., is characterized by a herbaceous habitat, with over 1000 species have a mainly pantropical distribution, but a few genera extend into temperate regions, excluding New Zealand.[6,7]

The genera *Borreria* and *Spermacoce*, the largest of the tribe Spermacoceae, comprises about 280 species distributed in tropical and subtropical America, Africa, Asia, and Europe.[8] In Brazil, 36 *Borreria* species were recorded, of which 22 are endemics.[9,10] Based on its fruits morphology, they are considered by many authors to be distinct genera and most others, however, prefer to combine the two taxa under the generic name *Spermacoce*.[6,11] In this work, they were considered as synonyms. This review reports an account of the species used in traditional medicine, their phytochemical profile, and biological activities of isolated compounds, mainly alkaloids and iridoids, and extracts. The data collected are based on the papers published up to September 2011 and the data bases assessed include Chemical Abstracts, Napralert, and ISI Web of Science.

Ethnomedicinal properties

Borreria and *Spermacoce* species are used medicinally in various manners and are reputed in traditional medicine of Latin America, Asia, Africa, and West Indies. The species most used as medicinal are described below:

B. alata (Aubl.) DC. [Syn.: S. alata Aubl., S. latifolia Aubl., B.

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latifolia (Aubl.) K. Schum.] is a herbaceous species native to South America.[12,13] In Nepal, the roots juice this plant is used to treat malaria.[14]

B. articularis (L. f.) F. N. Williams [Syn.: *S. articularis* L.f., *S. scabra* Willd. and *B. hispida* (L.) K. Schum.)], commonly known in Brazil as "poaia", is originally native to the temperate and tropical Asia regions and naturalized in Africa and Australia.[15] The leaves of this plant are used as ophthalmic, inflammation of eye and gums, blindness, carache, fever, spleen complaints, sore, conjunctivitis, hemorrhage, gallstones, dysentery, and diarrhoea,[15,16] and the decoction of the leaves, roots, and seeds is used in India for dropsy.[17]

B. centranthoides Cham. and Schltdl. (Syn.: *B. centranthoides* f. glabrior Chodat and Hassl.), known in Brazil as "sabugueirinho do campo", is a perennial herb originating from fields in southern Brazil, and possibly Uruguay and Argentina. In Brazil, these plants have been used for the treatment of liver ailments,[18,19] kidneys disorders,[20] and in Argentina as an abortifacient.[21]

B. eupatorioides Cham. and Schltdl. (Syn.: *B. polyana* DC, *S. eupatorioides* (Cham. and Schltdl.) Kuntze, and *Galianthe eupatorioides* (Cham. and Schltdl.) E.L. Cabral) is an herb which decoction of the leaves is used in Argentina with *Petroselinum crispum* (Mill.) Nyman ex. AW Hill. or *Gymnopteris tomentosa* (Lam.) as emmenagogue and the roots as a contraceptive,[22] and for diarrhea, and urinary and respiratory infections.[23]

B. hispida (Linn.) K. Schum. (Syn.: *S. hispida* L.) is being used as an alternative therapy for diabetes.[24] In India, decoction of the plant is used for headache[25] and the seeds as stimulant[26] and for the treatment of internal injuries of nerves and kidney.[27]

B. laevis (Lam.) Griseb. (Syn.: *S. laevis* Roxb. and *S. assurgens* Ruiz and Pavon) is a small herb found in the tropical regions of Asia.[28] Also occurs in Mexico, where decoction of the leaves is used to treat kidney pain and prevent menstruation[29] while the entire plant in admixture with *Cuscuta* L. and *Zebrina pendula* Schum is used for amenorrhea in Jamaica[30] and West India.[31] In Jamaica, the tea of the entire plant boiled with *Desmodium* Desv. and *Iresine paniculata* Kuntze also is used as diuretic.[30]

B. latifolia (Aubl.) K. Schum. (Syn.: *S. latifolia* Aubl.), known in Brazil as "poaia-do-campo", is an annual erect herb that occur in the Americas.[3,32]

B. ocymoides (Burm. *f.*) DC. (Syn.: *S. ocymoides Burm. f.*) is common in all America, also occurs in eastern Africa and East India.[9] In Nigeria, the juice of the leaves is applied for ring worm and eczema and the sap is squeezed on to the wound or lesion.[33]

B. princeae K. Schum. [Syn.: *S. princeae* (K. Schum.) Verdec.] is a scrambling or decumbent perennial herb, native to Africa, where is used for the treatment of skin diseases.[34]

B. pusilla (Wall.) DC. [Syn.: *B. stricta* (Linn. *f.*) K. Schum., *S. pusilla* Wall.] is an annual erect herb native to tropical Africa and Asia. In India, the fresh buds associated with flowers are used for cuts and wounds[35] and crushed of leaves are applied to the affected areas for bone fracture and scabies, and for snake and scorpion bites.[36]

B. verticillata (L.) G. F. W. Mey. (Syn.: *S. verticillata* L.), known in Brazil as "poaia", "poaia preta", "poaia miúda", "coroa-de-frade", and "vassourinha", is a small perene and erect herb, originating from South and Central Americas and distributed by the Old World, Southern United States to South America.[9,37] In Brazil, the infusion of the flowers is used as antipyretic and analgesic,[38,39] the roots as emetic and leaves as antidiarrheal, and for treat erysipelas and hemorrhoids.[40] In West India, the decoction of this plant is used for diabetes and dysmenorrhea, and when prepared with *Cuscuta* and *Zebrina* Schnizlein is used for amenorrhea;[31] while in Senegal it is used to treat bacterial skin infections and leprosy.[41] In Nigeria, fresh aerial part juice is applied for eczema[34] and in Jamaica the decoction of the endocarp, prepared jointly with *Iresine* P. Browne. and *Desmodium*, is used as a diuretic and as a remedy for amenorrhea mixed with *Cuscuta* and *Zebrina*.[30]

Spermacoce exilis (L.O. Williams) C.D. Adams [Syn.: *B. exilis* L.O. Williams, *B. gracilis* L.O. Williams, *B. repens* DC., *S. repens* (DC.) Fosberg and J. M. Powell, and *S. mauritiana* Gideon] is a weak erect, decumbent, or procumbent annual herb distributed in Africa and America and is used for headache.[42]

CHEMICAL CONSTITUENTS AND SOME OF THEIR BIOLOGICAL ACTIVITIES

The widespread uses of *Borreria* and *Spermacoce* species in traditional medicine have resulted in considerable chemical investigation of the plants and their active principles. The first phytochemical report was published in 1961, and revealed the detection of (-)-emetina (**7**) from roots of *B. verticillata*.[43] Today, over 60 compounds distributed in different classes have been isolated [Table 1]. Alkaloids, iridoids, flavonoids, and terpenoids are the main groups of constituents. Among them, alkaloids and iridoids displayed *in vivo* or *in vitro* some biological activities.

Alkaloids

A total of eleven alkaloids [Table 1 and Figure 1], containing indole [borrecapine (1), borrecoxine (2), borreline (3), borrerine (4), dehydroborrecapine (6), verticillatine A (10), and verticillatine B (11)], bis-indole [borreverine (**5**), isoborreverine (8) and spermacoceine (9)] and tetrahydroisoquinoline [(-)-emetine (**7**)] skeletons have been isolated from *B. capitata*,[44-46] *Borreria* spp.,[47] and *B. verticillata*.[39,41,43,48-52] Phytochemical screening indicated the presence of emetine in *B. poaya* DC., *B. suaveolens* var. *platyphylla* (K. Schum.) Standl., *B. verbenoides* Cham. and Schltdl., and *B. verticillata*.[48] Among isolated alkaloids, borreverine tartrate showed *in vitro* antibacterial activity against *Sarcina lutea* (MIC 3.0 µg/mL), *Vibrio cholerae* (MIC 12.5 µg/mL), and *Staphyloccocus aureus* (MIC 100 µg/mL).[41]

Table 1: Compounds isolated from *Borreria* and *Spermacoce* species

Compounds/number	Plant species	Plant parts	Collected place and references
Alkaloids			
Borrecarpine (1)	*B. capitata*	Not cited	Guiana[44-46]
		Aerial parts	French guiana[46]
Borrecoxine (2)	*B. capitata*	Aerial parts	French guiana[46]
Borreline (3)	*B. capitata*	Aerial parts	French guiana[46]
	Borreria spp.	Not cited	Guiana[47]
	Borreria spp.	Aerial parts	French guiana[47]
Borrerine (4)	*B. verticillata*	Leaves	Brazil[51]
		Entire plant	Senegal[49]
		Aerial parts	Belgium[52]
Borreverine (5)	*B. verticillata*	Entire plant	Senegal[41]
		Aerial parts	Belgium[52]
		Entire plant	Belgium[50]
Dehydroborrecapine (6)	*B. capitata*	Aerial parts	French guiana[46]
(-)-Emetine (7)	*B. verticillata*	Roots	Not cited[43]
		Flowers, leaves, stems, and roots	Brazil[48]
Isoborreverine (8)	*B. verticillata*	Aerial parts	Belgium[52]
Spermacoceine (9)	*B. verticillata*	Aerial parts	Belgium[52]
Verticillatine A (10)	*B. verticillata*	Roots	Brazil[39]
Verticillatine B (11)	*B. verticillata*	Roots	Brazil[39]
Iridoids			
Asperuloside (12)	*B. verticillata*	Flowers, roots	Brazil[38,39]
		Roots	Madagascar[67]
	S. laevis	Aerial parts	Thailand[28]
Asperulosidic acid (13)	*B. latifolia*	Aerial parts	Indonesia[66]
	B. verticillata	Roots	Madagascar[67]
	S. laevis	Aerial parts	Thailand[39]
6-*O*-Acetylscandoside (14)	*B. latifolia*	Aerial parts	Indonesia[66]
Borreriagenin (15)	*B. verticillata*	Flowers	Brazil[38]
Daphylloside (16)	*B. latifolia*	Aerial parts	Indonesia[66]
	B. verticillata	Flowers	Brazil[38]
		Roots	Madagascar[67]
Deacetylasperuloside (17)	*B. verticillata*	Roots	Madagascar[67]
Deacetylasperulosidic acid (18)	*B. latifolia*	Aerial parts	Indonesia[66]
	B. verticillata	Roots	Madagascar[67]
Feretoside (19)	*B. verticillata*	Roots	Madagascar[67]
(=Scandoside methyl ester)		Roots	Brazil[39]
6'-O-(2-glyceryl)scandoside methyl ester	*B. verticillata*	Roots	Brazil[39]
6α-Hydroxyadoxoside (21)	*S. laevis*	Aerial parts	Thailand[28]
10-Hydroxyloganin (22)	*B. latifolia*	Aerial parts	Indonesia[66]
Methyl deacetylasperulosidate (23)	*B. verticillata*	Roots	Madagascar[67]
Scandoside (24)	*B. latifolia*	Aerial parts	Indonesia[66]
		Roots	Brazil[39]
Flavonoids			
Astragalin (25)	*B. stricta*	Leaves	India[83]
Isorhamnetin (26)	*B. hispida*	Seeds	India[26]
Kaempferol 3-*O*-*β*-D-glucopyranoside (27)	*S. laevis*	Aerial parts	Thailand[28]
Kaempferol 3-*O*-rutinoside (28)	*S. laevis*	Aerial parts	Thailand[28]
Quercetin (29)	*B. stricta*	Seeds, leaves	India[83-84]
Quercetin 3-*O*-β-D-galactopyranoside (30)	*S. laevis*	Aerial parts	Thailand[28]
Quercetin 3-*O*-α-L-rhamnopyranosyl-(1→6)-β-D-galactopyranoside (B)	*S. laevis*	Aerial parts	Thailand[28]
Rutin (32)	*B. stricta*	Seeds, leaves	India[83-84]

Table 1: Contd....

Compounds/number	Plant species	Plant parts	Collected place and references
	S. laevis	Aerial parts	Thailand[28]
Terpenoids			
3α-Acetoxy-olean-12-en-29-oic acid (33)	*B. articularis*	Roots	Taiwan[87]
β-Amyrin (34)	*B. articularis*	Roots	Taiwan[87]
Campesterol (35)	*B. verticillata*	Stems	Madagascar[93]
Cariophyllene (36)	*B. verticillata*	Essential oil	Nigeria[34]
Daucosterol (37)	*B. stricta*	Leaves	India[83]
Epikatonic acid (38)	*B. articularis*	Entire plant	India[85]
Erythrodiol (39)	*B. articularis*	Entire plant	India[85]
Guiaene (40)	*B. verticillata*	Aerial parts	Nigeria[88]
3-Keto-olean-12-en-29-oic acid (41)	*B. articularis*	Entire plant	India[85]
Phytol (42)	*B. latifolia*	Aerial parts	Indonesia[66]
β-Sitosterol (43)	*B. articularis*	Entire plant	India[85]
	B. hispida	Entire plant	Not cited[89]
	B. stricta	Seeds, leaves	India[83-84]
	B. verticillata	Stems	Madagascar[93]
Stigmasterol (44)	*B. verticillata*	Stems	Madagascar[93]
Ursolic acid (45)	*B. articularis*	Entire plant	India[86]
	B. hispida	Entire plant	Not cited[89]
	B. stricta	Seeds, Leaves	India[83-84]
Ursolic acid methyl ester (46)	*B. articularis*	Entire plant	India[86]
Uvaol (47)	*B. articularis*	Entire plant	India[86]
Other classes of compounds			
Benzyl *O*-*α*-L-arabinopyranosyl-(1→6)-β-D-glucopyranoside (48)	*S. laevis*	Aerial parts	Thailand[28]
Benzyl *O*-β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside (49)	*S. laevis*	Aerial parts	Thailand[28]
(*Z*)-3-Hexenyl *O*-*α*-L-arabinopyranosyl-(1→6)-β-D-glucopyranoside (50)	*S. laevis*	Aerial parts	Thailand[28]
(*Z*)-3-Hexenyl diglycoside (51)	*S. laevis*	Aerial parts	Thailand[28]
(*Z*)-3-Hexenyl *O*-β-D-glucopyranoside (52)	*S. laevis*	Aerial parts	Thailand[28]
(*Z*)-3-Hexenyl *O*-*α*-L-rhamnopyranosyl-(1→6)-*β*-D-glucopyranoside (53)	*S. laevis*	Aerial parts	Thailand[28]
6-Methyl-5-cyclodecen-1-ol (54)	*B. articularis*	Aerial parts	Not cited[16]
Phenyethyl *O*-*α*-L-arabinopyranosyl-(1→6)-*β*-D-glucopyranoside (55)	*S. laevis*	Aerial parts	Thailand[28]
Phenyethyl *O*-*β*-D-glucopyranoside (56)	*S. laevis*	Aerial parts	Thailand[28]
Phenyethyl *O*-*α*-L-rhamnopyranosyl-(1→6)-*β*-D-glucopyranoside (57)	*S. laevis*	Aerial parts	Thailand[28]
(6*S*,9*R*)-Roseoside (58)	*S. laevis*	Aerial parts	Thailand[28]
Alcohol and carboxylic acids			
Hexacosan-1-ol (59)	*B. stricta*	Leaves	India[83]
Hentriacontan-1-ol (60)	*B. articularis*	Entire plant	India[85]
Linoleic acid (61)	*B. stricta*	Seeds	India[84]
Oleic acid (62)			
Palmitic acid (63)		Seeds, Leaves	India[84]
Stearic acid (64)	*B. stricta*	Seeds	India[84]
Amino acids and carbohydrates			
Alanine, arginine, aspartic acid, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tyrosine, valine	*B. stricta*	Seeds	India[84]
Galactose, glucose, mannitol, proteine	*B. stricta*	Leaves	India[84]

Emetine (**7**) is a tetrahydroisoquinoline alkaloid that occurs mainly in *Psychotria ipecacuanha* Stokes (Rubiaceae), also known as *Cephaelis ipecacuanha* A. Rich.[53,54] The first use of emetine in medicine was as emetic and expectorant.[55] Later, other properties were being discovered and today several important biological activities are reported for this compound. Among which are anticancer,[56-58] antiparasitic,[59-61] antiviral,[62,63] contraceptive,[64,65] inhibition of protein, DNA and RNA synthesis, reduction of T-2 toxin toxicity association with cells, and inhibition of the nonsense-mediated MRNA decay (NMD) pathway.[63] However, its medicinal use has been discouraged due to its toxicity.[63]

Iridoids

Thirteen iridoids (12–24) have been isolated from *B. latifolia*,[66] *B. verticillata*,[38,39,67] and *S. laevis*[27] [Table 1 and Figure 2]. Among these compounds, asperuloside (12) was claimed as muscle anabolic steroids,[68] inhibited TNF-α, decreased IL-1β prodution, reduced formation of PGE_2, and treated rheumatoid arthritis in mice.[69] This compound, along with deacetylasperulosidic acid (18) and scandoside (24) exhibited *in vitro* activity against the Epstein-Barr virus.[70] Deacetylasperulosidic acid (18, 63.8 ± 1.5%) and scandoside (24, 62.2 ± 1.6%), inhibited LDL-oxidation, at 20 μg/ml.[71] Compounds 12, 18 and methyl deacetylasperulosidate (23) showed purgative effects in mice[72] and 23 lowered the blood glucose level in normal mice.[73]

Asperolosidic acid (13) showed weak inhibition against TPA-induced inflammation in mice (ID_{50} > 1.0 mg/ear) and exhibited moderate effects against the EBV-EA activation induced by TPA (IC_{50} 578 mol).[74] It also was effective in suppressing TPA- or EGF-induced cell transformation and associated AP-1 activity. TPA- or EGF-induced phosphorylation of c-Jun was also blocked.[75] Compounds 12, 13, borreriagenin (15), deacetylasperuloside (17), and 6α-hydroxyadoxoside (21) were inactive as antioxidants (IC_{50} > 30 μmol)[76,77] and compounds 13 and 18 did not exhibit hypoglycemic effects in STZ-induced diabetic mice.[78]

Compounds 12 and 13 suppressed germination of large crabgrass, alfalfa, and white clover to 52 and 56, 58 and 80, and 30 and 40%, respectively, at 400 ppm.[79] Compounds 12 and 23 also were tested for their inhibitory activities toward germination and seedling growth of several plant species. Compound 12 inhibited growth of rice and lettuce seedlings at 10^{-4} to 10^{-3} mol, while 23 had no inhibitory activity.[80] Iridoid 13 did not show any effect *in vitro* on the soybean lipoxygenase and bovine testis hyaluronidase.[81]

The insecticidal activity of 13, 18, 10-hydroxyloganin (22), and 24 against ants (*Crematogaster scutellaris*) and termites (*Kalotermes flavicollis*) was evaluated. Significant levels of toxicity was observed only for 22.[82]

Flavonoids

Only eight flavonoids (25–32) have been isolated from *Borreria* and *Spermacoce* species [Table 1 and Figure 2]. All are free or glycosides flavonols derivatives and their occurrence are restricting to *B. stricta* [astragalin (25), quercetin (29) and rutin (32)],[83,84] *B. hispida* [isorhamnetin (26)][26] and *S. laevis* [kaempferol 3-*O*-β-D-glucopyranoside (27), kaempferol 3-*O*-rutinoside (28), quercetin 3-*O*-β-D-galactopyranoside (30), quercetin 3-*O*-*a*-L-rhamnopyranosyl-(1→6)-β-D-galactopyranoside (31), and rutin (32)].[28]

Terpenoids

The *Borreria* species also contains pentacyclic triterpenoids of

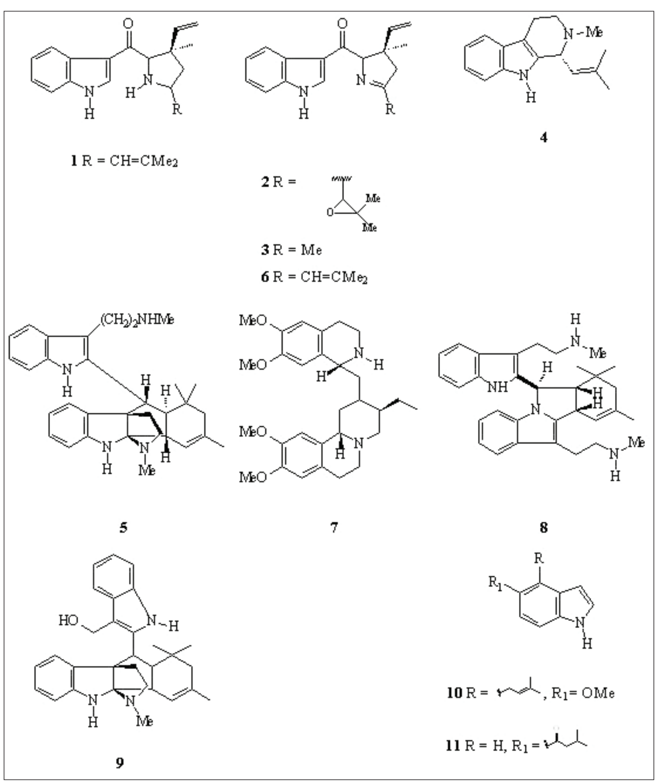

Figure 1: Alkaloids isolated from *Borreria* species

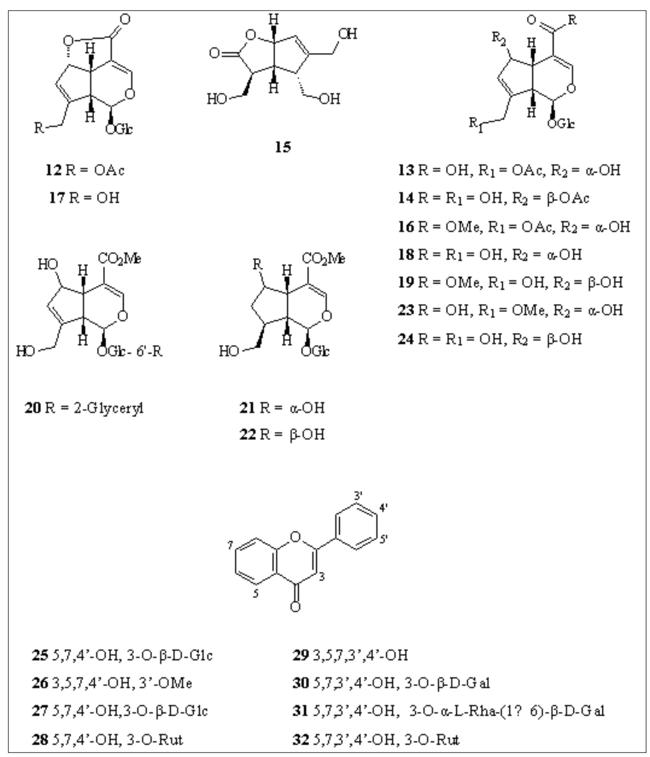

Figure 2: Iridoids and flavonoids isolated from *Borreria* and *Spermacoce* species

oleanane- and ursane-types [Table 1 and Figure 3]. From the chloroform extract of the aerial parts and roots of *B. auricularis*, a plant used in traditional medicine for several purposes,[15,16] seven triterpenes were isolated [3*a*-acetoxy-olean-12-en-29-oic acid (33), β-amyrin (34), 3-keto-olean-12-en-29-oic acid (41), epikatonic acid (38), ursolic acid (45), ursolic acid methyl ester (46), and uvaol (47)].[85-87] Furthermore, from the essential oil and aerial parts of *B. verticillata* two sesquiterpenes, caryophyllene (39) and guiaene (40), were isolated, respectively.[34,88] From the seeds of *B. stricta*[84] and *B. hispida*,[89] β-sitosterol (43) and ursolic acid (45) were isolated; and from aerial parts of *B. latifolia* the diterpene phytol (42) was isolated.[66]

Other classes of compounds

Besides the above-mentioned groups of compounds, two benzyl (48-49), four (*Z*)-3-hexenyl (50-53), three phenylethyl glycosides derivatives (55-57), and a megastigmane glycoside (58) [Table 1 and Figure 4] were isolated from aerial parts of *S. laevis*[28] and from aerial parts of *B. articularis* 6-methyl-5-cyclodecen-1-ol (54) was also isolated.[16] This compound exhibited antibacterial (MIC 500–2000 μg/mL and MBC 1000–3000 μg/mL) and antifungal (MIC 750–1500 mg/mL and MFC 1500–3000 mg/mL) activities against *Aspergillus niger*, *A. ustus*, *A. ochraceus*, *Bacillus cereus*, *B. megaterium*, *B. subtilis*, *C. albicans*, *E. coli*, *P. aeruginosa*, *S. aureus*, *S. dysenteriae*, *S. sonnei*, *S. typhi*, *S. paratyphi*, and *V. cholerae*.[16]

From *B. stricta*[83,84] and *B. articularis*[85] two alcohols (59-60) and four carboxylic acids (61-64) were isolated [Table 1 and Figure 4]. In addition, seventeen amino acids, including a protein and three carbohydrates have been identified from the leaves and seeds of *B. stricta*.[83,84] A recent study on *B. verticillata* roots has led to the isolation of mixtures of aliphatic acids, tri-*O*-acylglycerols and sucrose, and glucose and sucrose.[39]

Volatile components

Fatty acids, monoterpenoids, aromatic compound, and alcohol were identified by GC-MS from *S. ocymoides*[90] and some fatty acids and terpenoids, such as linalool, eugenol, β-bisabolene, *E*-β-farnesene, phytol and terpineol,[91] guaiene,[34] and phytol, 1,8-cineole, α-pinene, and *p*-cymene[92] were identified by GC-MS from the aerial parts of *B. verticillata*.

BIOLOGICAL ACTIVITIES OF CRUDE EXTRACTS

Borreria and *Spermacoce* species possess a wide variety of medicinal properties. So far, a few species have been screened for confirmation of their biological activities. Experimental results have shown some species as antimicrobial, antitumor, antioxidant, anti-inflammatory, hepatoprotective, larvicidal, etc. The various biological activities reported from different extracts of *Borreria* and *Spermacoce* species are summarized in Table 2.

CONCLUSIONS

Given the small of species chemically studied, no definite

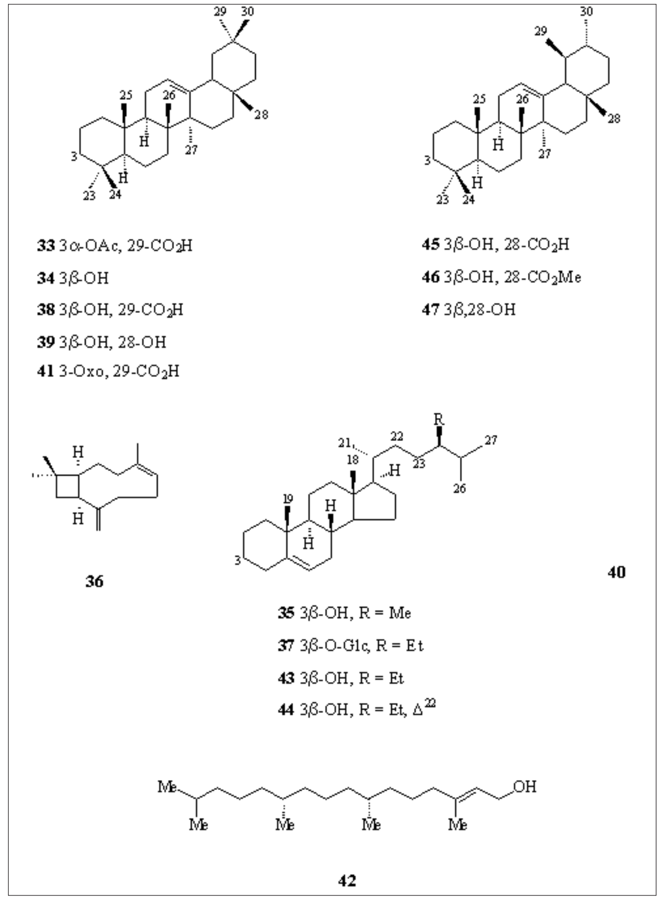

Figure 3: Terpenoids found in *Borreria* species

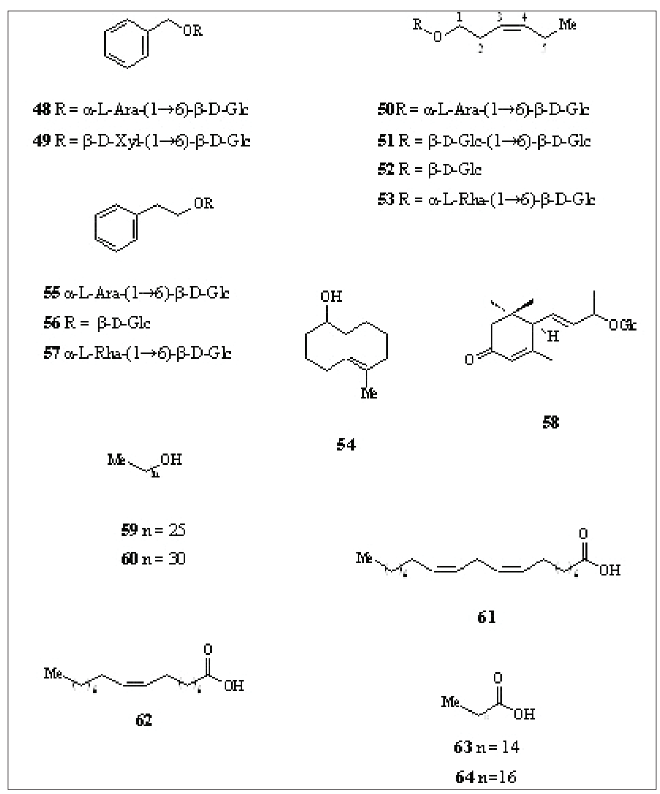

Figure 4: Miscellaneous compounds found in *Borreria* and *Spermacoce* species

Table 2: Biological activities for crude extracts and fractions of Borreria and *Spermacoce* species

Activity	Species and plant part[a]	Extracts/Species/References
Allelopathic	*B. hispida* (WP)	Aqueous—on two varieties of rape (*Brassica campestris* L.).[94]
Antibacterial	*B. articularis* (AP)	Ethyl acetate and ethanol (6–20 mm, at 2000 mg/disc) against *Bacillus cereus*, *B. megaterium*, *B. subtilis*, *E. coli*, *Shigella dysenteriae*, *S. sonnei*, *Salmonella typhi*, *S. paratyphi*, *P. aeruginosa*, *S. aureus*, and *V. cholerae*.[16]
	B. eupatorioides (R)	Aqueous—*S. typhi* (IC_{50} 10.1 mg/mL) and *E. coli* (IC_{50} 62.5 mg/mL).[23]
	B. ocymoides (L)	Aqueous and alkaloidic—against *Proteus mirabilis*, *P. aeruginosa*, and *Neisseria gonorrhoeae*.[33]
		Aqueous, ethanol, and alkaloidic and cardiac glycoside fractions against *S. aureus*, *K. pneumoniae*, *E. coli*, and β-hemolytic *Streptococci*.[33]
	B. verticillata	Extract unspecified—*S. aureus*, *E. coli*, and *Monilia albicans*.[95]
	B. verticillata (R)	Methanol—multiresistant strains of *P. aeruginosa*. [96]
	B. verticillata (AP)	Volatile oil (MIC 12.5-22.3 mg/mL).[92]
	S. hispida (WP)	Ethanol—*E. coli* (zone of inhibition of 20 mm).[97]
		Methanol (MIC 250 mg/mL)—against *B. subtilis*, *B. pumilus*, *S. aureus*, *P. aeruginosa*, *E. coli*, and *K. pneumoniae*.[98]
Antifungal	*B. articularis* (AP)	Ethyl acetate (37–45%) and ethanol (34.5–50%) against *Aspergillus niger*, *A. ustus*, *A. ochraceus*, and *C. albicans*.[16]
Anti-inflammatory	*S. articularis* (WP)	Pet. ether, chloroform, ethyl acetate, aqueous, and benzene—carrageenan-induced paw edema for 27.14%, 55.26%, 53.93%, 74.5%, and 53.5%, respectively, at 150 mg/kg.[15]
Anti-inflammatory	*S. hispida* (WP)	Methanolic-exhibited significant inhibition of the carrageenan-induced paw edema in Wistar albino male rats at the dose of 100 and 200 mg/kg body wt.[99]
Antihyperlipidemic	*S. hispida* (S)	Flavonoid-rich fraction improves antioxidant status and alleviates liver and kidney damage associated with HFD-fed-STZ (high-fat diet-fed-streptozotocin) rats by up-regulating PPAR-a (peroxisome proliferator activated receptor) mNRA.[100]
	S. hispida (WP)	Methanolic—significantly decreased the levels of lipid and lipoprotein in plasma and tissues (liver, heart, aorta in high fad rats).[101]
Antioxidant	*S. articularis* (WP)	Methanol—DPPH (65 μg/mL), and NO production (77.3%).[42]
	S. exilis (WP)	Methanol—DPPH (370 μg/mL) and NO production (91.16%).[42]
	S. hispida (WP)	Methanol—ABTS (3.91 mmol/100 g), DPPH (2.73 mmol/100 g), FRAP (0.92 μmol/g).[102]
Antioxidant	*S. hispida* (S)	Flavonoid-rich fraction *in vitro* ($DPPH^{\cdot}$ and $ABTS^{\cdot+}$ radicals) and *in vivo* (20, 40 and 80 mg/kg to high fat diet fed rats).[28]
	B. hispida (WP)	Pet. ether (IC_{50} 1150 and 970 μg/mL), ethyl acetate (IC_{50} 260 and 180 μg/mL) and methanol (IC_{50} 160 and 65 μg/mL) by phosphomolybdic acid and FRAP methods, respectively.[103]
Antitumoral	*B. pusilla* (NC)	Ethanol–H_2O 1:1—Leuk-P388 cell, at 115 mg/kg.[104]
Cardiovascular	*B. hispida* (WP)	Rats treated for 30 days with this plant showed that improves cardiac function and ameliorates various risk factors associated with cardiac disease.[24]
Gastrointestinal and anti-ulcer	*B. ocymoides* (L)	Aqueous (6.1%) and methanol (22.5%)—at 800 mg/kg, increased gastrointestinal motility in rats.[105]
Hepatoprotective	*B. articularis* (WP)	Aqueous—protected the rats from hepatotoxic action of paracetamol.[106]
Hepatoprotective	*S. hispida* (WP)	Ethanol—(200 mg/kg body wt.) on nitrobenzene (50 mg/kg body wt.)-induced hepatic damage rats.[107]
Larvicidal	*S. verticillata* (AP, R and St)	Hexane—LD_{50} 83.8 (AP); 91.8 (R) and 115.8 μg/mL (St) against fourth instar larvae of *A. aegypti*.[108]
Schistosomicidal	*B. verticillata* (L)	Essential oil—ova (MIC 500 mg/mL), miracidia and cercariae (MIC 100 μg/mL) of *Schistosoma hematobium*.[109]
Uterine stimulant	*B. verticillata* (R)	Aqueous[110]
Toxicity	*B. verticillata* (L and R)	Methanol—Brine shrimp (LC_{50} values > 250 μg/mL).[111]

[a]AP = Aaerial parts, L = Leaves, R = Roots, S = Seeds, St = Stems, NC = Not cited, and WP = Whole plant

conclusions can be drawn about chemical relationships among *Borreria* and *Spermacoce* species. However, the classes of compounds found are suggestive of chemical patterns in the tribe Spermacoceae. The most representative classes of compounds found were mainly alkaloids (only *Borreria* species) and iridoids (in two genera) which have been found in species from America (e.g. *B. capitata* and *B. verticillata*), Europe and Africa (e.g. *B. verticillata*) and Asia (e.g. *B. latifolia* and *S. laevis*) as well as in species of other genera of Spermacoceae. Flavonoids were found only in species from Asia (*B. hispida, B. stricta*, and *S. laevis*). Thus, the common possession of alkaloids and iridoids by few groups of species should be viewed as retention of an ancient characteristic or as a mark of natural affinity. Therefore, a molecular phylogeny of *Borreria* and *Spermacoce*, including plants with known chemistry, would be extremely helpful to clarify trends in the chemical evolution of the genera.

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