



Review article

Secondary metabolite compounds from *Sida* genus and their bioactivityN.S. Aminah^{a,*}, E.R. Laili^a, M. Rafi^b, A. Rochman^c, M. Insanu^d, K.N.W. Tun^{e,f}^a Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga, Komplek Kampus C, Jl. Mulyorejo, Surabaya, 60115, Indonesia^b Department of Chemistry, Faculty of Mathematics and Natural Sciences, Institut Pertanian Bogor, Jalan Tanjung Kampus IPB Dramaga, Bogor 16680, Indonesia^c Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, 55281, Indonesia^d Department of Pharmaceutical Biology, School of Pharmacy, Institut Teknologi Bandung, Bandung, West Java, Indonesia^e Postdoc Fellow Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga, Komplek Kampus C, Jl. Mulyorejo, Surabaya, 60115, Indonesia^f Department of Chemistry, Patheon University, Patheon, Myanmar

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ABSTRACT

Plants are the key source for the production of novel therapeutic products for new medicines. The biological properties of the plant species used world wide are mainly accountable for their secondary metabolites obtained from plants. The goal of this analysis is to summarize the chemical composition and biological effects of the genus *Sida* (Malvaceae) to identify potential research opportunities. This analysis draws on the literature review of scientific journals, and books from libraries, and electronic sources like ScienceDirect, Springer, PubMed, ResearchGate, Google Scholar, and the Website. Some groups of secondary metabolite compounds isolated from the genus *Sida* include alkaloids, flavonoids, coumarin, and others. Pharmacological experiments found that there are a wide variety of biological activities in extracts and compounds isolated from the genus *Sida* comprising antimalarial, antiplasmodial, antimicrobial, analgesic, antibacterial, antioxidant, vasorelaxant, wound healing, antifungal activities, the inhibition of quinone reductase, and mouse mammary organ culture.

1. Introduction

Metabolites are the transitional products of metabolism and restricted to small molecules. Plant produces a lot of chemicals that can be categorized into primary metabolites and secondary metabolites. Primary metabolites are necessary for cell function and they are omnipresent. Secondary metabolites are useful for human because of their diverse applications (Dufour and Rao, 2011; Olivoto et al., 2017; Yang et al., 2018).

The genus *sida* has relatively 200 species scattered in every part of tropical and subtropical regions in the world (Mabberley, 1997). The genus *sida* is originated in Brazil (Bovini, 2015). This plant can be used as traditional medicine, but no reviews have been made on the phytochemical, toxicological and pharmacological properties of the genus *Sida*. The main focus of this review is phytochemistry, pharmacological properties, botanical aspects of the herbs, their experimental application and translational investigation of genus *sida* (see Table 1).

2. Botanical description

2.1. *Sida cordifolia*

Sida cordifolia is an erect perennial growing up to 50–200 cm high. Leaves are oblong, hair-coated and 3.5 cm long. The trunks

are green-yellow, thick, long and short. The cycle of flora and fruit is from October to December (Shetu et al., 2019). *Sida cordifolia* plants according to Khurana et al. (2016) have the following categorization:

Kingdom	Plantae
Subkingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Dilleniidae
Superorder	Malvanae
Order	Malvales
Family	Malvaceae
Subfamily	Malvoideae
Tribe	Malveae
Genus	<i>Sida</i>
Species	<i>S. cordifolia</i>
Scientific name	<i>S. cordifolia</i> L.

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Table 1. Isolated compounds from Genus *Sida* and their biological activities.

Compound name	Species	Biological activities	References
Ψ-(pseudo)-ephedrine (1)	<i>S. cordifolia</i>		Ghosh and Dutta (1930)
β-phenethylamine (2)	<i>S. cordifolia</i>		Ghosal et al. (1975)
ephedrine (3)	<i>S. cordifolia</i>		Ghosal et al. (1975)
Ψ-ephedrine (4),	<i>S. cordifolia</i>		Ghosal et al. (1975)
S-(+) N ₆ -methyltrypto-phanmethyl ester (5)	<i>S. cordifolia</i>		Ghosal et al. (1975)
hypaphorine (6)	<i>S. cordifolia</i>		Ghosal et al. (1975)
vasicinone (7)	<i>S. cordifolia</i>		Ghosal et al. (1975)
vasicine(8)	<i>S. cordifolia</i>		Ghosal et al. (1975)
vasicol (9)	<i>S. cordifolia</i>		Ghosal et al. (1975)
quindolinone (10)	<i>S. acuta</i>	Quinone reductase	Jang et al. (2003)
cryptolepinone (11)	<i>S. acuta, S. rhombifolia</i>	Vasorelaxant, Mouse mammary organ culture, Quinone reductase	Jang et al. (2003), Chaves et al. (2013)
11-methoxyquindoline (12)	<i>S. acuta</i>	Quinone reductase	Jang et al. (2003)
N-trans-feruloyltyramine (13)	<i>S. acuta</i>	Mouse mammary organ culture	Jang et al. (2003)
5'-hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo[2,1-b]quinazolin-1-yl)-heptan-1-one (14)	<i>S. cordifolia</i>		Sutradhar et al. (2006)
1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-3-ylamine (15)	<i>S. cordifolia</i>		Sutradhar et al. (2007)
2-(1'-amino-butyl) indol-3-one (16)	<i>S. cordifolia</i>		Sutradhar et al. (2007)
2'-(3H-indol-3-ylmethyl)-butan-1'-ol (17)	<i>S. cordifolia</i>		Sutradhar et al. (2007)
a salt of cryptolepine (18)	<i>S. cordifolia</i>		Chaves et al. (2013)
11-methoxy-quindoline (19)	<i>S. cordifolia</i>		Chaves et al. (2013)
quindoline (20)	<i>S. cordifolia</i>		Chaves et al. (2013)
1,2,3,9-tetrahydro-pyrrolo[2,1-b]quinazolin-3-amine (21)	<i>Sida glutinosa</i>		Das et al. (2011)
3,4,5,6-tetrahydro-3-methyl-β-carboline-5-carboxylic acid (22)	<i>Sida szechuensis</i>		Yao and Xu (2000)
cryptolepine (23)	<i>S. acuta</i>	Antiplasmodial	Banzouzi et al. (2004)
3'-(3'',7''-dimethyl-2'',6''-octadiene)-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucoside (24)	<i>S. cordifolia</i>		Sutradhar et al. (2007)
3'-(3'',7''-dimethyl-2'',6''-octadiene)-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucosyl [1→4]-β-D-glucoside (25)	<i>S. cordifolia</i>		Sutradhar et al. (2007)
6-(3''-methyl2''-butene)-3'-methoxyl-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucosyl [1→4]-β-D-glucoside 3, 3'-(3'', 7''-Dimethyl 2'',6'' otadiene)-8-C β-D-glucosylkaempferol 3-O-β-D-glucoside (26)	<i>S. cordifolia</i>		Sutradhar et al. (2007)
5,7-dihydroxy-3-isoprenylflavone (27)	<i>S. cordifolia</i>		Sutradhar et al., (2008)
5-hydroxy-3-isoprenyl Flavone (28)	<i>S. cordifolia</i>		Sutradhar et al., (2008)
5,7-dihydroxy-4'-methoxyflavone (29)	<i>S. rhombifolia</i>		Chaves et al. (2013)
kaempferol (30)	<i>S. rhombifolia</i>		Chaves et al. (2017)
kaempferol-3-O-β-D-glycosyl-6''-α-D-rhamnose (31)	<i>S. rhombifolia</i>		Chaves et al. (2017)
Glutinoside (32)	<i>S. glutinosa</i>		Das et al. (2012)
Chrysin (33)	<i>S. glutinosa</i>		Das et al. (2012)
scopoletin (34)	<i>S. acuta, S. rhombifolia</i>		Jang et al. (2003)
scoporone (35)	<i>S. rhombifolia</i>		Jang et al. (2003)
20-hydroxy,24-hydroxymethyl ecdysone (36)	<i>S. spinosa</i>		Darwish and Reinecke (2003); Jadhav et al. (2007)
20-hydroxyecdysone (37)	<i>S. spinosa</i>		Darwish and Reinecke (2003); Jadhav et al. (2007)
turkesterone (38)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
makisterone C (39)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
20-Hydroxyecdysone-20,22-monoacetone (40)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
24(28)-Dehydromakisterone A (41)	<i>S. glutinosa</i>		Das et al. (2012)
2β,3β,14α,20,21,22R,24-heptahydroxycholest-7-en-6-one (42)	<i>S. szechuensis</i>		Yao and Xu (2000)
polypodine B (43)	<i>S. szechuensis</i>		Yao and Xu (2000)
α-ecdysone (44)	<i>S. szechuensis</i>		Yao and Xu (2000)
25-acetoxy-20-hydroxyecdysone-3-O-β-D-glucopyranoside (45)	<i>S. rhombifolia</i>		Jadhav et al. (2007)
Pterosterone-3-O-β-D-glucopyranoside ecdysteroid (46)	<i>S. rhombifolia</i>		Jadhav et al. (2007)
ecdysone-3-O-β-D-glucopyranoside (47)	<i>S. rhombifolia</i>		Jadhav et al. (2007)
2-deoxy-20-hydroxyecdysone-3-O-β-D-glucopyranoside (48)	<i>S. rhombifolia</i>		Jadhav et al. (2007)
20-hydroxyecdysone-3-O-β-D-glucopyranoside (49)	<i>S. rhombifolia</i>		Jadhav et al. (2007)
taraxast-1,20(30)-dien-3-one (50)	<i>S. acuta</i>	Antioxidant	Chen et al. (2007)
taraxasterone (51)	<i>S. acuta</i>	Antioxidant	Chen et al. (2007)
7a-methoxy-α-tocopherol (52)	<i>S. acuta</i>	Antioxidant	Chen et al. (2007)

(continued on next page)

Table 1 (continued)

Compound name	Species	Biological activities	References
β -tocopherol (53)	<i>S. acuta</i>		Chen et al. (2007)
α -tocopherol (54)	<i>S. acuta</i>		Chen et al. (2007)
α -tocospiro B (55)	<i>S. acuta</i>		Chen et al. (2007)
vomifoliol (56)	<i>S. acuta</i>		Jang et al. (2003)
Ioliolide (57)	<i>S. acuta</i>		Jang et al. (2003)
4-ketopinonesinol (58)	<i>S. acuta</i>		Jang et al. (2003)
evofolin-A (59)	<i>S. acuta</i>		Jang et al. (2003)
evofolin-B (60)	<i>S. acuta</i>		Jang et al. (2003)
glyceryl-1-eicosanoate (61)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
p-hydroxyphenethyl trans-ferulate (62)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
triacontane (63)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
1-eicosene (64)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
9-hydroxy-cis-11-octadecenoic acid (65)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
1-O- β -D-Glucopyranosyl-(2S,3S,4R,8Z)-2-[(2'R)-2'-hydroxypalmito-ylamino]-8-octadecene-1,3,4'-triol (66)	<i>S. spinosa</i>		Darwish and Reinecke (2003)
phaeophytin A (67)	<i>S. rhombifolia</i>		Chaves et al. (2013)
17 ³ -ethoxyphosphorbide A (68)	<i>S. rhombifolia</i>		Chaves et al. (2013)
13 ² -hydroxy phaeophytin B (69)	<i>S. rhombifolia</i>		Chaves et al. (2013)
17 ³ -ethoxyphosphorbide B (70)	<i>S. rhombifolia</i>		Chaves et al. (2013)

2.2. *Sida acuta*

There was no literature for plant description of *Sida acuta*. *Sida acuta* plants according to Mohideen et al. (2002) have the following categorization:

Kingdom	Plantae
Class	Dicotyledoneae
Order	Malvales
Family	Malvaceae
Genus	<i>Sida</i>
Specie	<i>S. acuta</i>
Scientific name	<i>Sida acuta</i> Burman f.

2.3. *Sida rhombifolia*

Sida rhombifolia is a member of the genus *Sida* which belongs to the Malvaceae family. Local names are called guri, sidaguri, saliguri (Sumatra), sadagori, sidaguri, otok-otok, taghuri, sidagori (Java), kahindu, mistaken (Nusa Tenggara) and hutugamo, bitumu, digo, sosapu (Maluku) (Dalimarta, 2003). Sidaguri plants (*Sida rhombifolia* L) according to Sivarajan and Pradeep (1994), have the following classification:

Divisio	Spermatophyta
Sub Divisio	Angiospermae
Classis	Dicotyledoneae
Sub classis	Dialypetalae
Ordo	Malvales/Columniferae
Familia	Malvaceae
Genus	<i>Sida</i>
Species	<i>S. rhombifolia</i>
Scientific name	<i>Sida rhombifolia</i> L.

2.4. *Sida spinosa*

Sida spinosais recognized as Kantakinibala (prickly fanpetals) is an erect perennial shrub. This plant is primarily found in the warmer parts of India at the height of 4400 ft. The plant is stellate, with filiform leaves 30

cm–1 m high, stipules 2–5 mm long, petiole length 2–20 mm, 1–3 spiny tubercles present on the stem at the base of petiole, lanceolate to ovate, oblong or rather orbicular, round at the base, acute or obtuse at the apex, and serrate at the apex. Moreover, flowers in terminal branches, axillary, solitary or 2–5 in fascicles, 2–5 mm pedicel, 0.2 cm long fruits, attached close to the center or tip. Calyx is 4–5 mm long and the fruits are compressed spherical with pubescent above. Furthermore, the length of the reddish brown glabrous seeds are 1.5 mm (Lin et al., 2010). *Sida spinosa* plants according to Singh and Navneet (2018) have the following classification:

Kingdom	Plantae
Division	Tracheophyta
Class	Mangnoliopsida
Order	Malvales
Genus	<i>Sida</i>
Species	<i>S. spinosa</i>
Scientific name	<i>Sida spinosa</i>

2.5. *Sida tuberculata*

In an area of South America, *Sida tuberculata* is mostly grown and is a well-known drink such as infusion or tea. *Sida tuberculata* is an herbaceous or subshrub plant that grows between 40 and 80 cm in length and expands by kernels. leaf blades elliptic or subrhombic to narrowly linear, upper surface with stellate trichomes; flowers and fruits crowded in subsessile axillary glomerules or, if solitary, the pedicels up to 15 mm long; calyx lobes with stellate trichomes and often with sparse simple trichomes in addition; and mericarps 6–8, muticous to submuticous, indehiscent (Rosa et al., 2015). *Sida tuberculata* plants according to <https://www.earth.com/earthpedia/plant/no/sida-tuberculata/> have the following classification:

Kingdom	Plantae
Class	Mangnoliopsida
Order	Malvales
Family	Malvaceae
Genus	<i>Sida</i>
Species	<i>S. tuberculata</i>
Scientific name	<i>Sida tuberculata</i>

2.6. *Sida cordata*

Sida cordata (Burm.f.), a medicinal plant, has been used for several illnesses. This plant belongs to the family Malvaceae which commonly grow in India. The plant is 30–80 cm tall. Soft hairy grows in its stems, petioles and pedicels pubescent. The heart-shaped leaves are 1–5.5 cm long and one at every node. The yellow flowers are produced on the axils of the leaf. Furthermore, flowers are axillary, solitary, 8–10 mm in diameter, Calyx 5 × 6 mm across, campanulate, 5-fid, simple and some stellate-hairy outside, glabrous within and around the margin, while the length of petioles is 1.5–30 mm. Moreover, the width of Corolla orange-yellow is 10 mm, the size of petals is 6 × 5 mm, obovate, base ciliate. There are 4 × 3 mm schizocarps, globose, enclosed in persistent calyx; mericarps 5, awnless. The colour of the seeds is brownish black. The plant is blooming and fruiting throughout the year, but it is mainly produced from September through November. The plant is also best to live in unused lands, damp and cool which needs up to one thousand and five hundred meter of area (Ugborogho, 1980). *Sida cordata* plants according to <https://www.gbif.org/species/5406739> have the following classification:

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Malvales
Family	Malvaceae
Genus	<i>Sida</i>
Species	<i>S. cordata</i>
Scientific name	<i>Sida cordata</i> (Burm. f.)

2.7. *Sida glutinosa*

Sida glutinosa is different from other species. It has a viscid dense stem with glandular and cutaneous hair, sometimes with star hair; leaves 2–4 × 1–3 cm, symmetrical, concolor, heart-shaped oval; solitary interest in axils or in diffuse terminal panicles; calyx 4.5–5.0 mm, unaccented, densely covered by viscid glandular hair and mixed with simple hair and stellate, obtrullate sepals; 1–2 cm in diameter; symmetrical petals, retuse, yellow with or without a red center, stamens 12–20, free filaments leading to the apex; and merger 5, apical 2-spined, dense thorn covered with antrorse hair (Baracho and Agra, 2016; Abat et al., 2017). This species can be found in tropical America, from northwestern Mexico and the Caribbean to Argentina and Brazil (Krapovickas, 2006). *Sida glutinosa* plants according to <http://plantamor.com/species/info/sida/glutinosa> have the following classification:

Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Dilleniidae
Order	Malvales
Family	Malvaceae
Genus	<i>Sida</i>
Species	<i>S. glutinosa</i>
Scientific name	<i>Sida glutinosa</i> Comm. ex Cav.

2.8. *Sida szechuensis*

Sida szechuensis is a Vietnamese plant. Its main uses are as an herb, the petiole and pedicle have slightly thick hair, penninerved leaves, axillary, solitary or in panicles; calyx campanulate, with 5 triangular lobes; pale yellow or orange crown, with pointed petals, mostly more or less

obliquely; staminal column ca. 5 mm long with long hair; ovaries with hair like a star; style more than 7; the outside of the protruding proticulate veined, short-tent; reniform seeds, dark brown or black, with white hair (Xuyen, 2006). *Sida szechuensis* plants according to <https://www.gbif.org/species/119199119> have the following classification:

Kingdom	Plantae
Family	Malvaceae
Genus	<i>Sida</i>
Species	<i>S. szechuensis</i>
Scientific name	<i>S. szechuensis</i> Matsuda

2.9. Methods

The documentation for this review was compiled from various data sources likes ScienceDirect, Springer, PubMed, ResearchGate, Google Scholar, and the Website.

3. Chemical constituents

3.1. Alkaloid

Ghosh and Dutt (1930) isolated Ψ-(pseudo)-ephedrine (1) from the *S. cordifolia*. From the roots of *S. cordifolia*, Ghosal et al. (1975), reported β-phenethylamine (2), ephedrine (3), Ψ-ephedrine (4), S-(+) N_B-methyltryptophanmethyl ester (5), hypaphorine (6), vasicinone (7), vasicine (8), and vasicinol (9) Jang et al. (2003), isolated quindolinone (10), cryptolepinone (11), 11-methoxyquindoline (12), N-trans-feruloyltyramine (13) from the whole plants of *S. acuta*. From the aerial parts of *S. cordifolia*, Sutradhar et al. (2006), isolated a new alkaloid, 5'-hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-1-yl)-heptan-1-one (14). Sutradhar et al. (2007), studied the aerial parts of *S. cordifolia* revealed the presence of four new alkaloids., 1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-3-ylamine (15), 5'-hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-1-yl)-heptan-1-one (14), 2-(1'-amino-butyl) indol-3-one (16), and 2'-(3H-indol-3-ylmethyl)-butan-1'-ol (17). Chaves et al. (2013), isolated cryptolepinone (11) and a salt of cryptolepine (18). From the aerial parts of *S. rhombifolia*. Chaves et al. (2017), reported quindolinone (10), the cryptolepine salt (18), 11-methoxy-quindoline (19), and quindoline (20) from the aerial parts of *S. rhombifolia*. Das et al. (2011) isolated 1,2,3,9-tetrahydro-pyrrolo[2,1-b] quinazolin-3-amine (21) from the aerial parts of *Sida glutinosa*. Yao and Xu (2000) reported 3,4,5,6-tetrahydro-3-methyl-β-carboline-5-carboxylic acid was isolated from *Sida szechuensis*. Banzouzi et al. (2004), isolated cryptolepine (23) from the ethanolic extract of *S. acuta*. Alkaloid group compounds in the genus *Sida* are presented in Figure 1.

3.2. Flavonoid

Sutradhar et al., (2007), isolated three new flavonol C-glycosides: 3'-(3'',7''-dimethyl-2'',6''-octadiene)-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucoside (24), 3'-(3'',7''-dimethyl-2'',6''-octadiene)-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucosyl [1→4]-β-D-glucoside (25), and 6-(3''-methyl-2''-butene)-3'-methoxyl-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucosyl [1→4]-β-D-glucoside 3, 3'-(3'', 7''-Dimethyl 2'',6'' otadiene)-8-C β-D-glucosylkaempferol 3-O-β-D-glucoside (26) from the aerial parts of *S. cordifolia*. Sutradhar et al., (2008), isolated two new flavones, 5,7-dihydroxy-3-isoprenylflavone (27) and 5-hydroxy-3-isoprenyl Flavone (28) from the chloroform extract of *S. cordifolia*. In 2013, Chaves et al. isolated 5,7-dihydroxy-4'-methoxyflavone (29) from the aerial parts of *S. rhombifolia*. Chaves et al. (2017), also isolated kaempferol (30) and kaempferol-3-O-β-D-glycosyl-6''-α-D-rhamnose (31) from the aerial parts of *S. rhombifolia*. Das et al. (2012) isolated

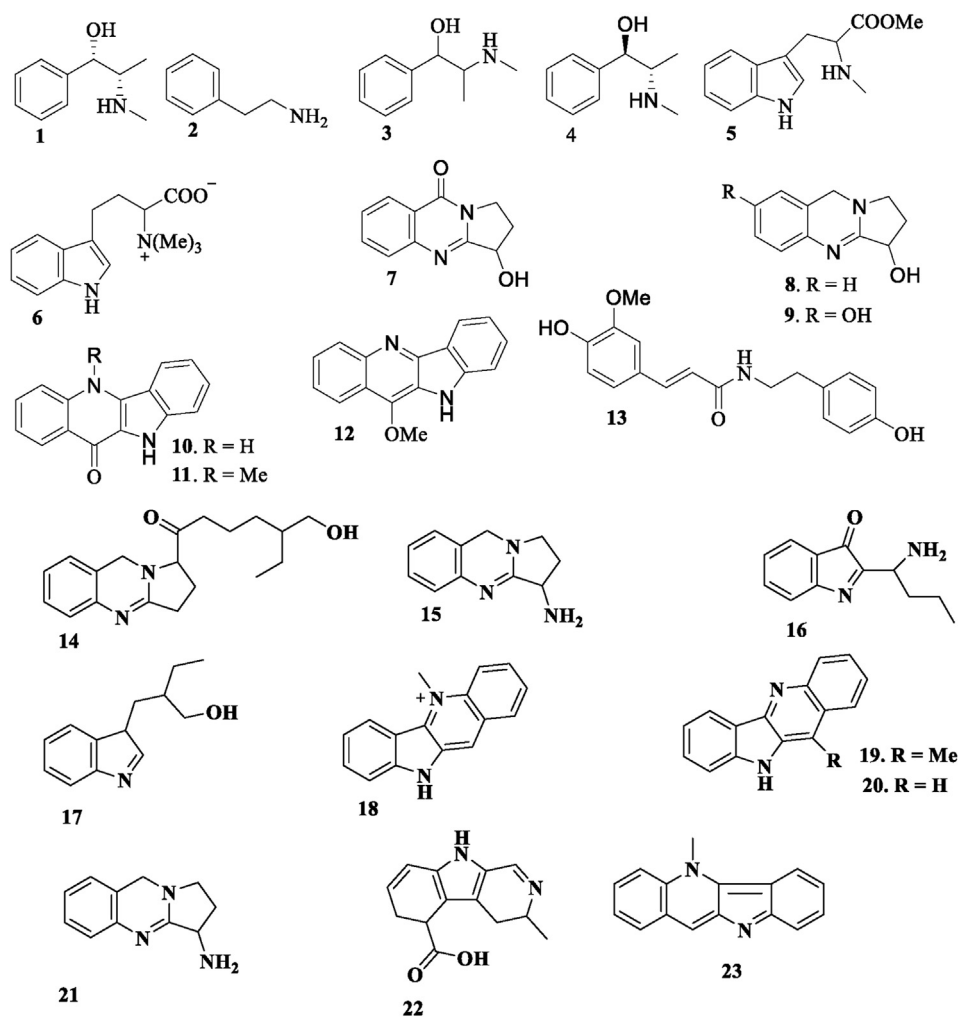


Figure 1. Alkaloids 1–23 isolated from genus *Sida*.

Glutinoside (32) and Chrysin (33) from the aerial parts of *Sida glutinosa*. Figure 2 presents the reported flavonoid compounds isolated from the genus *Sida*.

3.3. Coumarins

Jang et al. (2003), isolated scopoletin (34) from the whole plants of *S. acuta*. Chaves et al. (2017), reported scopoletin (34) and scoporone (35) from the aerial parts of *S. rhombifolia*. The two structures of coumarin compound are shown in Figure 3.

3.4. Ecdysteroids

From the aerial parts of *S. spinosa*, Darwish and Reinecke (2003), reported five ecdysteroids, 20-hydroxy,24-hydroxymethyl ecdysone (36), 20-hydroxyecdysone (37), turkesterone (38), makisterone C (39), and 20-Hydroxyecdysone-20,22-monoacetone (40). Das et al. (2012) reported 24(28)-Dehydromakisterone A (41) found in dried aerial parts of *Sida glutinosa*. Yao and Xu (2000) isolated 2 β ,3 β ,14 α ,20,21,22R, 24-heptahydroxycholest-7-en-6-one (42), polypodine B (43), and α -ecdysone (44) from *Sida szechuensis*. Jadhav et al. (2007) isolated ecdysone (36), 20-hydroxyecdysone (37), 25-acetoxy-20-hydroxyecdysone-3-O- β -D-glucopyranoside (45), Pterosterone-3-O- β -D-glucopyranoside ecdysteroid (46), ecdysone-3-O- β -D-glucopyranoside (47), 2-deoxy-20-hydroxyecdysone-3-O- β -D-glucopyranoside (48), and 20-hydroxyecdysone-3-O- β -D-glucopyranoside from the whole plant of

S. rhombifolia. Figure 4 shows the molecular structure of the ecdysteroid group of compound of the genus *Sida*.

3.5. Triterpenes

Chen et al. (2007), reported two triterpenes, including a new taraxast-1,20(30)-dien-3-one (50) and taraxasterone (51) from the whole plant of *S. acuta*. The two triterpenes structure can be seen in Figure 5.

3.6. Tocopherols

Chen et al. (2007), reported a new tocopherol derivative, 7 α -methoxy- α -tocopherol (52), along with β -tocopherol (53), α -tocopherol (54), and α -tocospiro B (55) from the whole plant of *S. acuta*. The structure of the tocopherol's derivatives is shown in Figure 6.

3.7. Other compounds

Jang et al. (2003), isolated vomifoliol (56), Ioliolide (57), 4-ketopinoresinol (58), evofolin-A (59), and evofolin-B (60) from the whole plants of *S. acuta*. Darwish and Reinecke (2003) reported two new compounds, namely glyceryl-1-eicosanoate (61) and p-hydroxyphenethyl trans-ferulate (62), together with four known compounds, triacontane (63), 1-eicosene (64), 9-hydroxy-cis-11-octadecenoic acid (65), and 1-O- β -D-Glucopyranosyl-(2S,3S,4R,8Z)-2-[(2'R)-2'-hydroxypalmito-ylamino]-8-octadecene-1,3,4'-triol (66), from the aerial parts of *S. spinosa*. Chaves et al. (2013), isolated phaeophytin A (67),

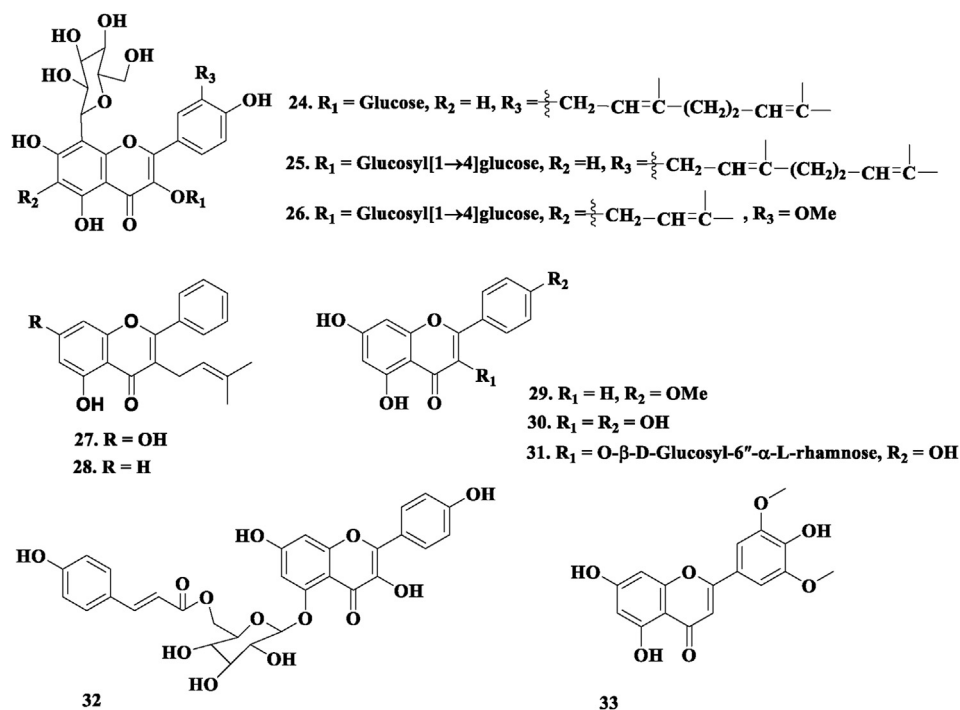


Figure 2. Flavonoids 24–33 isolated from genus *Sida*.

17³-ethoxyphosphoride A (68), 13²-hydroxy phaeophytin B (69), 17³-ethoxyphosphoride B (70), from the aerial parts of *S. rhombifolia*. The structure of compounds's 56–70 is presented in Figure 7.

4. Biological activities

4.1. Antimalarial activity

Karou et al. (2003), reported that various fractions of *S. acuta* showed the antimalarial activity with the IC₅₀ values in the range of 0.05–57.04 µg/mL.

4.2. Antiplasmodial activity

The EtOH roots extract of *S. acuta* displayed the antiplasmodial activity with the IC₅₀ values in the range of 3.9–5.4 µg/mL. In addition, compound 23 from *S. acuta* also showed potent antiplasmodial activity (Banzouzi et al., 2004).

4.3. Antimicrobial activity

Momin et al. (2014), evaluated the antimicrobial activity of *S. cordifolia* EtOH extract using five pathogenic bacteria with standard antibiotic kanamycin. The extract of *S. cordifolia* has no antimicrobial activity against five selected bacteria.

4.4. Analgesic activity

Momin et al. (2014), evaluated the analgesic activity *S. cordifolia* EtOH extract using acetic acid-induced writhing reflex model in mice with standard drug diclofenac. The extract displayed a significant ($P > 0.001$) decrease in the writhing reflex of mice induce acetic acid at a dose

of 500 mg/kg. Moreover, the aqueous acetone extract of *S. acuta* and *S. cordifolia* was reported to inhibit dose-dependent analgesic activity (Konaté et al., 2012).

4.5. Anti-inflammatory activity

Moreover, aqueous leaves extract of *S. cordifolia* was found to inhibit the carrageenin-induced rat paw edema at a dose of 400 mg/kg administered orally (Franzotti et al., 2000).

4.6. Antibacterial activity

Islam et al. (2003) studied the antibacterial activity of various extracts of *S. rhombifolia* with Gram-positive and Gram-negative test organisms. The results revealed that all extracts exhibited weak activity. Karou et al. (2005), conducted the antibacterial activity of *S. acuta* alkaloids fraction using agar-well diffusion assay and broth microdilution assay. The highest zone inhibition diameters were identified by Gram-positive bacteria in accordance with agar-well diffusion assay. From the broth microdilution assay, the MIC and MBC values observed in the range of 16–400 µg/mL and 80–400 µg/mL. In 2007, Oboh et al. evaluated the antibacterial activity of the 90% EtOH extract of *S. acuta* aerial parts with agar-dilution method. The results of the MIC were found values in the range of 5–10 mg/mL. In other studies, Assam et al. (2010) evaluated antibacterial activity of the aqueous-methanol extract of *S. rhombifolia* (1:4, v/v) using agar disc diffusion and agar dilution methods. The results found that aqueous-methanol extract of *S. rhombifolia* displayed moderate activity. Moreover, Halilu et al. (2016) evaluated antibacterial activity of *S. cordifolia* ethanolic leaves extract using cup plate method against Gram-positive and Gram-negative microorganisms. The results showed that the extract has potent activity on all tested organisms.

4.7. Antioxidant activity

In 2003, Auddy et al. (2003) assessed the antioxidant activity of EtOH extract and water infusions of *S. cordifolia* with ABTS radical cation decolorization assay and lipid peroxidation. According to the ABTS assay,

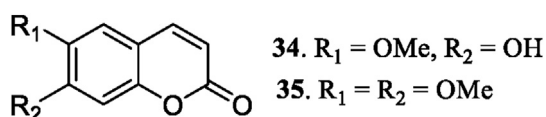
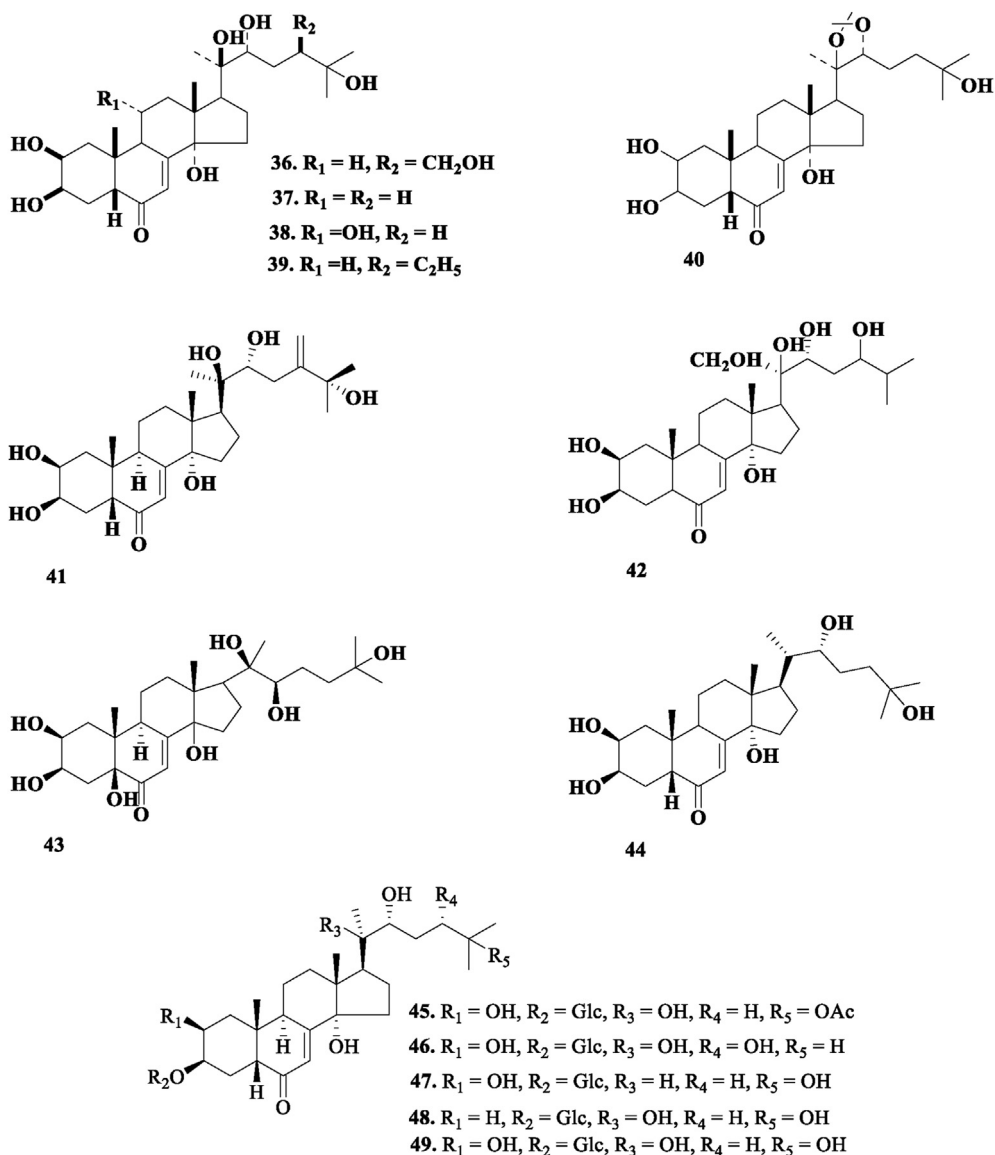
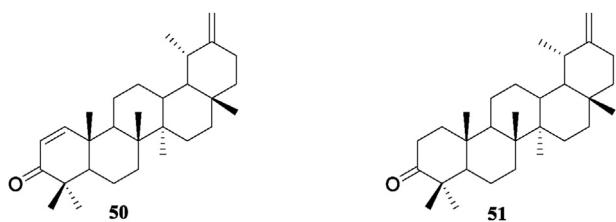
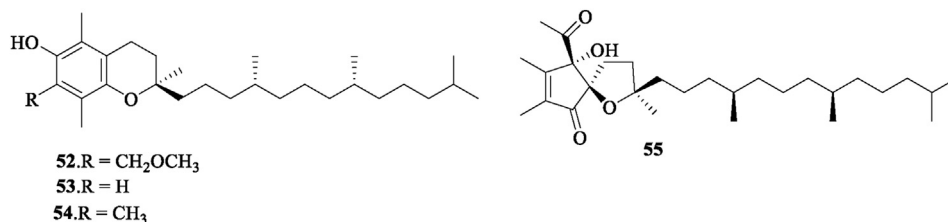


Figure 3. Coumarins 34–35 isolated from genus *Sida*.

Figure 4. Ecdysteroids 36–49 isolated from genus *Sida*.Figure 5. Triterpenes 50–51 isolated from genus *Sida*.Figure 6. Tocopherols 52–55 isolated from genus *Sida*.

the EtOH extract displayed potent activity (IC_{50} 16.07 $\mu g/mL$). [Chen et al. \(2007\)](#), studied the antioxidant activity of compounds 52–55 with DPPH assay, and the result showed that compound 52, 53, and 54 displayed significant activities with the EC_{50} values of 86.9, 68.2, and 70.9 μM . [Momin et al. \(2014\)](#), evaluated the antioxidant activity of EtOH extract of *S. cordifolia* using DPPH assay with standard ascorbic acid. According to the results, the IC_{50} values of the extract and standard ascorbic acid was 50 and 1.16 $\mu g/mL$. In addition, [Kumar et al. \(2019\)](#), assessed the antioxidant activity of various extracts of *S. cordifolia* using DPPH assay with standard ascorbic acid. The results found that various

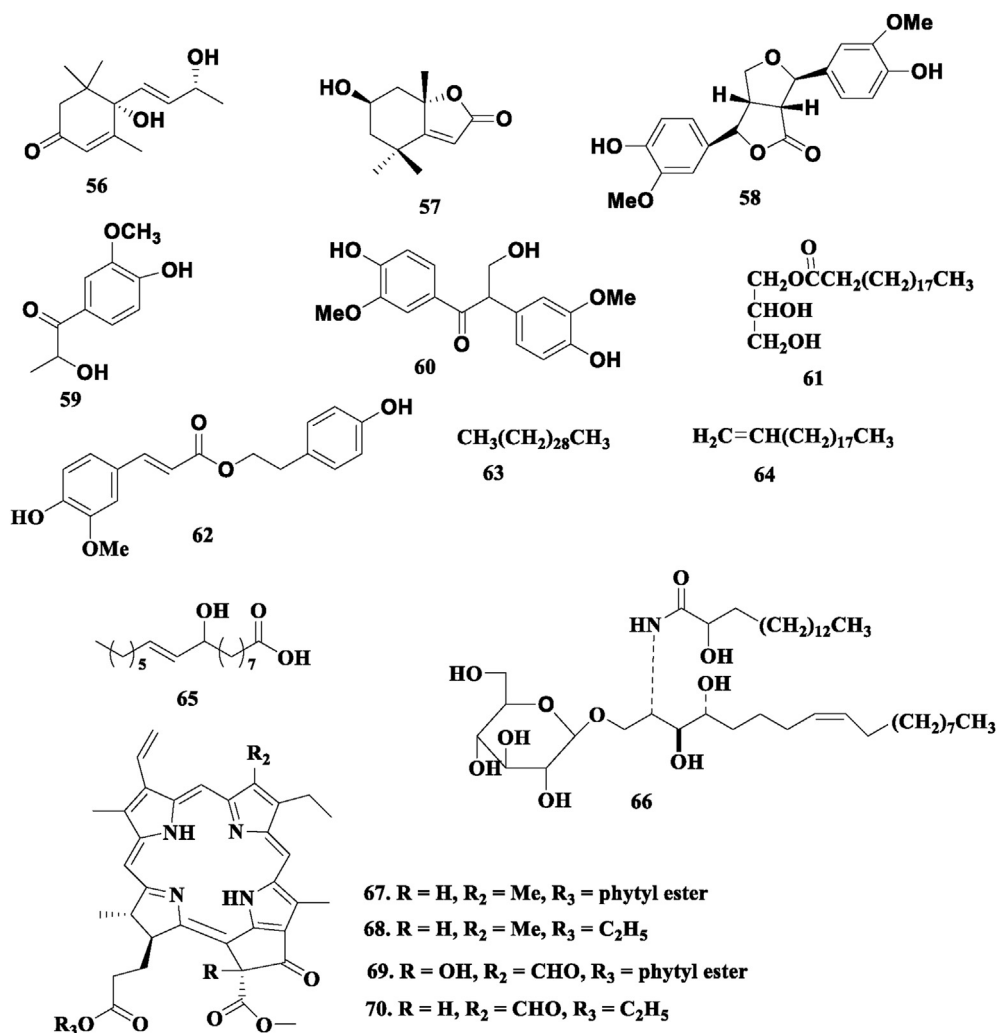


Figure 7. Other compounds 56–70 isolated from genus *Sida*

extracts and standard ascorbic acid displayed concentration-dependent percent inhibition of DPPH radical.

4.8. Vasorelaxant activity

In another study, the vasorelaxant activity was detected in the rodent isolated mesenteric arteries by the compound **11** (Chaves et al., 2013).

4.9. Wound healing activity

Pawar et al. (2013), informed that the EtOH extract of *S. cordifolia* displayed wound healing activity in rats. Moreover, Francis et al. (2018), also informed that EtOH leaves extract of *S. rhombifolia* has a prospective advantage in enhancing wound healing. In another study, Kumar et al. (2019), studied wound healing activity of various extract of *S. cordifolia* against dexamethasone-induced retardation in rats. According to the results, aqueous extract of *S. cordifolia* displayed significant activity.

4.10. Antifungal activity

Rosa et al. (2015), evaluated the antifungal activity of aqueous infusion from *S. tuberculata* leaves and roots, using the broth micro-dilution method against 37 clinical isolates of opportunistic yeasts.

The MIC (minimal inhibitory concentration) and MFC (minimal fungicidal concentration) were identified toward *Candida krusei* isolates.

4.11. Antidiabetic activity

Ahmad et al. (2014) documented that the alcoholic extract of *S. cordifolia* displayed antihyperglycemic action when administered to streptozotocin-induced diabetic rats.

4.12. Toxicity

Islam et al. (2003) evaluated the toxicity of various extracts of *S. rhombifolia* using brine shrimp bioassay with standard reference gallic acid. According to the results, EtOAc extract of *S. rhombifolia* exhibited significant cytotoxic activity with LC₅₀ value of 5.41 ppm. In addition, the aqueous extract of *S. cordifolia* has low acute toxicity in mice (Franzotti et al., 2000).

4.13. Antiarthritic activity

Gupta et al. (2009) assessed the antiarthritic activity of various extracts of *S. rhombifolia*. According to the results, EtOH and aqueous extracts displayed significant activity.

4.14. Quinone reductase induction assay

Jang et al. (2003), evaluated quinone reductase induction activity of compounds (10–14, 34, and 56–60) with culture mouse Hepa 1c1c7 cell. The results showed that compounds 10–11 have the most potent activity.

4.15. Mouse mammary organ culture assay

Jang et al. (2003), studied the prospective of compounds (10–14, 34, and 56–60) to inhibit the 7,12-dimethylbenzene (DMBA)- induced pre-neoplastic lesion in a mouse mammary organ culture. According to the results, compounds 11 (83.3%) and 13 (75.0%) displayed the activity to inhibit 7,12-dimethylbenzene (DMBA)- induced preneoplastic lesion at a dose of 10 µg/mL.

5. Conclusion

Eight species of the genus *Sida* have been explained and discussed in this review article. The eight species produce a variety of secondary metabolite compounds, namely alkaloids, flavonoids, coumarins, ecdysteroids, triterpenes, tocopherols, and other compounds. The compounds depicted a variety of interesting biological activities. So they can be used as a reference for the researchers to develop further research or exploration.

Declarations

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

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Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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