REVIEW



Phytochemistry and pharmacological activities of the genus *Rhynchosia*: a comprehensive review

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Abstract

Main conclusion The genus *Rhynchosia* is a rich source of natural compounds especially flavonoids and prenylated isoflavonoids. Further experimental studies on *Rhynchosia* members may be result new and novel secondary metabolites with potent biological activities.

Abstract Traditionally, medicinal plants have played a significant role on human life since ancient days. At present, natural compounds are the major source for the modern drug discovery owing to their therapeutic selectivity, minutest of side effects, inexpensive source and serve as lead molecules for the discovery of new drugs. *Rhynchosia* species (Fabaceae) are extensively circulated throughout the tropical and subtropical areas around the world. A few plants of this genus were used in traditional medicine for the treatment of various ailments such as antibacterial, antidiabetic, abortifacients, healing of wounds, hepatoprotective, remedial of boils, rheumatic pains and skin infections. The present review compiles traditional uses, isolated chemical compounds and pharmacological activities of *Rhynchosia* species. So far, in total, seventy-seven compounds were isolated from the genus *Rhynchosia*, including flavonoids, isoflavonoids, flavan-3-ols, xanthones, biphenyls, simple polyphenols and sterols. It is interesting to note that the genus *Rhynchosia* is a rich source of *C*-glycosylflavonoids and prenylated isoflavonoids. Further, phytochemical and pharmacological studies on this genus are required since only few species have been investigated so far.

Keywords Flavonoids · Phytochemistry · Pharmacology · Rhynchosia · Traditional medicine

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Introduction

Medicinal plants are worthy source of biologically active compounds for the development of new therapeutic drug candidates over the past centuries (Harvey 2008; Koehn and Carter 2005; Newman and Cragg 2012). Plants are treasure house of bioactive compounds which can be developed as safe drugs for the treatment of various human diseases. It is the time to recall the significance and past invention of some of the most illustrative examples of successful and promising drugs from natural source are listed. Aspirin: an anti-inflammatory agent (Newman et al. 2000); Digitoxin: used as a drug for congestive heart failure (Buss et al. 2003); Morphine: is a commercial drug and its derivative apomorphine used to treat Parkinson's disease (Dias et al. 2012); Penicillin: an important antibacterial agent (Wainwright 1990), Quinine: the anti-malarial drug (Achan et al. 2011); Taxol: promising anticancer drug (Kingston 1993), etc. are



still used for therapeutic applications. Even today, people in several countries are extensively using plant species as a remedy for the treatment of various kinds of diseases such as bacterial infections, cardiovascular, diabetic, digestive, kidney, mental-nervous, nutritional, respiratory, reproductive, sensory, skin infections and several wounds (González-Tejero et al. 2008). Thus, the plants have valuable source of natural compounds and played significant role in the current drug discovery with clinically enriched efficacy besides fewer side effects (Butler 2004). Hence, many researchers have been focusing their research interest on medicinal plants in terms of biological activity and drug discovery.

Among the plants of Fabaceae family which are used in traditional medicine, Rhynchosia species have occupied a prominent role. Rhynchosia genus consists of approximately 300 species circulated throughout the tropical and subtropical areas around the world, out of which twenty-two species occur in India (Chadha 1976; Willis 1966). The species belonging to the genus Rhynchosia (Fabaceae) are herbs, twining or erect shrubs. Previous phytochemical investigations on several species of *Rhynchosia* showed that the genus is exclusive to profuse production of C-glycosylflavonoids (Rao et al. 1991). Some of the isolated compounds of Rhynchosia genus and their plant extracts exhibit interesting biological activities, including antioxidant, anti-inflammatory, antimycobacterial and antiproliferative (Coronado-Aceves et al. 2017; Kinjo et al. 2001; Rondo 2017). A tiny review on chemical constituents of Rhynchosia genus was published in 1991 from our laboratory (Rao et al. 1991); however, the review covers only few phytochemistry reports but not on pharmacology perspective. To the best of our knowledge, no comprehensive, updated phytochemical and pharmacology review was published on Rhynchosia species which covers the literature up to date. The present review aimed to deliver an outline on the traditional uses, chemical constituents and pharmacology activities of the genus Rhynchosia which includes the literature up to date for future research opportunities.

Traditional uses

Based on folkloric medications, a few plants of *Rhynchosia* genus were used in indigenous medicine (Bakshu and Raju 2001; Bangalore and Agrahari 2009; Gamble and Fischer 1935; Kritikar and Basu 1975) such as antibacterial, antidiabetic, abortifacients, healing of wounds, hepatoprotective, rheumatic pains, remedial for boils and skin infections by Adivasi tribes. For example, *Rhynchosia scarabaeiods* L. (known as 'gadi chikkudu kaya') has been used to treat various bacterial diseases like dysentery, diarrhea and skin infections (Challa et al. 2011). Another endemic species of South India, *Rhynchosia suaveolens* DC is reported as

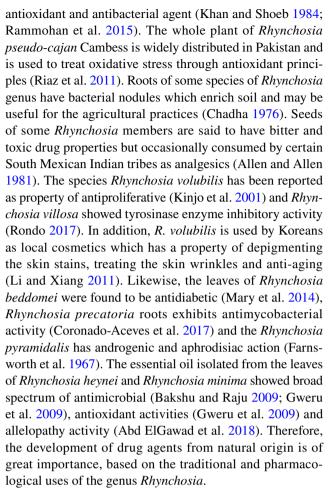


Table 6 represents the reported traditional uses of *Rhynchosia* species used for treating various ailments. These documented data represent that most of the species are used to treat oxidative stress-related (antioxidants), antibacterial, anti-inflammation and skin disorders. Also, they are used as analgesic and for the digestive disorders.

Phytochemistry

In the past few decades, some *Rhynchosia* species have been investigated from a phytochemical and pharmacological point of view. So far, in total, seventy-seven compounds were isolated; their structures, names and the corresponding plant source are compiled in Tables 1, 2, 3, 4, 5 and Figs. 1, 2, 3, 4, 5, 6, 7, 8, 9. A comprehensive of chemical constituents so far reported from the genus *Rhynchosia* can be conveniently grouped into the following types.

Flavones and flavone glycosides

Fifteen compounds (1–15, Fig. 1) were isolated from the genus *Rhynchosia* so far. Among them, most of the reported *C*-glycosylflavones are derivatives of apigenin and luteolin.



 Table 1
 Naturally occurring flavones and flavone glycosides of the genus Rhynchosia

Compounds/trivial names	Plant source	Plant part	References
Apigenin (1)	R. beddomei	Leaves	Adinarayana et al. (1985)
	R. heynei	Leaves	Adinarayana et al. (1985)
	R. rothii	Leaves	Rao and Gunasekar (1987)
Luteolin (2)	R. heynei	Leaves	Adinarayana et al. (1985)
	R. suaveolens	Leaves	Adinarayana et al. (1985)
Tricin (3)	R. volubilis	Roots	Li and Xiang (2011)
Apigenin-7- <i>O</i> -β-D-glucopyranoside (4)	R. volubilis	Roots	Li and Xiang (2011)
Luteolin-7- <i>O-β</i> -D-glucopyranoside (5)	R. volubilis	Roots	Li and Xiang (2011)
8',4'-Di- <i>O</i> -methylluteolin-7- <i>O</i> -glucuronide (6)	R. beddomei	Leaves	Adinarayana et al. (1980b)
Vitexin (7)	R. beddomei	Leaves	Adinarayana et al. (1980b)
	R. rufescens	Leaves	Adinarayana et al. (1979)
	R. bracteata	Leaves	Ali et al. (1992)
	R. sublobata	Leaves	Ali et al. (1992)
	R. cana	Leaves	Adinarayana and Ramachandraiah (1986
	R. capitata	Leaves	Praveena et al. (2013)
	R. heynei	Leaves	Adinarayana et al. (1985)
	R. minima	Leaves	Adinarayana et al. (1985)
	R. sericea	Leaves	Adinarayana et al. (1985)
	R. suaveolens	Leaves	Adinarayana and Ramachandraiah (1985
	R. jacobii	Leaves	Seetharamamma et al. (1989)
sovitexin (8)	R. beddomei	Leaves	Adinarayana et al. (1980b)
•	R. beddomei	Flowers	Rammohan et al. (2019)
	R. rufescens	Leaves	Adinarayana et al. (1979)
	R. bracteata	Leaves	Ali et al. (1992)
	R. sublobata	Leaves	Ali et al. (1992)
	R. cana	Leaves	Adinarayana and Ramachandraiah (1986
	R. capitata	Leaves	Praveena et al. (2013)
	R. heynei	Leaves	Adinarayana et al. (1985)
	R. minima	Leaves	Adinarayana et al. (1985)
	R. sericea	Leaves	Adinarayana et al. (1985)
	R. rothii	Leaves	Rao and Gunasekar (1987)
	R. suaveolens	Leaves	Adinarayana et al. (1985)
	TH SHAFFESTERS	Flowers	Rammohan et al. (2015)
	R. jacobii	Leaves	Seetharamamma et al. (1989)
Vicenin-1 (9)	R. jacobii	Leaves	Seetharamamma et al. (1989)
Vicenin-2 (10)	R. beddomei	Leaves	Adinarayana et al. (1980b)
(10)	R. rufescens	Leaves	Adinarayana et al. (1979)
	R. bracteata	Leaves	Ali et al. (1992)
	R. sublobata	Leaves	Ali et al. (1992)
	R. cana	Leaves	Adinarayana and Ramachandraiah (1986
	R. capitata	Leaves	Adinarayana et al. (1985)
	R. capnaia R. heynei	Leaves	Adinarayana et al. (1985) Adinarayana et al. (1985)
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	R. jacobii R. minima	Leaves	Seetharamamma et al. (1989)
		Leaves	Adinarayana et al. (1985)
	R. rothii	Leaves	Rao and Gunasekar (1987)
	R. sericea	Leaves	Adinarayana et al. (1985)
7 2 (11)	R. suaveolens	Leaves	Adinarayana et al. (1985)
Vicenin-3 (11)	R. minima	Leaves	Besson et al. (1977)
	R. sericea	Leaves	Adinarayana et al. (1985)
Schaftoside (12)	R. minima	Leaves	Besson et al. (1977)



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 Table 1 (continued)

Compounds/trivial names	Plant source	Plant part	References
Orientin (13)	R. beddomei	Leaves	Adinarayana et al. (1980b)
	R. rufescens	Leaves	Adinarayana et al. (1979)
	R. bracteata	Leaves	Ali et al. (1992)
	R. sublobata	Leaves	Ali et al. (1992)
	R. cana	Leaves	Adinarayana and Ramachandraiah (1986
	R. capitata	Leaves	Adinarayana et al. (1985)
	R. heynei	Leaves	Adinarayana et al. (1985)
	R. jacobii	Leaves	Seetharamamma et al. (1989)
	R. minima	Leaves	Adinarayana et al. (1985)
			•
	R. rothii	Leaves	Rao and Gunasekar (1987)
	R. sericea	Leaves	Adinarayana et al. (1985)
	R. suaveolens	Leaves	Adinarayana et al. (1985)
soorientin (14)	R. beddomei	Leaves	Adinarayana et al. (1979)
	R. beddomei	Flowers	Rammohan et al. (2019)
	R. rufescens	Leaves	Adinarayana et al. (1979)
	R. bracteata	Leaves	Ali et al. (1992)
	R. sublobata	Leaves	Ali et al. (1992)
	R. cana	Leaves	Adinarayana and Ramachandraiah (1986
	R. capitata	Leaves	Praveena et al. (2013)
	R. heynei	Leaves	Adinarayana et al. (1985)
	R. jacobii	Leaves	Seetharamamma et al. (1989)
	R. minima	Leaves	Adinarayana et al. (1985)
	R. rothii	Leaves	Rao and Gunasekar (1987)
	R. sericea	Leaves	Adinarayana et al. (1985)
	R. suaveolens	Leaves	Adinarayana et al. (1985)
	R. suaveolens	Flowers	Rammohan et al. (2015)
Lucenin-2 (15)	R. beddomei	Leaves	Adinarayana et al. (1980a)
2400 2 (40)	R. rufescens	Leaves	Adinarayana et al. (1979)
	R. bracteata	Leaves	Ali et al. (1992)
	R. sublobata	Leaves	Ali et al. (1992)
	R. heynei	Leaves	Adinarayana et al. (1985)
	R. rothii	Leaves	Rao and Gunasekar (1987)

Table 2 Naturally occurring flavonols and flavonol glycosides of the genus *Rhynchosia*

Compounds/trivial names	Plant source	Plant part	References
Kaempferol (16)	R. volubilis	Roots	Li and Xiang (2011)
Quercetin (17)	R. volubilis	Roots	Li and Xiang (2011)
Kaempferol-3-O-methylether (18)	R. rufescens	Leaves	Adinarayana and Ramachandraiah (1984)
Kaempferol-3- <i>O</i> -rutinoside (19)	R. cyanosperma	Leaves	Adinarayana et al. (1980a)
Quercetin-3-O-methylether (20)	R. rufescens	Leaves	Adinarayana and Ramachandraiah (1984)
Quercetin-7-O-methylether (21)	R. beddomei	Flowers	Rammohan et al. (2019)
Rutin (22)	R. beddomei	Leaves	Adinarayana et al. (1980b)
	R. cyanosperma	Leaves	Adinarayana et al. (1980a)
Rhynchosin (23)	R. beddomei	Leaves	Adinarayana et al. (1980c)
Rhynchospermin (24)	R. cyanosperma	Leaves	Adinarayana et al. (1981)



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Table 3 Naturally occurring dihydroflavonols of the genus *Rhynchosia*

Compounds/Trivial Names	Plant Source	Plant part	References	
Tirumalin (27)	R. cyanosperma	Leaves	Adinarayana et al. (1980a)	
Isotirumalin (28)	R. cyanosperma	Leaves	Rao and Gunasekar (1988)	
6- <i>C</i> -Prenyltoxifolin-7,3′-dimethylether (29)	R. densiflora	Leaves	Rao and Gunasekar (1998)	
Lupinifolinol (30)	R. precatoria	Roots	Coronado-Aceves et al. (2017)	

Table 4 Naturally occurring isoflavones and isoflavanones of the genus *Rhynchosia*

Compounds/trivial names	Plant source	Plant part	References
Diadzein (31)	R. volubilis	Roots	Li and Xiang (2011)
Calycosin (32)	R. volubilis	Roots	Li and Xiang (2011)
Genistein (33)	R. viscosa	_	Bohni et al. (2013)
	R. villosa	Roots	Rondo (2017)
Biochanin A (34)	R. volubilis	Roots	Li and Xiang (2011)
	R. beddomei	Flowers	Rammohan et al. (2019)
2'-Hydroxygenistein (35)	R. villosa	Roots	Rondo (2017)
3'-O-Methylorobol (36)	R. viscosa	_	Bohni et al. (2013)
3'-Hydroxybiochanin A (37)	R. volubilis	Roots	Li and Xiang (2011)
Cajanin (38)	R. villosa	Roots	Rondo (2017)
Licoisoflavone A (39)	R. viscosa	_	Bohni et al. (2013)
4'-(1"-Methoxy)-propylgenistein (40)	R. volubilis	Roots	Li and Xiang (2011)
Rhynedulin A (41)	R. edulis	Bark	Guo et al. (2011)
Rhynedulin B (42)	R. edulis	Bark	Guo et al. (2011)
Rhynedulin C (43)	R. edulis	Bark	Guo et al. (2011)
Cyclochandalone (44)	R. edulis	Bark	Guo et al. (2011)
Ulexin B (45)	R. edulis	Bark	Guo et al. (2011)
Rhynedulinal (46)	R. edulis	Bark	Guo et al. (2011)
Scandelinal (47)	R. edulis	Bark	Guo et al. (2011)
Cajanone (48)	R. precatoria	Roots	Coronado-Aceves et al. (2017)
	R. volubilis	_	Bohni et al. (2013)
	R. edulis	Bark	Guo et al. (2011)
Precatorin C (49)	R. precatoria	Roots	Coronado-Aceves et al. (2017)
Sophoraisoflavone A (50)	R. viscosa	_	Bohni et al. (2013)
Precatorin A (51)	R. precatoria	Roots	Coronado-Aceves et al. (2017)
Precatorin B (52)	R. precatoria	Roots	Coronado-Aceves et al. (2017)
Rhynchoviscin (53)	R. viscosa	_	Bohni et al. (2013)

[&]quot;-" Indicates plant part not mentioned in publication

Flavonols and flavonol glycosides

Till now, only eight flavonols (16–24, Fig. 2) were reported from the species of *Rhynchosia*. Except compound 23, all the flavonols and flavonol glycosides reported in the genus *Rhynchosia* are the derivatives of kaempferol and quercetin. An interesting note that Rhynchosin (23), is the only 5-deoxyflavnol is isolated from the leaves of *Rhynchosia beddomei* (Adinarayana et al. 1980c) up to now in the genus *Rhynchosia*.

Flavanones

Naringenin (25) and lupinifolin (26) were isolated from the leaves of *Rhynchosia beddomei* and the roots of *Rhynchosia precatoria*, respectively (Adinarayana et al. 1979; Coronado-Aceves et al. 2017), which are the only two flavanones so far reported in this genus (Fig. 3).



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Table 5 Naturally occurring simple phenolic compounds of the genus *Rhynchosia*

Compounds/trivial names	Plant source	Plant part	References	
Protocatechuic acid (62)	R. minima	Pericaps	Krishnamurty et al. (1975)	
Gallic acid (63)	R. volubilis	Seeds	Kinjo et al. (2001)	
	R. minima	Pericaps	Krishnamurty et al. (1975)	
Vanillic acid (64)	R. suaveolens	Leaves	Adinarayana et al. (1985)	
	R. cyanosperma	Leaves	Adinarayana et al. (1980a)	
Ethyl gallate (65)	R. minima	Pericaps	Krishnamurty et al. (1975)	
Methyl gallate (66)	R. volubilis	Seeds	Kinjo et al. (2001)	
Glucogallin (67)	R. volubilis	Seeds	Kinjo et al. (2001)	
1,6-Di- <i>O</i> -galloylglucose (68)	R. volubilis	Seeds	Kinjo et al. (2001)	
Trigalloylgallic acid (69)	R. volubilis	Seeds	Kinjo et al. (2001)	
2-Hydroxy-3,4-dimethoxybenzo- phenone (70)	R. suaveolens	Flowers	Rammohan et al. (2015)	
Hydroquinone Diacetate (71)	R. minima	Pericaps	Krishnamurty et al. (1975)	
D-Pinitol (72)	R. beddomei	Leaves	Adinarayana et al. (1979)	
	R. cyanosperma	Leaves	Adinarayana et al. (1980a)	
p-inositol (73)	R. beddomei	Leaves	Adinarayana et al. (1980c)	

Dihydroflavonols

Only four dihydroflavonols (27–30, Fig. 4) are reported in the genus *Rhynchosia* and all the listed compounds are *C*-prenylated derivatives. Also, the compounds 27–29 were reported as new dihyroflavols from the species *R. cyanosperma* (Adinarayana et al. 1980a; Rao and Gunasekar 1988) and *R. densiflora* (Rao and Gunasekar 1998).

Isoflavones and Isoflavanones

A total of nineteen isoflavones (31–49, Fig. 5) and three isoflavanones (50-53) to date were reported from the genus Rhynchosia. Most of the isoflavones isolated from the species R. edulis (Ogungbe et al. 2011) are substituted with either prenyl or dimethylpyrano group in both ring A and ring B, except in 46 and 47 in which prenylation in ring B is absent. Two isoflavone derivatives, rhynedulinal (46) and candelinal (47) are isolated from R. edulis which have an unusual formyl group at 3'-position. Furthermore, two new isoflavanones reported as precatorin A (50) and B (51) from the roots of *R. precatoria* (Coronado-Aceves et al. 2017) are structural isomers, as they differed only in the location of dimethylpyrene ring fusion in an ring A of isoflavanoid moiety. An unusual method was attempted using 1-butyl-3-methyl tetrafluoroborate ionic liquid for the isolation of isoflavones such as biochanin A (34), 4'-(1"-methoxy)-propoylgenistein (40) and cajanone (48) from the Rhynchosia volubilis (Ogungbe et al. 2011) and this report was very typical compared with conventional methods. This approach for the extraction and isolation of flavonoids using ionic liquids is environmental benign and green method. An unusual new isoflavanoid derivative,

Rhynchoviscin (53) reported from *R. viscosa* with novel skeleton basis of benzodihydrofuran moiety fused with benzodihydropyran ring, was established with 2D NMR spectral studies. The isolation of compound 53 is achieved through Zebrafish bioassay-guided microfractionation (Bohni et al. 2013) and this report is unique in this genus.

Flavan-3-ols

Catechin (**54**) (Rondo 2017), epicatechin (**55**) (Li and Xiang 2011), 7-*O*-galloylcatechin (**56**) (Kinjo et al. 2001) and proanthocyanidin (**57**) (Rangaswamy et al. 1974), are the four flavan-3-ols (Fig. 6) so far isolated from various *Rhynchosia* species.

Other phenolic compounds

These are non-flavonoid class simple polyphenolic compounds and listed below.

Xanthones

Besides the above revealed flavonoids, two xanthone-*C*-glycosides (Fig. 7), mangiferin (**58**) and isomangiferin (**59**) (Adinarayana and Chetty 1985; Rammohan et al. 2015) have been isolated from *R. suaveolens*. It is expected that the co-occurrence *C*-glycosylflavonoids and *C*-glycosylxanthones in the same source *R. suaveolens* is due to chemotaxonomic prominence.



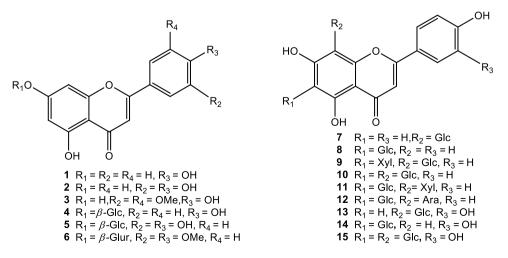
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 Table 6
 Scientific names and traditional uses of studied plants of the genus Rhynchosia

No.	Plant name	Distribution	Traditional uses	References
1.	R. beddomei Baker	India	Antioxidant, antidiabetic, anti-inflamma- tory, antimicrobial, analgesic, diuretic activity, rheumatic pains and remedial for wounds and boils	Bakshu and Raju (2001), Rammohan et al. 2019
2.	R. bracteata Benth	India	_	Gamble and Fischer (1935)
3.	R. cana DC.	India	-	Adinarayana et al. (1985); Kritikar and Basu (1975)
4.	R. capitata DC.	India, Pakistan	Antioxidant, constipation, gastric problems	Praveena et al. (2013)
5.	R. cyanosperma Benth.	India	_	Gamble and Fischer (1935)
6.	R. densiflora (Roth) DC.	India	_	Gamble and Fischer (1935)
7.	R. edulis	India	Antiproliferative activity	Ogungbe et al. (2011)
8.	R. heynei Wt. & Arn.	India	Antimicrobial, Arthritis and rheumatic pains, skin disorders	Bakshu and Raju (2009)
9.	R. jacobii	India	_	Gamble and Fischer (1935)
10.	R. minima (L.) DC.	Africa, India, Sri Lanka and USA	Antimicrobial, Antioxidant, Anthelmintic, Allelopathic activity	Abd ElGawad et al. (2018), Gweru et al. (2009)
11.	R. pseudo-cajan Cambess	Pakistan	Antioxidant	Riaz et al. (2011)
12.	R. precatoria (Humb. & Bonpl. Ex Willd.) DC.	North America	Antimycobacterial activity	Coronado-Aceves et al. (2017)
13.	R. pyramidalis (synm: pega palo)		Androgenic and aphrodisiac action	Farnsworth et al. (1967)
14.	R. rothii	India	-	Adinarayana et al. (1985), Kritikar and Basu 1975
15.	R. rufescens DC.	India	_	Gamble and Fischer (1935)
16.	R. scarabaeoides (L.) DC.	India	Antibacterial, Diarrhea, dysentery and skin infections	Challa et al. (2011)
17.	R. sericea Span.	India	_	Gamble and Fischer (1935)
18.	R. sublobata (Schumach.)	India	-	Adinarayana et al. (1985), Kritikar and Basu 1975
19.	R. suaveolens DC.	India	Antioxidant, antibacterial agent, abortifacients	Rammohan et al. (2015), Khan and Shoeb (1984), Kritikar and Basu (1975)
20.	R. villosa	Africa	Tyrosinase enzyme inhibitory activity	Rondo (2017)
21.	R. viscosa (Roth) DC.	Africa	Antinflammatory, Anti-angiogenic, Inflammatory skin disorders	Bohni et al. (2013)
22.	R. volubilis Lour.	Japan, Korea	Antiproliferative, Anti-aging agent	Kinjo et al. (2001), Rondo (2017)

[&]quot;-" Symbol indicates no significant traditional uses and activity studies are acknowledged

Fig. 1 Flavones and flavone glycosides (1–15) isolated from the genus *Rhynchosia*





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Fig. 2 Flavanol and flavonol glycosides (16–24) isolated from the genus *Rhynchosia*

Fig. 4 Dihydroflavonols (27–30) isolated from the genus *Rhynchosia*

MeO
$$R_2$$
 OR_3 OR_4 OR_3 OR_4 OR_4 OR_4 OR_5 OR_4 OR_5 OR_6 OR_7 OR_8 OR_8 OR_8 OR_8 OR_8 OR_9 OR_9

27 $R_1 = R_3 = H$, $R_2 = Pre$, $R_4 = Me$ **28** $R_1 = Pre$, $R_2 = R_3 = H$, $R_4 = Me$ **29** $R_1 = Pre$, $R_2 = R_4 = H$, $R_3 = Me$

23 R₁ = R₃ = R₄ = H, R₂ = OH, 24 R₁ = OH, R₂ = H, R₃ = Pre, R₄ = Me

Biphenyls

Two new biphenyls, 4-(3-methyl-but-2-enyl)-5-methoxy-(1,1'-biphenyl)-3-ol (**60**) and 2-carboxyl-4-(3-methyl-but-2-enyl)-5-methoxy-(1,1'-biphenyl)-3-ol (**61**) were isolated from the whole plant of *R. suaveolens* (Khan and Shoeb 1984, Fig. 7). The existence of biphenyls in plants was believed that the aldol-type condensation of shikimate derived β -triketo ester.

Simple polyphenols

Twelve simple polyphenolic compounds (62–73, Fig. 8) such as gallic acid (63), vanillic acid (64) and gallic acid derivatives (65–69) so far reported from the genus

Rhynchosia. Moreover, two polyhydric alcohols such as p-pinitol and p-inositol were also isolated from the leaves of *R. beddomei* (Adinarayana et al. 1979 and Adinarayana et al. 1980c). A unique trioxygenated simple benzophenone (70) was reported as a new chemical constituent from the flowers of *R. suaveolens* (Rammohan et al. 2015).

Sterols

 β -Sitosterol (74), Stigmasteryl galactoside (75), Lupeol (76) and ergosterol peroxide (77) are the four steroid compounds isolated from the whole plant of *R. minima* so far reported in *Rhynchosia* genus (Ahmed et al. 1992; Krishnamurty et al. 1975, Fig. 9).



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Fig. 5 Isoflavones (**31–50**) and Isoflavanones (**51–53**) isolated from the genus *Rhynchosia*



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Fig. 6 Flavan-3-ols (54–57) isolated from the genus Rhynchosia

Fig. 7 Xanthones (58–59) and biphenyls (60–61) isolated from the genus *Rhynchosia*

Pharmacology

Most of the reports are either isolation of chemical constituents or preliminary pharmacological screening of plant extracts of *Rhynchosia* species. There are very few reports are on the bioassay guided isolation of natural compounds and their biological activity studies. In the above section, under traditional uses, we have summarized the activity studies of plant extracts of *Rhynchosia* members and in the current section, the study focusing mostly on stated biological activities of isolated compounds of *Rhynchosia* members. Most of the reported activities are antibacterial, allelopathic activity, anti-angiogenic activity,

anti-inflammatory activity, antimycobacterial, antioxidant, antiproliferative, antityrosinase and cytotoxic activity.

Antioxidant studies

The reactive oxygen species termed as free radicals are formed in human tissue cells during metabolic process, which cause general oxidative damage leading to cellular damage, several types of cancers, inflammation, hypertension and age related diseases. Therefore, many researchers have focused on natural antioxidants because they serve as primary ingredients to balance the oxidative damage against free radicals. Flavonoids are the hugest group of secondary metabolite occuring in plants which show



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Fig. 8 Simple polyphenols (**62–73**) isolated from the genus *Rhynchosia*

wide range of therapeutic applications including antioxidant activities. The bioassay-guided isolation of flowers of Rhynchosia suaveloens resulted in four flavonoids, isovitexin (8), isoorientin (14), mangiferin (58) and 2-hydroxy-3,4-dimethoxybenzophenone (70), which were tested for 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity (Rammohan et al. 2015). Among them, compounds 58 and 14 showed prominent antioxidant activity with IC₅₀ 51.7 and 57.7 µg/mL, respectively, comparably with positive control ascorbic acid (IC₅₀ 34.2 µg/mL). In another study, the aerial parts of *Rhynchosia capitata* were studied through DPPH and nitric oxide antioxidant principles (Praveena et al. 2013) which resulted in five C-glycosylflavanoids namely, vitexin (7), isovitexin (8), vicenin 2 (10), orientin (13) and isoorientin (14). The C-glycosyl flavonoids were studied through density functional theory (DFT) to understand the molecular properties, factors and mechanism of radical scavenging ability. This study declares that the antioxidant activity of C-glycosyl flavonoids was exhibited by donating the

electrons instead of seizing the free radicals. As a result, this report concludes that the compound vitexin (7) acts as good radical scavenger based on quantum chemical computation and theoretical analysis.

Antimicrobial activity

Recently, four flavonoids namely, isovitexin (8), isoorientin (14), quercetin-7-O-methylether (21) and biochanin A (34) were isolated from the flowers of *Rhynchosia beddomei* (Rammohan et al. 2019). All the compounds were tested for their antimicrobial activity against gram-positive and gramnegative bacteria and fungi using disc diffusion method. Isoorientin (14) and quercetin-7-O-methylether (21) showed potent inhibition concentrations 20.1 and 15.8 nm; and 20.4 and 15.7 nm, respectively, against *Pseudomonas aeruginosa* and *Candida albicans*. Further, the in silico and Lipinski's rule analysis of the isolated compounds concluded that the compounds 14 and 21 act as prominent antimicrobial agents.



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Fig. 9 Sterols (**74–77**) isolated from the genus *Rhynchosia*

Antimycobacterial activity

The roots of Rhynchosia precatoria DC was tested for in vitro inhibitory and bactericidal activity against Mycobacterium tuberculosis and Mycobacterium smegmatis with redox indicator Alamar Blue (Coronado-Aceves et al. 2017). Further, isolation of dichloromethane fraction of roots of Rhynchosia precatoria resulted in six flavonoids, lupinifolin (26), lupinifolinol (30), cajanone (48), precatorin C (49), precatorin A (51) and precatorin B (52). All the isolated compounds, except compound 30, were screened for antimycobacterial activity. The compounds lupinifolin (26) and cajanone (48) exhibited highest activity against Mycobacterium tuberculosis (Mtb) with MIC 31.25 and 62.5 µg/mL, respectively. While, the compounds precatorin A (51) and cajanone (48) showed potent activity Mycobacterium smegmatis (Msm) with MIC 125 μg/mL (297.29 μM) and 125 μg/ mL (295.87 μM), respectively.

Anti-inflammatory and anti-angiogenic activities

Recent report on the Zebrafish integrated microfractionation of *Rhynchosia viscosa* resulted in five flavonoid compounds such as genistein (33), 3'-O-methylorobol (36), licoisoflavone A (39), sophoraisoflavone A (50) and a novel new compound, Rhynchoviscin (53) (Bohni et al. 2013). Further, the isolated compounds were tested for anti-inflammatory activity using LPS-enhanced leukocyte migration assay. Genistein (33) and sophoraisoflavone A (50) showed

significant inhibition of leukocyte migration with IC $_{50}$ 12.5 and 25 μ M, respectively. The other two compounds **36** and **39**, did not show any significant inhibition. Further, the angiogenic activity of extracts and compounds was also carried out using Zebrafish-based vascular outgrowth assay. The compounds, genistein (**33**) and licoisoflavone A (**39**) showed good potency of anti-angiogenic activity with IC $_{50}$ 24.2 and 16.7 μ M, respectively (Bohni et al. 2013).

Antityrosinase activity

The bioassay-guided isolation of roots of *Rhynchosia villosa* resulted in five compounds viz., genistein (33), 2'-hydroxygenistein (35), cajanin (38), catechin (54) and 7-O-galloylcatechin (56). Besides, the isolated compounds exhibited prominent tyrosinase activities (Bohni et al. 2013) such as genistein (31.45 μ M), catechin (36.86 μ M), cajanin (38.97 μ M), galloylcatechin (60.40 μ M) and 2'-hydroxygenistein (69.49 μ M). The compounds 33 and 38 exhibited the highest tyrosinase inhibitory activity, which may be used as depigmenting agent to treat hyperpigmentation (Bohni et al. 2013).

Cytotoxic activity

The phytochemical analysis of roots of *Rhynchosia precatoria* DC yielded six compounds such as lupinifolin (26), lupinifolinol (30), cajanone (48), precatorin C (50), precatorin A (51) and precatorin B (52). Further, the roots and



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isolated compounds (except lupinifolinol) of *Rhynchosia precatoria* were screened for cytotoxic activity against murine macrophages cells (RAW 264.7) using MTT reduction assay (Coronado-Aceves et al. 2017). The IC $_{50}$ values of the isolated compounds from 13.73 to 160.52 μ M indicate that these compounds exhibit less prominent activities and may not be appropriate to treat disease cancer but they may serve as lead molecules for the development of new synthetic molecules.

Antibacterial activity

The antibacterial activity of ethanol extract of whole plant of *Rhynchosia suaveloens* was studied against *Bacillus subtilis* and *Staphylococcus aureus* pathogens (Khan and Shoeb 1984). The active fraction further purification yields two biphenyls, 4-(3-methyl-but-2-enyl)-5-methoxy-(1,1'-biphenyl)-3-ol (**60**) and 2-carboxy-4-(3-methyl-but-2-enyl)-5-methoxy-(1,1'-biphenyl)-3-ol (**61**). These both biphenyls also showed activity against *Bacillus subtilis* and *Staphylococcus aureus* with minimum inhibitory concentration (MIC) 15.63 and 31.25 µg/mL, respectively.

Antiproliferative activity

The antiproliferative properties of seeds of *Rhynchosia vol*ubilis were tested against human gastric adenocarcinoma cells (MK-1), human uterus carcinoma (HeLa) and murine melanoma (B16F10) using MTT assay (Kinjo et al. 2001). The MeOH extract showed potent growth inhibition of MK-1 (GI₅₀: 25 μg/ml), HeLa (GI₅₀: 30 μg/ml) and B16F10 cells (GI₅₀: 8 µg/ml). Further, bioassay-guided isolation of MeOH extract results in six polyphenols, 7-O-galloylcatechin (56), gallic acid (63), methyl gallate (66), glucogallin (67), 1,6-di-O-galloylglucose (68) and trigalloylgallic acid (69) which showed good inhibition against B16F10 than HeLa and MK-1 cells. Among all the isolates, trigalloylgallic acid showed the highest activity with B16F10, HeLa and MK-1 cells (GI₅₀: 2.9, 9.3 and 10 μ g/ml) followed by the gallic acid (GI₅₀: 7.1, 22 and 19 μ g/ml). From the results and structure-antiproliferative activity studies of gallic acid derivatives, it is concluded that the number of galloyl groups and either presence/absence of three adjacent free hydroxyl groups or free carboxyl group for polyphenols are not the prominent reason for weak inhibition of cancer cells by other gallic acid derivatives (56, 66–68).

Allelopathic activity

The essential oil isolated from the roots of *Rhynchosia* minima *L*. consists of majorly volatile compounds such as α -eudesmol, trans-caryophyllene, caryophyllene oxide, 2-allyl-5-tert-butylhydroquinone and τ -cadinol (Abd

ElGawad et al. 2018). This essential oil showed significant inhibition of *D. aegyptium* and *R. dentatus* germination. Hence, it is recommended as green bio-herbicides such as allelochemicals.

Conclusions

Though approximately 300 Rhynchosia species are distributed all over the world, only 22 species, R. bracteata, R. beddomei, R. cana, R. capitate, R. cyanosperma, R. densiflora, R. edulis, R. heynei, R. jacobii, R. minima, R. precatoria, R. pyramidalis, R. pseudo-cajan, R. rothii, R. rufescens, R. sericea, R. suaveolens, R. sublobata, R. scarabaeoides, R. villosa, R. viscosa and R. volubilis, have been investigated so far. Phytochemical studies on the species of this genus led to the isolation of 77 compounds including flavonoids, isoflavonoids, flavan-3-ols, xanthones, biphenyls, simple polyphenols and sterols. Literature survey demonstrated that the genus Rhynchosia is a rich source of C-glycosylflavonoids and prenylated isoflavonoids. From the published reports on the phytochemical and pharmacological perspective, the genus Rhynchosia is a potent source of novel bioactive compounds such as rhynchoviscin, cajanone, genistein, mangiferin, vitexin, precatorin A. The authors of this review believe that insufficient work has been done on this genus and hence, the further work on *Rhynchosia* species may result in novel natural compounds with potent biological activities. Therefore, this review may give a bird view for the future experimental studies in the discovery of new drugs.

Author contribution statement The authors AR and DG were outline and collected the literature associated to the review. AR, GMR and BVB were performed manuscript writing and analysis the data. GVZ and DG contributed with their attentive discussions during manuscript preparation.

Compliance with ethical standards

Conflict of interest All the authors declare no conflict of interest.

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