ISSN 2462-2052 *Journal of Science and Mathematics Letters*
DOI: https://doi.org/10.37134/jsml.vol11.sp.18.2023 *Volume 11 (Special Issue), 163-174, 2023*

Review on Anthraquinones Isolated from Rubiaceae Family

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Received: 10 October 2023; **Accepted:** 29 November 2023; **Published:** 22 December 2023

ABSTRACT

A current economic trend is to highlight natural resources and many plant species are rich sources of anthraquinones. Anthraquinones are a diverse group of natural compounds extensively studied in various articles. Commonly used for dyes with 30% of it contributed to textile industry. Anthraquinone plays an important chromophore in cancer chemotherapy. They are widely distributed in Rubiaceae family and exhibit various biological activities. Malaysian Rubiaceae, especially plants from *Morinda, Rennellia, Psychotria,* and *Prismatomeris* genera, have been known to be rich in anthraquinone content, especially in the roots. The current review aims to provide a comprehensive update on the isolation of anthraquinones from Rubiaceae family in Malaysia. It also discussed the taxonomy, chemistry, and pharmacology studies of the genus. Through the years, 45 anthraquinones have been reported from various species of Rubiaceae demonstrating promising pharmacological activities. The information presented in this review can provide a scientific foundation for future research on the possible therapeutic applications of the species. Enhancing the links between plant biological effects and traditional uses with their chemical characterization.

Keywords: anthraquinone; Rubiaceae; *Morinda*; *Rennellia*; *Psychotria*; *Prismatomeris*

1. RUBIACEAE FAMILY

Rubiaceae, a family of coffee plants belonging to the Gentianales order in the eudicots. It comprises approximately 13,600 species grouped in 620 genera and 60 tribes. This makes it the fourth most species-rich and diverse family among flowering plants (Ly et al., 2020). Rubiaceae mainly grow as trees, shrubs, or, less often, as perennial to annual herbs, as in Rubieae (subfamily Rubioideae), which are found in temperate regions (Ahmad et al., 2010). They inhabit a wide range of habitats, from dry desert conditions to wet tropical rainforests. Their altitudinal range extends from low altitudes in tropical rainforests and mangrove coastline vegetation to alpine areas, exceeding 4000 m (Wilkstrom et al., 2015). Rubiaceae were divided into four subfamilies, namely, Cinchonoideae, Ixoroideae, Antirheoiseae, and Rubioideae, according to Mongrand et al. (2005). The Rubiaceae family can be recognized by certain characteristics. The flower's visual features include enlarged petals resembling sepals and secondary pollen presented on the style (Endress, 1996). The Rubiaceae family can also be differentiated by leaves with stipules between the base of each pair of leafstalks, an inferior ovary, and a flower with a small calyx tube enclosed and joined to the ovary (Handerson, 1974).

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Most members of this family produce a capsule or a berry with numerous seeds (Elpel, 2013). Figure 1 illustrates the characteristics of Rubiaceae family plants.

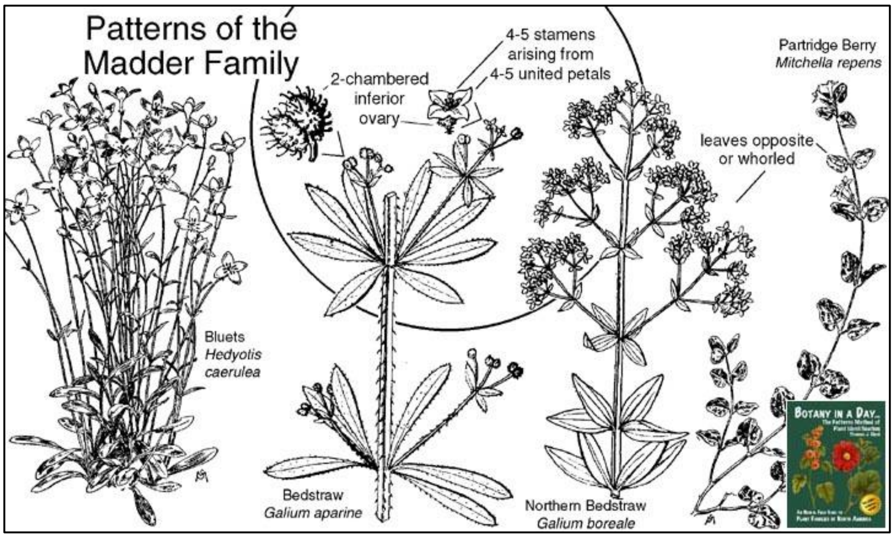


Figure 1. Rubiaceae family illustration (Elpel, 2013)

Most of the species in Rubiaceae have been widely used by various people, particularly for traditional practices as remedies. Rubiaceae is well known for its medicinal uses to treat malaria, diarrhea, digestive problems, skin diseases, fever, haemorrhage, urinary and respiratory infections, headache, inflammation of eyes and gums (Wong et al., 2015). Some Malaysian Rubiaceae, especially plants from *Morinda, Rennellia, Psychotria,* and *Prismatomeris* genera, have been known to be rich in anthraquinone content, especially in the roots. In traditional practice, some of these plants are consumed for vitality and various health problems. Anthraquinones possess three fused aromatic rings with two keto groups located on the central ring. They typically appear as yellow-orange crystals with a high melting point and exhibit good stability. One of the most well-known anthraquinone containing Rubiaceae plants commonly found in Malaysia is *Morinda citrifolia* or Noni. This plant has been used for prevention and treatment of various diseases and is widely known as a health, food, and supplement. Phytochemical analysis of Noni has long been known to contain a substantial amount of damnacanthal and nordamnacanthal. Interestingly, both anthraquinones showed a broad spectrum of bioactivities such as antimicrobial (Ali et al., 2000; Ayo et al., 2007; Garcia-Sosa et al., 2006), antifungal (Kanokmedhakul et al., 2005), antioxidant (Ahmad et al., 2005), anticancer (Ayo et al., 2007), antiviral, antimalaria (Oben et al., 2006; Osman et al., 2010), anti-inflammatory and antinociceptive properties (Kusada et al., 2011).

2. GENUS *Rennelia*

Rennellia is a small genus native to Southeast Asia, with eight recorded species (Suratman, 2008). The species include *R. amoena, R. borneensis, R. elliptica, R. elongata, R. microcephala, R. morindiformis, R. paniculata,* and *R. speciosa* (WFO, 2021). In the Malay Peninsula, five species are identified, among which *R. elliptica* and *R. elongata* have been recognized as distinct species and are not synonymous (Wong, 1984; Osman and Ismail, 2017). *Rennellia* is closely related to *Morinda*. The two genera belong to the tribe Morindeae and share similar characters. In the Malaysia Peninsula, *Rennellia* can be distinguished from *Morinda* by its lianas, flowering heads, stalked flower petals, and ovules (Wong, 1984).

The *Rennellia* genus is restricted to the humid region of West Malaysia, including Borneo, Sumatra, and Peninsular Malaysia, extending northwards to the western coast of Peninsular

Thailand and the Tenasserim District in Burma. Most of the species inhabit tropical evergreen forest, mostly in the lowland (Jalaluddin and Bruhl, 2008). Not all *Rennellia* species are known for their medicinal uses. In Peninsular Malaysia, five species of *Rennellia* have been used for various treatments by the locals. For instance, the water decoction of *R. elliptica* is used for the treatment of jaundice and body aches, serving as a postpartum tonic and aphrodisiac (Osman and Ismail, 2017). The *R. morindiformis* bark is used to treat wounds, while the decoction of *R. speciosa* bark or roots are used to treat dropsy and swollen abdomens in children. In the meantime, the decoction of the combination of leaves and root are used in a bath to treat rheumatism and as a protective medicine after childbirth (Ong, 2003).

Among all eight recorder species of *Rennellia*, only *R. elliptica* was the only species that fully studied in terms of its phytochemistry and biologically. It was reported that *R. elliptica* is rich in anthraquinones, with coumarins, phenolic compounds, and terpenoids identified as minor compounds.

3. GENUS *Morinda*

The *Morinda* genus is described as the largest genus within the pantropical tribe Morindeae of the Rubiaceae family (Hutchinson, 1973). The genus comprises about 102 species, including trees, shrubs, and vines, scattered widely in tropical, sub-tropical, and temperate regions (Ban et al., 2013). *Morinda* plants are characterized within the Rubiaceae family based on their growth habits, often appearing as small trees or shrubs, and less commonly as lianas. The leaves are petiolate or subsessile with a stalked head of flowers that fuse together at their ovaries. The fruits were produced in ellipsoidal shapes that fused together known as syncarp (Kesonbuaa and Chantaranothai, 2013). Taxonomic studies in Malaysia have identified the *Morinda* genus as comprising nine species in Peninsular Malaysia, including three species with reported phytochemistry (*M. citrofolia, M. elliptica*, and *M. umbellate*), and six recorded species (*M. corneri, M. lacunose, M. rigida, M. calciphila, M. scortechinii,* and *M. ridleyi*) (Wong, 1984; Abdullah et al., 1998).

Globally, various parts of *Morinda* are widely used in traditional medicine for treating both acute and chronic infections (Solomon et al., 2022). In Taiwan, the juice of *M. citrifolia* is used to cure diabetes and hypertension, while in tropical Pacific islands, the juice acts as an antidote for headache, high blood pressure, diarrhea and diabetes. In South-East Asian countries, including Brunei, Malaysia, Burma (Myanmar), Indonesia, Timor-Leste, Cambodia, Singapore, Thailand, Laos, Vietnam, and the Philippines, powdered leaves of *M. lucida* are macerated with fresh palm wine to treat high blood pressure, swollen spleen, diabetes, cough, and malaria (Ee et al., 2009). In Malaysia, *M. citrifolia* fruits are consumed raw to purify the blood, while the roots of *M. elliptica* are brewed to treat jaundice and gastric complaints. The heated leaves of *M. elliptica* are placed on the abdomen to address flatulence and fever, and crushed leaves are inserted into the nose to stop nose bleeding (Ong and Norzalina, 1999).

The most commonly used *Morinda* for its beneficial properties is *M. citrifolia*. This plant possessed anti-inflammatory, antidyslipidemic, and antioxidant properties from the isolation of β-carotene, kaempferol, quercetin, rutin, and ursolic acid. An experiment on the antiatherosclerotic properties of *M. citrifolia* leaf extract revealed lipid elimination and anti-inflammatory activity (Kah Hui et al., 2020). The antioxidant test was evaluated using the DPPH radical method, resulting in a dose-dependent response higher than that of ascorbic acid.

The antimicrobial showed inhibition against various bacteria. The results supported for new drug development from *M. citrifolia* for dietary conditions and chronic diseases that associate with oxidative stress (Sina et al., 2021). Another well-known *Morinda* species, *M. elliptica*, exhibited interesting biological activity in cytotoxicity and antioxidant assays. Compounds found in the species, damnacanthal and nordamnacanthal, developed active reactions against many cell lines and a high potential in developing anticancer agents (Ismail, 1999). A study on human pathogenic strains of *E. coli* and *S. typhi* showed effective results from *M. elliptica* leaf extract, indicating its potential in the development of new pharmaceutical products (Wakawa et al., 2022).

4. GENUS *Prismatomeris*

The genus *Prismatomeris*, a member of the Rubiaceae family, consists of twenty-nine species that are widely distributed in tropical and subtropical areas (Son, 2017). According to some researchers, this genus belongs to the subtribe Prismatomerinae within the tribe Morindeae. *Prismatomeris* is classified under the tribe Morindeae based on features such as a downward radicle, valvate aestivation of corolla lobes, and the appearance of raphides. However, it differs from Morindeae in the presence of free flowers, a bolicular ovary, and a peltate ovule attached to the upper half of the septum (Zhen, 1998). A research paper by Johnsson and Wong (1988) stated that *Prismatomeris* is closely related to the genera *Gentingia, Rennellia,* and *Motleyia* in terms of morphology, including branches, stipules, inflorescence, and calyx. Genus *Prismatomeris* resembles *Gentingia* based on ridged brachelts, free bilobed stipules, and the inner side of the calyx tube lacking colleters. Meanwhile, *Prismatomeris* was included to the genus *Motleyia* at the genus level and genus *Rennellia* at the species level due to important inflorescence characteristics (Zhen, 1988).

Prismatomeris species are known for their various traditional medicinal uses. In Malaysia, *P. tetrandra*, also known as 'tongkat haji samat' is popular among locals for treating wounds, bronchitis, and snake bites, while the water extracted from the roots of *P. glabra* is traditionally used to increase stamina, promote health, and provide an ergogenic effect (Abdullah et al., 2016). In Indochina, locals use a decoction of *P. fragrans* mixed with coconut and henna to treat bronchitis (Salleh et al., 2019). In folk Chinese medicine, the roots of *P. connata* are used to treat hepatitis and pneumoconiosis (Hao et al., 2011).

From a literature survey conducted, only six species of *Prismatomeris* have been reported globally. These species include *P. connata, P. fragrans, P. glabra, P. malayana, P. sessiliflora,* and *P. tetrandra.* The species include *P. connata*, *P. fragrans*, *P. glabra*, *P. malayana*, *P. sessiliflora*, and *P. tetrandra*. The phytochemistry of the genus includes anthraquinones, anthraquinone glycosides, iridoids, and triterpenoids, known for their therapeutic uses such as cytotoxic, antitumor, anticancer, antifungal, antimalarial, antiplasmodial, and antituberculosis activities (Salleh et al., 2019). *P. glabra* showed positive results for cytotoxicity and anti-inflammatory effects from isolated compounds, including 5,7,4'-hydroxyflavonoid, amentoflavone, and stigmasterol (Alkadi et al., 2021). The same species was tested for anticancer properties using leaf extract, which induced apoptosis and served as an alternative to anticancer treatment (Rohayu, 2020).

5. GENUS *Psychotria*

Psychotria Linnaeus is considered the largest genus in the Rubiaceae family, encompassing over 2000 species. It predominates among woody plants and is mainly distributed in tropical and subtropical regions (Somer and David, 2007; Marques et al., 2013). Upon reviewing its morphological features and geographical distribution, the genus has been classified into three subgenera: *Psychotria* (pantropical), *Tetramerae* (comprising some African and Madagascan species), and *Heteropsychotria* (housing neotropical species) (Steyermark, 1972). However, Nepokroeff et al. (1999) reorganized the genus based on molecular phylogenetic studies. Southeast Asia abounds with species of *Psychotria*, excluding New Guinea and the Philippines (Sohmer, 1988; Sohmer and David, 2017).

The genus *Psychotria* is characterized by sheathing and caducous interpetiolar stipules, along with conspicuous colleters found on the lower part of the adaxial surface of the stipules. The corolla tube is short and straight, with valvate petals in the bud. The drupaceous fruits come with two pyrenes, displaying hemispherical imagery in the seed cross-section, flattened furrow patterns on the seed surface, and a ribbed to rounded dorsal seed surface. Additionally, the seeds are coated with an ethanol-soluble pigment and exhibit ruminate endosperm (Robbrecht, 1989; Nepokroeff et al., 1999; Sohmer and Davis, 2007; Srisuk et al., 2020). In the Malay Peninsula, Ridley (1923) conducted a review of the genus, while Wong (1989) focused on tree and shrub species. Simultaneously, Turner and Kumar (2018) provided an in-depth analysis of climbing taxa within the *Psychotria* genus for Peninsular Malaysia and Singapore. Their compilation identified a total of 19 *Psychotria* species, encompassing climbing and/or hemi-epiphytic habits, as native to Peninsular Malaysia and Singapore (Turner and Kumar, 2018).

Psychotria species are widely recognized in folk medicine globally for treating various ailments. In the Amazon, 'caboclos' uses *P. colorata* fruits and flowers to alleviate earache and abdominal pain. In Malaysia, the leaves of *P. rostrata* are employed for treating constipation. Conversely, *P. viridis* is known for its hallucinogenic properties and is used as an ingredient in the beverage known as ayahuasca (De Carvalho et al., 2016). Various parts of *Psychotria* plants, including leaves, roots, and rhizomes, have been traditionally used for treating conditions such as cough, bronchitis, ulcers, stomachache, and infections of the female reproductive system (Calixto et al., 2016). *P. malayana*, locally known as 'meroyan sakat' in Malaysia, has been reported to contain multiple alkaloids, including hodgkinsine and other compounds. Studies have investigated the antibacterial activities of these compounds, including hodgkinsine, against LPM-547. Additionally, research has explored their analgesic activities with hodgkinsine, (+)-chimonanthine, and *meso*-chimonanthine, and calycanthine for anti-convulsant effects. Notably, leaf extracts exhibited the highest inhibition on alpha-glucosidase (Nipun et al., 2020). *P. sarmentosa* has demonstrated significant anti-inflammatory activity in a rat paw edema model induced by carrageenan, a model reflecting the acute phase of inflammation involving chemical mediators such as histamine, serotonin, and prostaglandins (Ratnayake et al., 2017). Simultaneously, the leaf extract also exhibited potent activity against mycobacterial strains, suggesting its potential use as a component in anti-TB drug development (Jayantha et al., 2022).

6. ATHRAQUINONES

Anthraquinones are commonly utilized as dyes, with 30% of their usage attributed to the textile industry. These compounds produce a diverse range of colors contingent upon the nature and position of auxochromic groups substituting hydrogen on the anthraquinone skeleton. Anthraquinones play a crucial role as chromophores, particularly in cancer chemotherapy. They can be found in various biological sources, including bacteria, marine sponges, fungi, lichens, and higher plants. Notably, plants from the Rubiaceae family, such as *Rubia, Galium,* and *Morinda,* are recognized for substantial amounts of anthraquinones, especially in their roots (Wijnsma and Verpoorte, 1986). In Malaysian Rubiaceae, anthraquinones are predominantly categorized as Rubia type, characterized by substitution only on ring C, while the remaining substitutions occur on rings A and C (Ismail et al., 2012).

For clarity, the structure and names of ring-C substituted anthraquinones are summarized in Table 1, and ring A and C substituted anthraquinones are detailed in Table 2. Besides Rubia anthraquinones, two pyranoanthraquinones, namely, rennellianone A **44** and rennellianone B **45** were reported from the root of *R. elliptica* (Osman et al., 2016).

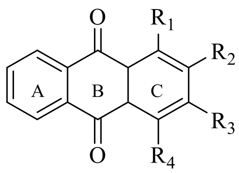
Table 1. Ring C anthraquinone and its distribution

No.	Compounds	Origin	References
1	1,2-Dihydroxyanthraquinone	*M. citrifolia*	Hemwimon et al., 2007
2	1,2,3-Trimethoxyanthraquinone	*M. pandurifolia*	Ruksilp et al., 2011
3	1,3-Dihydroxy-2-methylanthraquinone	*M. elliptica* *M. lucida* *M. officinalis* *R. elliptica* *P. malayana*	Bao et al., 2011 Chiang et al., 2007 Osman & Ismail., 2018 Tuntiwachwuttikul et al., 2008
4	1,3-Dihydroxy-2 methoxy methylanthraquinone	*M. elliptica,* *M. pandurifolia* *R. elliptica*	Chiang et al., 2007 Osman and Ismail, 2018 Ruksilp et al., 2011
5	1,3-Dihydroxy-2-(methoxymethyl) anthraquinone 3-O-β-primerveroside	*P. connata*	Hao et al., 2011
6	1,3-Dimethoxy-2-hydroxyanthraquinone	*M. citrifolia*	Kamiya et al., 2005
7	1-Hydroxy-2-primeverosyloxymethyl-anthraquinone-3-olate	*M. citrifolia*	Kamiya et al., 2009
8	1-Hydroxy-2-methylanthraquinone	*M. elliptica* *M. lucida* *P. malayana*	Abdullah et al., 1998; Tuntiwachwuttikul et al., 2008
9	1-Methoxy-2-hydroxyanthraquinone	*M. citrifolia* *M. elliptica* *M. lucida* *M. officinalis* *P. malayana*	Ahmad et al., 2005 Chiang et al., 2007 Tuntiwachwuttikul et al., 2008
10	1-Methoxy-2-methylanthraquinone	*M. lucida* *M. pandurifolia*	Ruksilp et al., 2011 Tuntiwachwuttikul et al., 2008
11	2-Formyl-1-hydroxyanthraquinone	*M. elliptica*	Abdullah et al., 1998
12	2-Formyl-3-hydroxy-9,10-anthraquinone	*R. elliptica*	Osman and Ismail, 2018
13	2-Methylanthraquinone	*M. lucida* *P. malayana*	Rath et al., 1995 Tuntiwachwuttikul et al., 2008
14	3-Hydroxy-1-methoxy-2-methoxymethyl anthraquinone	*M. pandurifolia*	Ruksilp et al., 2011
15	3-Hydroxy-2-hydroxymethylanthraquinone	*R. elliptica*	Osman and Ismail, 2018
16	3-Hydroxy-2-methylanthraquinone	*R. elliptica*	Osman and Ismail, 2018
17	Anthragallol 2-methyl ether	*M. citrifolia*	Kamiya et al., 2005
18	Anthraquinone-2-aldehyde	*M. lucida*	Rath et al., 1995
19	Damnacanthal	*M. elliptica* *M. lucida* *M. pandurifolia* *M. royoc* *R. elliptica* *P. malayana*	Chiang et al., 2007 Herna et al., 2008 Osman and Ismail, 2018 Rath et al., 1995 Tuntiwachwuttikul et al., 2008 Ruksilp et al., 2011
20	Damnacanthol-11-O-β-primeveroside	*M. citrifolia*	Kamiya et al., 2009
21	Damnacanthol-3-O-β-primeveroside	*P. connata*	Hao et al., 2011

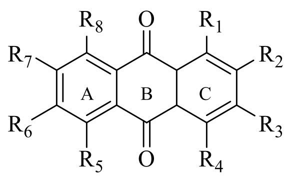
22	Digiferruginol-1-methylether-11-O-β-gentiobioside	*M. citrifolia*	Kamiya et al., 2009
23	Digiferruginol-11-O-β-primeveroside	*M. citrifolia*	Kamiya et al., 2009
24	Digiferruginol ω-gentiobiose	*P. connata*	Hao et al., 2011
25	Lucidin	*M. pandurifolia* *M. royoc*	Herna et al., 2008 Ruksilp et al., 2011
26	Lucidin-3-O-β-primeverosideo	*P. connata*	Hao et al., 2011
27	1-Methoxy-2-primeverosyloxymethyl-anthraquinone-3-olate	*M. citrifolia*	Kamiya et al., 2009
28	Nordamnacanthal	*M. elliptica* *M. lucida* *M. pandurifolia* *M. royoc* *R. elliptica* *P. malayana*	Chiang et al., 2007 Osman and Ismail, 2018 Rath et al., 1995 Ruksilp et al., 2011
29	Rubiadin-1-methyl ether	*M. elliptica* *M. lucida* *M. royoc* *R. elliptica* *P. malayana*	Chiang et al., 2007 Herna et al., 2008 Osman and Ismail, 2018 Rath et al., 1995 Tuntiwachwuttikul et al., 2008
30	1-O-Methylrubiadin 3-O-β-primeveroside	*P. connata*	Hao et al., 2011
31	Rubiadin-3-O-β-primeveroside	*P. connata*	Hao et al., 2011

Table 2. Ring A and C anthraquinone and its distribution

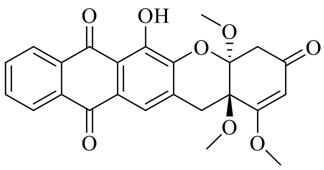
No.	Compounds	Origin	References
32	1-Hydroxy-2-methoxy-6- methyl-9,10-anthraquinone	*R. elliptica*	Osman et al., 2010
33	1,2-Dimethoxy-6-methyl-9,10-anthraquinone	*R. elliptica*	Osman et al., 2010
34	1,3-Dihydroxy-5,6-dimethoxy-2-methyl-9,10-anthraquinone	*P. malayana*	Tuntiwachwuttikul et al., 2008
35	1,3-Dihydroxy-5,6-dimethoxy-2-methoxymethyl-9,10-anthraquinone	*P. malayana*	Tuntiwachwuttikul et al., 2008
36	1,3,8-Trihydroxy-2-methoxyanthraquinone	*M. officinalis*	Bao et al., 2011
37	1,6-Dihydroxy-2- methylanthraquinone	*M. elliptica,* *M. lucida* *M. pandurifolia* *M. royoc*	Abdullah et al., 1998 Herna et al., 2008 Ruksilp et al., 2011
38	3-Hydroxy-2-methoxy-6-methyl-9,10-anthraquinone	*R.elliptica*	Osman et al., 2010
39	5,15-Dimethylmorindol	*M. citrifolia*	Kamiya et al., 2009
40	6-Hydroxy-anthragallol-1,3-dimethyl ether	*M. citrifolia*	Kamiya et al., 2009
41	Flavopurpurin	*M. pandurifolia*	Ruksilp et al., 2011
42	Morindone	*M. elliptica*	Abdullah et al., 1998
43	Morindone-5-methyl ether	*M. elliptica*	Abdullah et al., 1998



	R_1	**R_2**	**R_3**	**R_4**
1	OH	OH	H	H
2	OH	OH	OH	H
3	OH	CH_3	OH	H
4	OH	CH_2OCH_3	OH	H
5	OH	CH_2OCH_3	O-primeverose	H
6	OCH_3	OH	OCH_3	H
7	OH	CH_2O-primeverose	O^-	H
8	OH	CH_3	H	H
9	OCH_3	OH	H	H
10	OCH_3	CH_3	H	H
11	OH	CHO	H	H
12	H	CHO	OH	H
13	H	CH_3	H	H
14	OCH_3	CH_2OCH_3	OH	H
15	H	CH_2OH	OH	H
16	H	CH_3	OH	H
17	OH	OCH_3	OH	H
18	OCH_3	CHO	OH	H
19	OCH_3	CH_2O-primeverose	OH	H
20	OCH_3	CH_2OH	O-primeverose	H
21	OCH_3	CH_2O-gentibiose	H	H
22	OCH_3	CH_2O-primeverose	H	H
23	OCH_3	CH_2O-gentibiose	CH_3	H
24	OH	CH_2OH	OH	H
25	OH	CH_2OH	O-glucose	H
26	OH	CH_2OH	O-primeverose	H
27	OCH_3	CH_2O-primeverose	O^-	H
28	OH	CHO	OH	H
29	OCH_3	CH_3	OH	H
30	OCH_3	CH_2CH_3	O-primeverose	H
31	OH	CH_2CH_3	O-primeverose	H



	R_1	**R_2**	**R_3**	**R_4**	**R_5**	**R_6**	**R_7**	**R_8**
32	OH	OCH_3	H	H	H	CH_3	H	H
33	OCH_3	OCH_3	H	H	H	CH_3	H	H
34	OH	CH_3	OH	H	OCH_3	OCH_3	H	H
35	OH	CH_2OCH_3	OH	H	OCH_3	OCH_3	H	H
36	OH	OCH_3	OH	H	H	H	H	OH
37	OH	CH_3	H	H	H	OH	H	H
38	H	OCH_3	OH	H	H	CH_3	H	H
39	OH	CH_2OCH_3	H	H	OCH_3	OH	H	H
40	OCH_3	OH	OCH_3	H	H	OH	H	H
41	OH	OH	H	H	H	OH	H	H
42	OH	OH	H	H	OH	CH_3	H	H
43	OH	CH_3	H	H	OCH_3	OH	H	H



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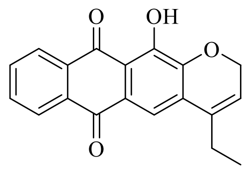

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7. CONCLUSION

In conclusion, this review comprehensively surveys various genera in the Rubiaceae family, emphasizing their abundance in anthraquinones. The research underscores the potential of these plants as promising candidates for developing new drugs. The diverse range of bioactive anthraquinones exhibits various biological activities, particularly in chemotherapeutic agents for early cancer management. The study highlights the need for further exploration, considering that most species within this family are yet to be thoroughly investigated for their phytochemical composition and pharmacological activities. Notably, the genera *Psychotria* and *Morinda*, categorized as the largest genera in the Rubiaceae family, represent a vast reservoir of untapped potential for discovering novel bioactive compounds with potential therapeutic applications. Future research should aim to fully characterize the compounds in the Rubiaceae genus, elucidate their mechanisms of action, and explore their potential applications in drug development. Despite current limitations, the exciting prospect of abundant anthraquinone-rich plants holds promise for the development of novel therapies and inventions to address various health conditions, including the creation of new anthraquinone-based anticancer agents. These innovations may translate into safer and more effective chemotherapeutics.

Declaration of Interest

The authors hereby declare that there is no conflict of interest.

Acknowledgment

The first author was supported by *Geran Insentif Penyeliaan* (600-RMC/GIP 5/3 (127/2021) from Universiti Teknologi MARA, Malaysia.

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