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GENUS *MALLOTUS* (EUPHORBIACEAE): A REVIEW ON TRADITIONAL MEDICINAL USE, PHYTOCHEMISTRY, AND BIOLOGICAL ACTIVITIES

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Abstract. *Ethnopharmacological relevance*: The genus *Mallotus* (Euphorbiaceae family) includes 124 accepted names and is distributed in tropical and subtropical regions. Some *Mallotus* species are used in traditional medicines for the treatment of chronic hepatitis, enteritis, mental disorders, cholelithiasis, anti-cancer, gastric, and duodenal ulcers.

Aim of the study: According to the Scifinder database, this is the first review study that focuses on the phytochemistry and pharmacology of *Mallotus* genus (17 *Mallotus* species) to understand the link between the traditional medicinal uses, phytochemistry, and bioactivities. Thus, they provide a scientific foundation for further research in the phytochemical and pharmacological activities of their species.

Materials and methods: Information about the *Mallotus* genus was collected using various databases, such as Web of Science, SciFinder, PubMed, Sci-hub, Google Scholar, Wiley, Elsevier, ACS publications, and SpringerLink between 1978 and 2021. Plant names were validated by "The Plant List" (www.theplantlist.org).

Results: Up to now, total 325 compounds were reported from *Mallotus* species, including phloroglucinols, steroids, coumarins, benzopyrans, flavonoids, chalcones, gallic acid and bergenin derivatives. The extracts and phytochemical constituents of the *Mallotus* genus are a rich source of biological activities, including anti-cancer, anti-inflammatory, immunoregulatory, antioxidant, antibacterial, antifungal, anti-virus, and other activities.

Conclusions: The review indicated that the *Mallotus* genus is a promising source of biological compounds, special anti-cancer chromanes. The results of this review confirm the great potential of *Mallotus* species. Thus, it will be helpful for further research in the phytochemistry and pharmacology of the *Mallotus* genus.

Keywords: Mallotus, Euphorbiaceae, anti-cancer, anti-inflammatory, phloroglucinol, benzopyran.

Classification numbers: 1.1.1, 1.1.6

1. INTRODUCTION

Nowadays, researchers from the worldwide are interested in new drugs from plant sources due to their low cost and may offer safer medicine than synthetic drugs, which are more costly and have many adverse side effects. Thus, the interest is increasing in the structure-activity relationships of secondary metabolites with potential pharmacological activity.

Mallotus (Euphorbiaceae) is a large genus of trees and shrubs distributed throughout tropical and subtropical regions. Some species of the genus have been used in traditional medicine. Phytochemical studies of the genus have indicated the presence of a large number of phloroglucinols, coumarins, benzopyrans, along with some chalcones, steroids, gallic acid and bergenin derivatives. Furthermore, there are many biological activities of the plants in the genus, such as cytotoxic, anti-inflammatory, immunoregulatory, antioxidant, antibacterial, antifungal, and anti-virus. Herein, we will summarize the literature data concerning the phytochemistry and the biological activities of the *Mallotus* genus with the aim of providing a comprehensive survey on the traditional medicinal uses of the *Mallotus* genus in line with their structural and pharmacological data.

2. MATERIAL AND METHODS

The review was carried out with the help of databases of scientific publications, such as Web of Science, SciFinder, PubMed, Sci-hub, Google Scholar, Wiley, Elsevier, ACS publications, and SpringerLink by using keywords "*Mallotus"*. The cited articles were collected from 1978 to 2021. The Plant List (www.theplantlist.org) was used for confirming species names.

3. RESULTS AND DISCUSSION

3.1. Ethnopharmacology properties

Many *Mallotus* species have been used as medicinal plants in traditional medicine in Viet Nam and Southeast Asian countries to treat various ailments ranging from minor infections such as gastrointestinal disorders to dysentery, hepatic and cutaneous diseases, fever, and malaria, and a series of other indications. The parts of the *Mallotus* species that have been studied include barks, stem barks, heartwoods, seeds, leaves, roots, aerial parts, and whole plants. The barks of *M. barbatus* have been used in Vietnamese oriental medicine to treat stomach ache and duodenal ulcer [1, 2]. In India, the decoctions of *M. peltatus* leaves and stem barks are widely used to treat stomachache [3], intestinal ailments, and skin infections [4]. The ethanol extract of leaves is reported to be helpful in the treatment of trematodic infection [5]. *M. repandus* has been used in an herbal formula to relieve muscle pain in Thailand [6]. In Taiwan, the leaves of *M. repandus* have been used as anti-inflammatory drugs [7]. *M. apelta* has been used in traditional medicine for the treatment of chronic hepatitis. *M. furetianus*, a kind of tropical plant, is a herb indigenous to Hainan Island of China. Its leaves have been used as a popular aromatic beverage for indigestion. It is also used as a folk medicine for the treatment of cholecystitis disease [8]. *M.*

paxii has played an important role in folk medicine for hundreds of years. Its stems have been used for the treatment of viral infections [9]. The leaves of *M. japonicus* are used as food wrap while the bark is used to treat various diseases such as gastric ulcer, duodenal ulcer, and gastric hyperacidity [10]. *M.roxburghianus* has long been traditionally used by the tribal people of Mizoram as a dietary supplement and therapeutic agent for diabetes, ulcer, hypertension, and liver disorders. The leaves of *M.roxburghianus* are eaten as vegetable (used as greens for salad or cooked with meat or fish) or consumed as a decoction (50 mL thrice daily) for six months to 1 year based on the clinical complications [11].

3.2. Phytochemistry

To date, chemical constituents of the *Mallotus* genus have been widely studied but with more focus on the following seventeen species: *M. apelta, M. oppositifolius, M. furetianus, M. paxii, M. philippensis, M. resinosus, M. conspurcatus, M. mollissimus, M. barbatus, M. nanus, M. japonicus, M. metcalfianus, M. pallidus, M. roxburghianus, M. anisopodus, and M. macrostachyus*. From this genus, 325 compounds have been reported, belonging to benzopyrans and coumarins (**1**–**51**), flavonoids and chalcones (**52**–**104**), phloroglucinols (**105**–**140**), gallic acidand bergenin derivatives (**141**–**169**), tannins (**170**–**193**), lignans (**194**–**199**), other phenolics (**200**–**219**), triterpenoids (**220**–**255**), diterpenoids and terpenoids (**256**–**285**), megastigmanes (**286**–**294**), other terpenoids (**295**–**297**), steroids (**298**–**311**), and other compounds (**312**–**325**) (Figures 1-15, Tables 1-15). The parts of *Mallotus* genus have been studied, including leaves, branches, stem barks, roots, and whole plants The leaves and barks have been found to contain triterpenoids and phenolics. The fruits yielded chalcones and phloroglucinols, while the other parts are characterized by the appearance of flavonoids, steroids, and terpenoids, etc.

3.2.1. Benzopyrans and coumarins

There are 40 benzopyrans and 11 coumarins reported from the *Mallotus* genus. Benzopyrans (**1**-**40**) have been reported from *M. apelta* (leaves), *M. oppositifolius* (leaves), *M. furetianus* (leaves), *M. paxii* (stems), and *M. philippensis* (fruits) (Table 1). Coumarins (**41**-**51**) have been reported from *M. apelta* (all parts: leaves, branches, roots, barks, and fruits), *M. repandus* (stems), *M. oppositifolius* (leaves), *M. resinosus* (leaves and fruits), and *M. japonicus* (leaves) (Table 2).

Table 1. Benzopyrans from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
1	5-hydroxy-2,8,6-trimethyl-8-(3,7- dimethyl-2,6-octadienyl)-2H-1-benzopyran-4,7(3H,8H)-dione	*M. apelta*	leaves	[12]
2	6*β*-hydroxy-2*α*,6*α*,8*β*-trimethyl-8-(3,7-dimethyl-2,6-octadienyl)-2H-1-benzopyran-4,5,7(3H,6H,8H)-trione	*M. apelta*	leaves	[13]
3	6*β*-hydorxy-2*α*,8*β*-dimethyl-6-(3-methyl-2-butenyl)-8-(3,7-dimethyl-2, 6-octadienyl)-2H-1-benzopyran-4,5,7(3H,6H,8H)-trione	*M. apelta*	leaves	[13]
4	5-hydroxy-2,8-dimethyl-6-(3-melhyl-2-butenyl)-8-(3,7-dimethyl-2.6-octadienyl)-2H-1-benzopyran-4,7(3H, 8H)-dione	*M. apelta*	leaves	[12]
5	2,3-dihydro-5,7-dihydroxy-2,6-dimethyl-8-(3-methyl-2- butenyl)-4H-1-benzopyran-4-one	*M. apelta*	leaves	[12]
6	2,3-dihydro-5,7-dihydroxy-2,8-dimethyl- 6-(3-methyl-2-butenyl)-4H-1-benzopyran-4-one	*M. apelta*	leaves	[12]
7	6-[l′-oxo-3′(*R*)-hydroxy-butyl]-5,7-dimethoxy-2,2-dimethyl-2H-l-	*M. apelta*	leaves	[14]

	benzopyran			
8	6-[l′-oxo-3′(*R*)-methoxy-butyl]-5,7-dimethoxy-2,2-dimethyl-2H-l-benzopyran	*M. apelta*	leaves	[14]
9	4-hydroxy-2,6-dimethyl-6-(3,7-dimethyl-2,6-octadienyl)- 8-(3-methyl-2-butenyl)-2H-1-benzopyran-5,7(3H,6H)-dione	*M. apelta*	leaves	[12]
10	4-hydroxy-2,6,8-trimethyl-6-(3,7-dimethyl-2,6-octadienyl)-2H-1-benzopyran-5,7(3H,6H)-dione	*M. apelta*	leaves	[12]
11	2,3-dihydro-5,7-dihydroxy-2,6,8-trimethyl-4H-1-benzopyran-4-one.	*M. apelta*	leaves	[12]
12	acronyculatin U	*M. oppositifolius*	leaves	[15]
13	3,3,8,9,10-pentahydroxydibenzo[b,d]pyran-6-one	*M. furetianus*	leaves	[8, 16]
14	paxiione D	*M. paxii*	stems	[9]
15	(+)-α-tocopherol	*M. oppositifolius* *M. apelta*	leaves leaves	[17] [18]
16	paxiione A	*M. paxii*	stems	[9]
17	paxiione B	*M. paxii*	stems	[9]
18	lichenxanthone	*M. oppositifolius*	leaves	[15]
19	mallopenin B	*M. philippensis*	fruits	[19]

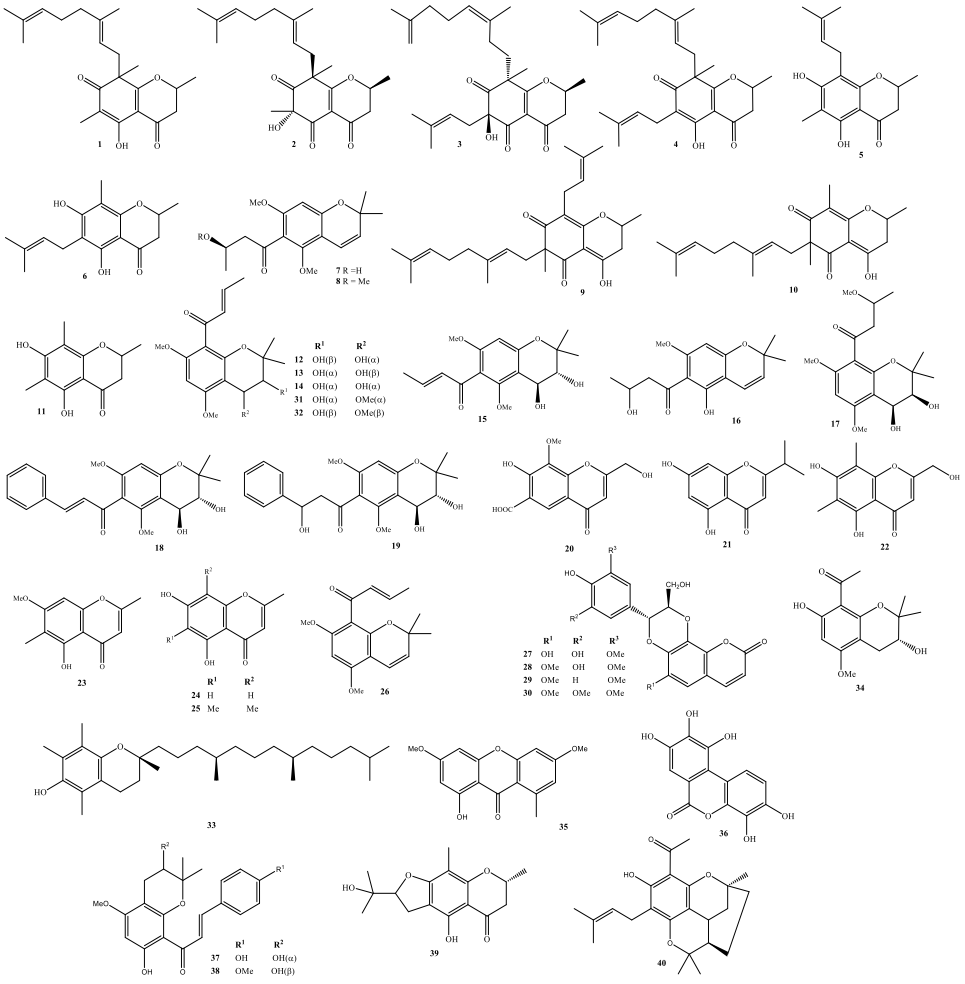


Figure 1. Chemical structures of benzopyrans from *Mallotus* genus (**1**-**40**).

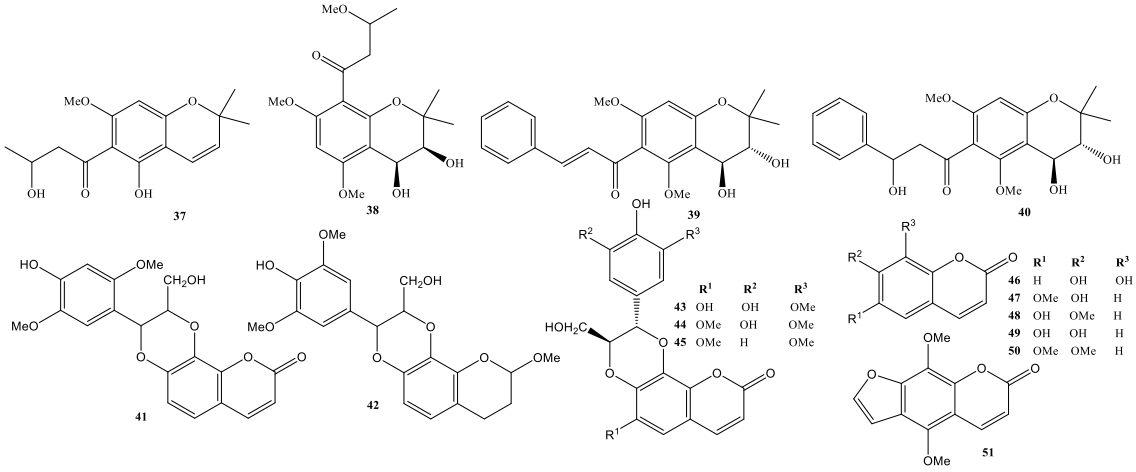


Figure 2. Chemical structures of coumarins from *Mallotus* genus (**41**-**51**).

Table 2. Coumarins from *Mallotus genus.*

No.	Compound names	Sources	Part	Ref.
20	7-hydroxy-2-hydroxymethyl-8-methoxy-4-*O*-4H-chromene-6-carboxylic acid	*M. apelta*	branches	[20]
21	5,7-dihydroxy-2- propylchromone	*M. apelta*	branches	[20]
22	melachromone	*M. apelta*	branches	[20]
23	eugenitol	*M. apelta*	branches	[20]
24	noreugenin	*M. apelta*	branches	[20]
25	5,7-dihydroxy-2,6,8-trimethylchromone	*M. apelta*	branches	[20]
26	malloapelta B	*M. apelta*	leaves	[18]
27	malloapelin A	*M. apelta*	roots	[21]
28	cleomiscosin A	*M. apelta*	roots	[21, 22]
29	cleomiscosin B	*M. apelta*	roots	[21]
30	aquillochin	*M. apelta*	roots	[22]
31	(+)-malloapelta C	*M. apelta*	leaves	[23]
32	(-)-malloapelta C	*M. apelta*	leaves	[23]
33	(+)-malloapelta D	*M. apelta*	leaves	[23]
34	(-)-malloapelta D	*M. apelta*	leaves	[23]
35	malloapelta E	*M. apelta*	leaves	[23]
36	malloapelta G	*M. apelta*	leaves	[23]
37	malloapelta H	*M. apelta*	leaves	[23]
38	malloapelta J	*M. apelta*	leaves	[23]
39	malloapelta I	*M. apelta*	leaves	[24]
40	malloapelta II	*M. apelta*	leaves	[24]
41	repandusin	*M. repandus*	stems	[25]
42	repanduthylin	*M. repandus*	stems	[25]
43	malloapelin B	*M. apelta*	roots	[21]
44	malloapelin C	*M. apelta*	roots	[21]

45	5′-demethylaquillochin	*M. apelta*	roots	[21]
46	daphnetin	*M. apelta*	branches	[20, 22]
47	scopoletin	*M. oppositifolius* *M. apelta* *M. resinosus* *M. japonicus*	leaves branches fruits leaves	[15] [20] [26] [27]
48	isoscopoletin	*M. resinosus*	roots	[28]
49	esculetin	*M. resinosus*	roots	[28]
50	dimethoxycoumarin	*M. resinosus*	roots	[28]
51	isopimpinellin	*M. apelta*	leaves	[18]

3.2.2. Flavonoids and chalcones

There are 34 flavonoids and 19 chalcones reported from the *Mallotus* genus. Flavonoids (**52-85**) have been reported from *M. apelta* (leaves and branches), *M. barbatus* (leaves), *M. conspurcatus* (roots), *M. metcalfianus* (leaves and stems), and *M. japonicus* (leaves) (Table 3). Chalcones (**86-104**) have been reported from *M. philippinensis* (fruits) and *M. philippensis* (fruits) (Table 4).

Table 3. Flavonoids from *Mallotus genus.*

No.	**Compound names**	**Sources**	**Part**	**Ref.**
52	6-prenylnaringenin	*M. conspurcatus*	roots	[29]
53	7-*O*-methyl-6-prenylnaringenin	*M. conspurcatus*	roots	[29]
54	4′-*O*-methyl-6-prenylnaringenin	*M. conspurcatus*	roots	[29]
55	(2*S*)-5,4′-dihydroxy-7-methoxy-6-(3″,3″-dimethylallyl)flavanone	*M. mollissimus*	leaves	[30]
56	5,7-dihydroxy-8-methyl-6-prenylflavanone	*M. philippensis*	fruits	[31]
57	5,7-dihydroxy-8-methyl-6-prenylfIavanone	*M. philippensis*	fruits	[32]
58	malloapeltic acid	*M. apelta*	leaves	[33]
59	(2″*S*/2″*R*)-(2*S*)-5,7-dihydroxy-4’ -methoxy-6-(2″-hydroxy-3″-methylbut-3″-enyl)flavanone	*M. mollissimus*	leaves	[30]
60	gallocatechin	*M. conspurcatus*	roots	[34]
61	catechin	*M. conspurcatus*	roots	[34]
62	8-prenylnaringenin	*M. mollissimus* *M. conspurcatus*	leaves roots	[30] [29]
63	7-*O*-methyl-8-prenylnaringenin	*M. conspurcatus*	roots	[29]
64	(2*S*)-5,7- dihydroxy-4′-methoxy-8-(3″,3″-dimethylallyl)flavanone	*M. mollissimus*	leaves	[30]
65	apigenin-7-*O*-*β*-D-glucopyranoside	*M. mollissimus*	leaves	[30]
66	isovitexin	*M. philippensis*	leaves	[35]
67	mallopenin D	*M. philippensis*	fruits	[19]
68	mallopenin E	*M. philippensis*	fruits	[19]
69	apigenin	*M. apelta* *M. mollissimus*	branches leaves	[20] [30]
70	kaempferol	*M. apelta* *M. barbatus*	branches leaves	[20] [36]

71	quercitrin	*M. japonicus* *M. barbatus* *M. nanus* *M. metcalfianus*	leavesle aves leavesle aves	[15] [37] [38] [39]
72	quercetin	*M. japonicus* *M. barbatus*	leaves	[15] [15, 36]
73	kaempferol-3-*O*-*β*-D-glucopyranoside	*M. barbatus*	leaves	[36]
74	kaempferin	*M. barbatus* *M. nanus* *M. metcalfianus*	leavesle aves leaves	[37] [38] [39]
75	juglanin	*M. nanus*	leaves	[38]
76	myricitrin	*M. nanus*	leaves	[38]
77	rhoifolin	*M. nanus*	leaves	[38]
78	quercetin-3-*O*-*β*-neohesperidoside	*M. metcalfianus*	stems	[39]
79	isoquercitrin	*M. japonicus*	leaves	[15]
80	rutin	*M. japonicus*	leaves	[15]
81	kaempferol-3-rutinoside	*M. conspurcatus*	leaves	[15]
82	6,6-dimethylpyrano(2″,3″:7,6)-5-hydroxy-8-methylflavanone	*M. philippensis*	fruits	[32]
83	astilbin	*M. metcalfianus*	stems	[39]
84	ampelopsin	*M. philippensis*	leaves	[35]
85	paxiione C	*M. paxii*	stems	[9]

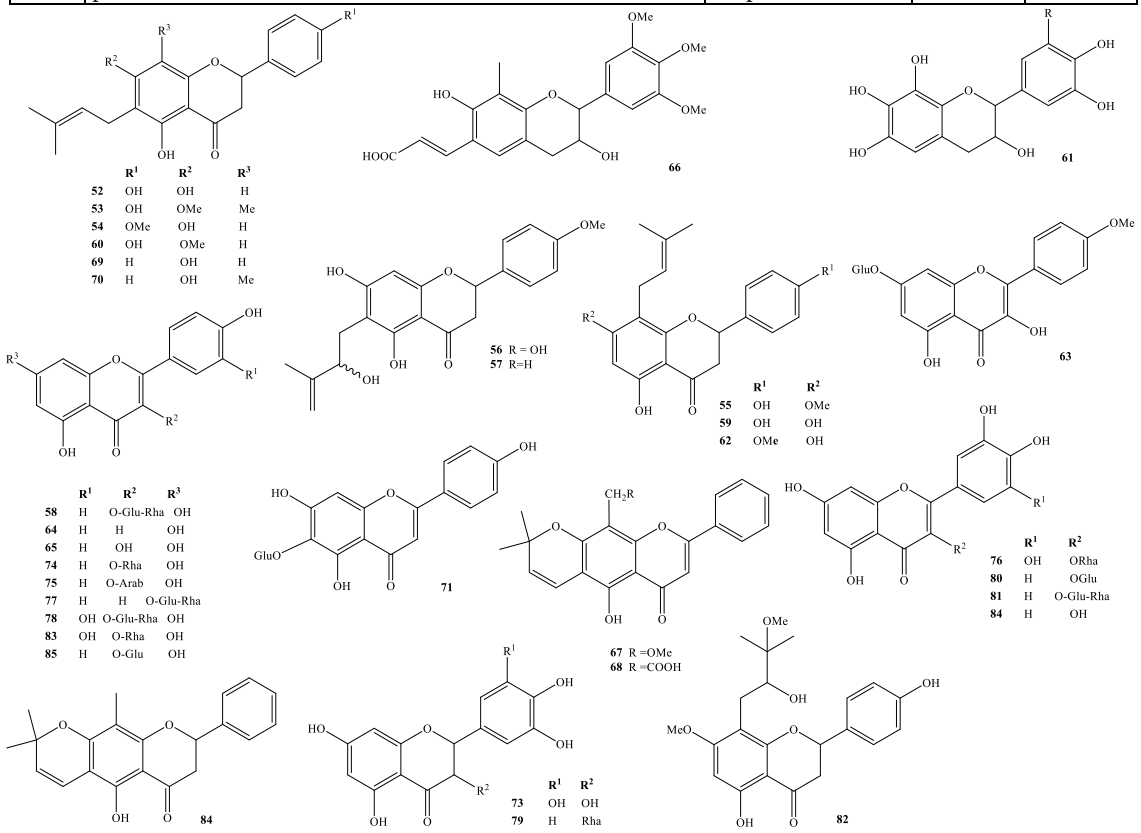


Figure 3. Chemical structures of flavonoids from *Mallotus* genus (**52-85**).

Table 4. Chalcones from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
86	kamalachalcone E	*M. philippinensis*	fruits	[40]
87	1-(5,7-dihydroxy-2,2,6-trimethyl-2H-1-benzopyran-8-yl)-3-phenyl-2-propen-1-one	*M. philippinensis*	fruits	[40]
88	rotterin	*M. philippensis* *M. philippinensis*	fruits fruits	[19, 31, 32, 41] [40]
89	4′-hydroxyrottlerin	*M. philippensis*	fruits	[19]
90	kamalachalcone D	*M. philippensis*	fruits	[32]
91	mallotophilippen F	*M. philippensis*	fruits	[19, 41]
92	3-prenylrubranine	*M. philippensis*	fruits	[31]
93	kamalachalcone A	*M. philippensis*	fruits	[32, 42]
94	8-cinnamoyl-2,2-dimethyl-7- hydroxy-5-methoxychromene	*M. philippensis*	fruits	[41]
95	8-cinnamoyl-5,7-dihydroxy-2,2,6-trimethylchromene	*M. philippensis*	fruits	[41]
96	kamalachalcone C	*M. philippensis*	fruits	[32]
97	mallotophilippen C	*M. philippinensis*	fruits	[43]
98	mallotophilippen D	*M. philippinensis*	fruits	[43]
99	mallotophilippen E	*M. philippinensis*	fruits	[43]
100	mallotoate A	*M. phillipensis*	stems	[44]
101	mallotoate B	*M. phillipensis*	stems	[44]
102	mallopenin A	*M. philippensis*	fruits	[19]
103	mallopenin C	*M. philippensis*	fruits	[19]
104	kamalachalcone B	*M. philippensis*	fruits	[32, 42]

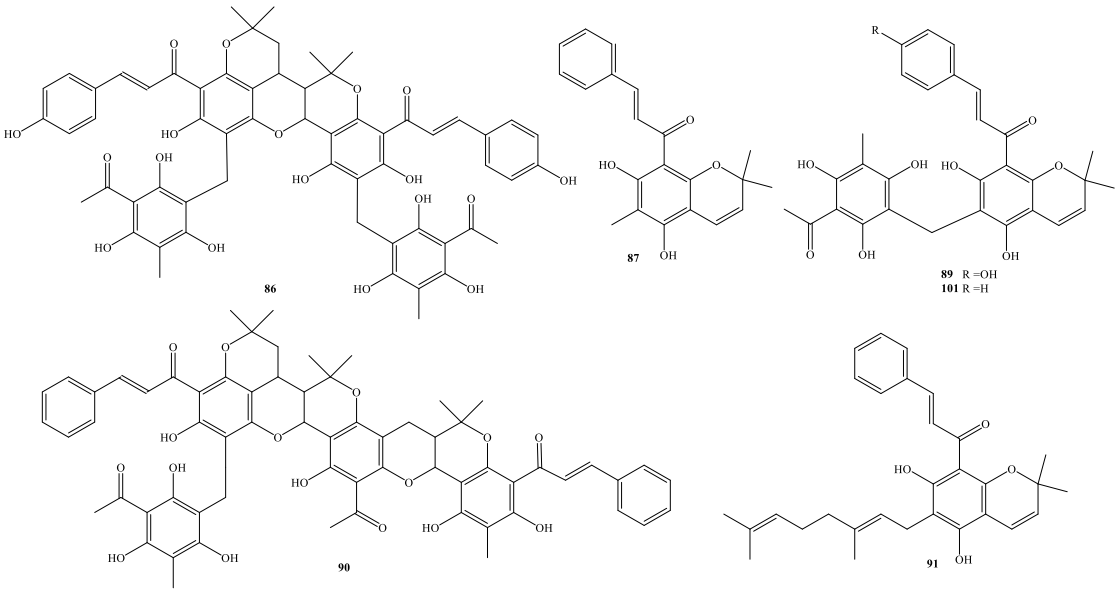


Figure 4. Chemical structures of chalcones from *Mallotus* genus **86**-**91**.

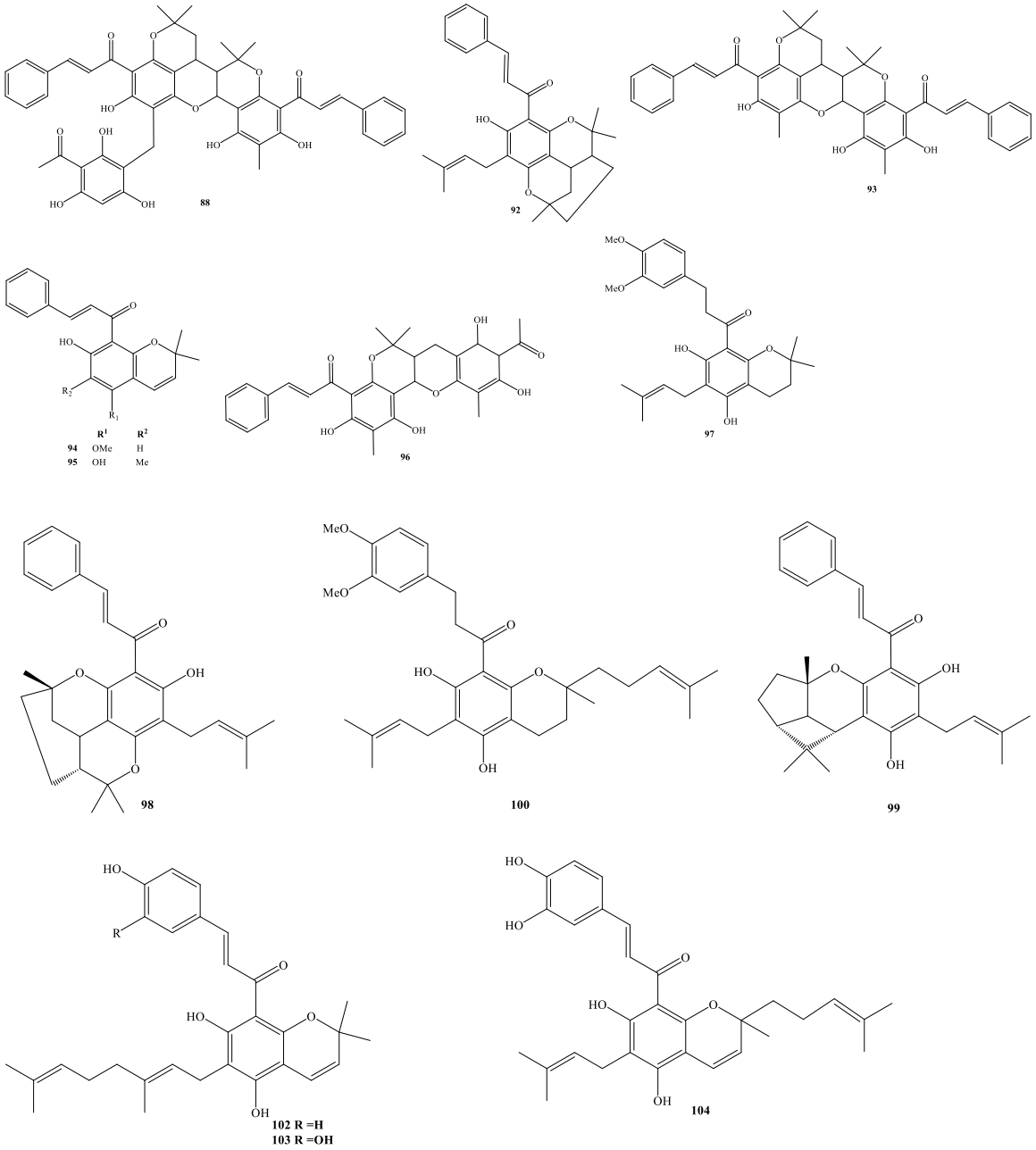


Figure 5. Chemical structures of chalcones from Mallotus genus (**88**-**104**) (Continue).

3.2.3. Phloroglucinols

There are 36 phloroglucinols reported from the *Mallotus* genus. Phloroglucinols (**105**-**140**) have been reported from *M. japonicus* (fruits and leaves), *M. oppositifolius* (fruits and leaves), *M. pallidus* (leaves), *M. philippinensis* (fruits), and *M. philippensis* (fruits) (

Table 5).

Table 5. Phlorogulcinols from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
105	mallotophilippen A	*M. japonicus*	fruits	[45]
106	mallotophilippen B	*M. japonicus*	fruits	[45]
107	mallotochromene	*M. japonicus*	fruits	[26, 46-49]
108	butyrylmallotochromene	*M. japonicus*	fruits	[49, 50]
109	isobutyrylmallotochromene	*M. japonicus*	fruits	[49, 50]
110	methylene-bis-aspidinol AB	*M. oppositifolius*	leaves	[17]
111	methylene-bis-aspidinol	*M. oppositifolius*	leaves	[17]
112	mallotophenone	*M. oppositifolius* *M. japonicus*	fruits	[51, 52] [26, 46-49]
113	mallotochromanol	*M. japonicus*	fruits	[26, 47-50, 52, 53]
114	isobutyrylmallotochromanol	*M. japonicus*	fruits	[48, 49, 52, 54]
115	mallotochroman	*M. japonicus*	fruits	[26, 48, 49]
116	butyrylmallotochromanol	*M. japonicus*	fruits	[49, 54]
117	butyrylmallotolerin	*M. japonicus*	fruits	[48, 49, 52]
118	mallotolerin	*M. japonicus*	fruits	[26, 47, 49]
119	isobutyrylmallotolerin	*M. japonicus*	fruits	[49]
120	isomallotolerin	*M. japonicus*	fruits	[53]
121	malloterin	*M. japonicus*	fruits	[53]
122	mallopposinol	*M. oppositifolius*	leaves	[17]
123	isomallotochromene	*M. japonicus*	fruits	[26, 48, 49, 52]
124	isomallotochromanol	*M. japonicus*	fruits	[26, 48, 49, 52, 53]
125	isomallotochroman	*M. japonicus*	fruits	[49]
126	mallotojaponin B	*M. oppositifolius*	leaves	[15, 51]
127	mallotojaponin	*M. japonicus*	fruits	[26, 46-49, 52, 55, 56]
128	butyrylmallotojaponin	*M. japonicus*	fruits	[27, 49]
129	isobutyrylmallotojaponin	*M. japonicus*	fruits	[27, 49]
130	3-(3,3-dimethylallyl)-5-(3-acetyl-2,4-dihydroxy-5-methyl-6-methoxybenzyl)-phlorobutyrophenone	*M. japonicus*	fruits	[47, 56, 57]
131	3-(3,3-dimethylallyl)-5-(3-acetyl-2,4-dihydroxy-5-methyl -6-methoxy benzyl)-phloroisobutyrophenone	*M. japonicus*	fruits	[47, 57]
132	mallopallidol	*M. pallidus*	leaves	[58][59]
133	homomallopallidol	*M. pallidus*	leaves	[59]
134	mallopallidusol	*M. pallidus*	leaves	[60]
135	mallotojaponol	*M. japonicus*	fruits	[54]
136	mallotojaponin D	*M. oppositifolius*	leaves	[15]
137	isoallorottlerin	*M. philippensis*	fruits	[19, 32]

138	4′-hydroxyisorottlerin	*M. philippensis*	fruits	[19, 32]
139	isorottlerin	*M. philippensis* *M. philippinensis*	fruits	[19, 31, 41] [32, 61]
140	mallotojaponin C	*M. oppositifolius*	leaves	[15, 51]

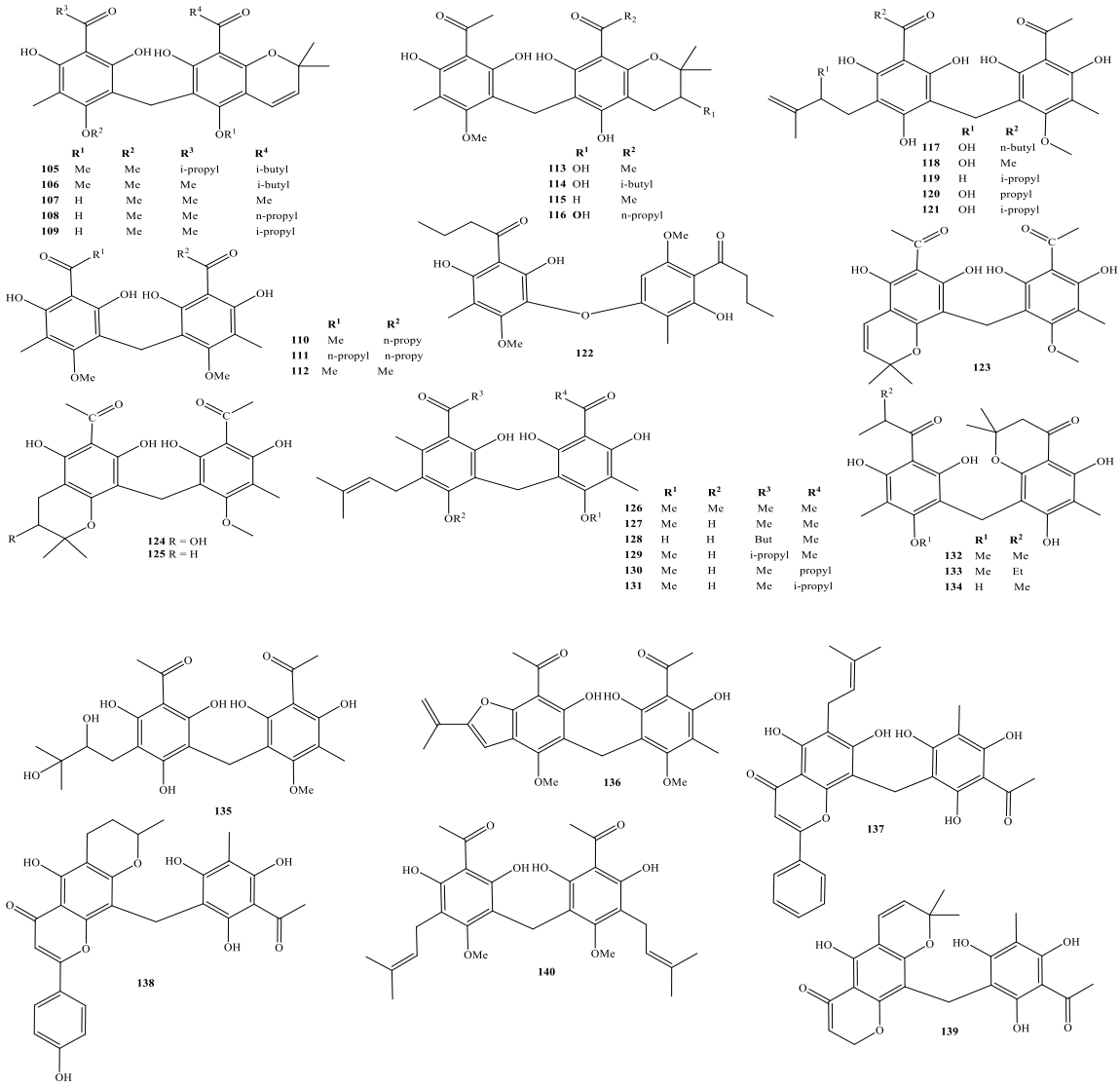


Figure 6. Chemical structures of phlorogulcinols from *Mallotus* genus (**105**-**139**).

3.2.4. Phenolics

There are 53 phenolics reported from the *Mallotus* genus. Among of them, gallic acid and bergenin derivatives (**141**-**169**) have been reported from *M. anisopodus* (leaves), *M. barbatus* (leaves), *M. conspurcatus* (barks), *M. furetianu* (leaves), *M. japonicus* (barks and leaves), *M. nanus* (leaves), *M. oppositifolius* (leaves), *M. oppositifolius* (leaves), *M. philipinesis* (leaves), *M. philippensis* (leaves), *M. philippensis* (leaves), *M. repandus* (leaves and barks), *M. resinosus*

(leaves), and *M. roxburghianus* (leaves) (Table 6). Tanins (**170-193**) have been reported from *M. conspurcatus* (leaves), *M. furetianus* (barks and leaves), *M. japonicus* (barks and leaves), *M. philipinesis* (leaves), and *M. repandus* (leaves) (Table 7).

Table 6. Gallic acid and bergenin derivatives from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
141	gallic acid	*M. furetianus* *M. barbatus*	leaves leaves	[8, 16] [36]
142	methyl gallate	*M. furetianu* *M. oppositifolius* *M. barbatus*	leaves leaves leaves	[16] [17] [36]
143	protocatechuic acid	*M. barbatus*	leaves	[36]
144	mallonanoside A	*M. nanus*	leaves	[38]
145	mallonanoside B	*M. nanus*	leaves	[38]
146	4-hydroxy-3- methoxyphenol l-*O*-*β*-D-(2′,6′-di-*O*-galloyl)glucoside	*M. japonicus*	barks	[62]
147	4-hydroxy-3-methoxyphenol l-*O*-*β*-D-(2,3,6′-tri-*O*-galloyl)glucoside	*M. japonicus*	barks	[62]
148	4-hydroxy-2-methoxyphenol 1-*O*-*β*-D-(6′-*O*-galloyl)glucoside	*M. japonicus*	barks	[62]
149	mallophenol A	*M. furetianus* *M. resinosus*	leaves	[8, 16]
150	3,4,5-trimethoxyphenol 1-*O*-*β*-D-(2′,6′-di-*O*-galloyl) glucoside	*M. japonicus*	barks	[62]
151	3-(1-C-*β*-D-glucopyranosyl)- 2,6-dihydroxy-5-methoxybenzoic acid	*M. roxburghianus*	leaves	[63]
152	glucogallin	*M. repandus*	leaves	[7]
153	brevifolin carbonxilic acid	*M. philipinesis* *M. repandus*	leaves	[64] [7]
154	11-*O*-galloylbergenin	*M. japonicus*	barks	[65]
155	bergenin	*M. anisopodus* *M. oppositifolius* *M. philippensis* *M. conspurcatus* *M. roxburghianus* *M. japonicus*	leaves leaves leaves barks leaves barks	[66] [15, 17, 34, 35] [35, 64] [34] [63] [63, 65, 67, 68]
156	bergenin-8-*O*-*α*-L-rhamnoside	*M. repandus*	barks	[69]
157	4-*O*-galloylbergenin	*M. philippensis* *M. japonicus*	leaves barks	[35] [65]
158	8,10-di-*O*-methylbergenin	*M. japonicus*	barks	[65]
159	4,8,10-tri-*O*-methylbergenin	*M. japonicus*	barks	[65]
160	3,8,10-tri-*O*-methylbergenin	*M. japonicus*	barks	[65]
161	8,10,11-tri-*O*-methylbergenin	*M. japonicus*	barks	[65]
162	permethylated bergenin	*M. japonicus*	barks	[65]
163	4,5,4′-trimethylellagic acid	*M. apelta*	roots	[70]

164	nasutin B	*M. japonicus*	leaves	[27]
165	nasutin C	*M. japonicus*	leaves	[27]
166	6-*O*-galloylbergenin	*M. philipinesis*	leaves	[64]
167	3-*O*-galloylnorbergenin	*M. philipinesis*	leaves	[64]
168	11-*O*-galloyldemethylbergenin	*M. philipinesis*	leaves	[64, 65]
169	norbergenin	*M. philipinesis*	leaves	[64]

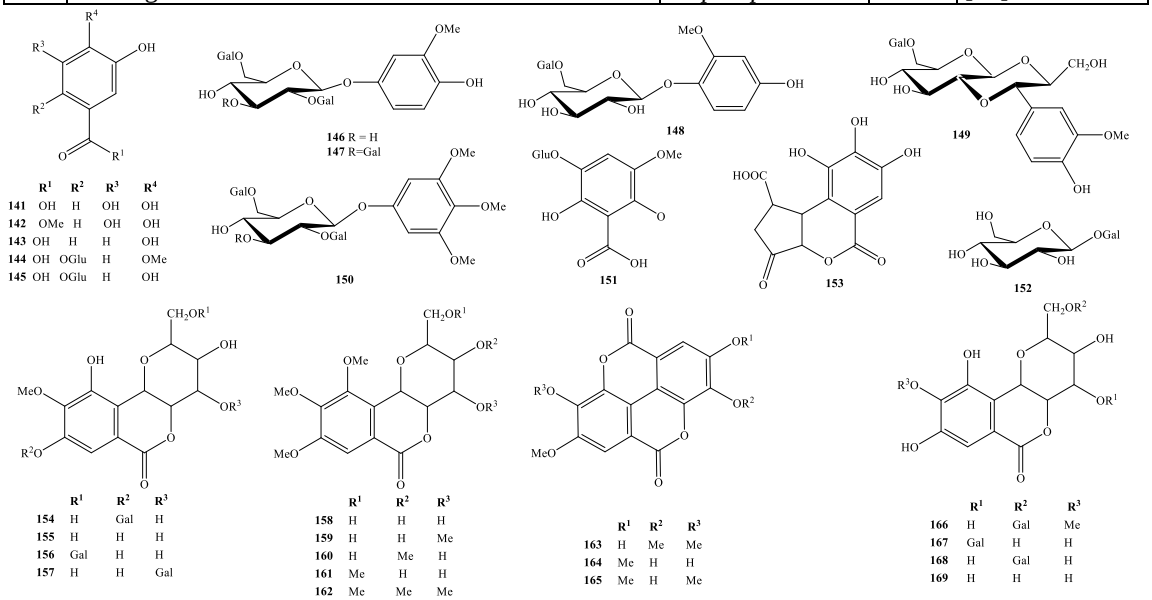
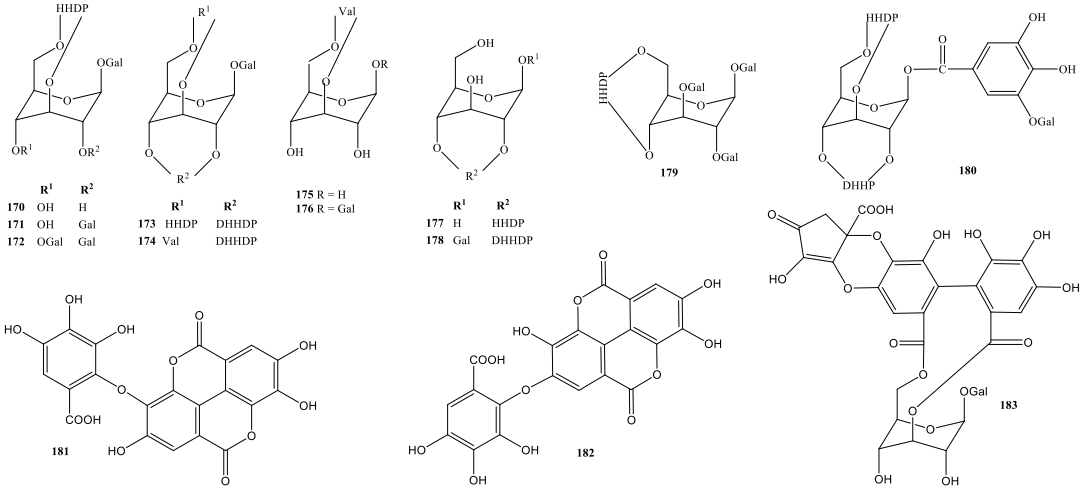


Figure 7. Chemical structures of gallic acid and bergenin derivatives (**141**-**169**).

Table 7. Tannins from *Mallotus genus.*

No.	**Compound names**	**Sources**	**Part**	**Ref.**
170	corilagin	*M. furetianus,* *M. philipinesis* *M. repandus*	barks leaves leaves	[16, 71, 72] [64] [7]
171	1,2-di-*O*-galloyl-3,6-(*R*)- hexahydroxydiphenoyl-*β*-D-glucopyranose	*M. japonicus*	barks	[73]
172	punicafolin	*M. repandus*	leaves	[7]
173	geraniin	*M. japonicus* *M. philipinesis* *M.repandus*	leaves leaves leaves	[71, 72, 74] [64] [7]
174	mallotusinic acid	*M. japonicus* *M. philipinesis* *M. repandus*	barks leaves leaves	[71, 72, 74] [7, 64] [62]
175	1-desgalloylmallotinic acid	*M. philipinesis*	leaves	[64]
176	mallotinic acid	*M. japonicus* *M. philipinesis* *M. repandus*	barks leaves leaves	[71, 72, 74] [64] [7]
177	2,3-(*S*)-hexa-dihidroxydiphenoyl-*D*-glucose	*M. philipinesis*	leaves	[64]
178	furosin	*M. phlipinesis*	leaves	[64]

		M. repandus	leaves	[7]
179	eugenin	*M. repandus*	leaves	[7]
180	1-*O*-digalloyl-3,6-(*R*)-hexahydroxydiphenoyl-*β*-D-glucopyranose	*M. japonicus*	barks	[73]
181	tergallic acid dilactone	*M. philipinesis*	leaves	[64]
182	flavogallonic acid	*M. philipinesis*	leaves	[64]
183	repandinin B	*M. furetianus*	leaves	[16]
184	mallotanin A	*M. japonicus*	leaves	[64]
185	mallotanin B	*M. japonicus*	leaves	[64]
186	repandusinic acid A(K)	*M. philipinesis*	leaves	[7, 64]
187	repamdusinic acid B	*M.repandus*	leaves	[7]
188	mallonin	*M. japonicus*	barks	[73]
189	mallojaponin	*M. japonicus*	barks	[73]
190	mallotinin	*M. repandus*	leaves	[7]
191	phyllanthusiin D	*M. conspurcatus*	leaves	[75]
192	mallotusinin	*M. japonicus*	barks	[73]
193	repandusinin	*M. repandus*	leaves	[7]



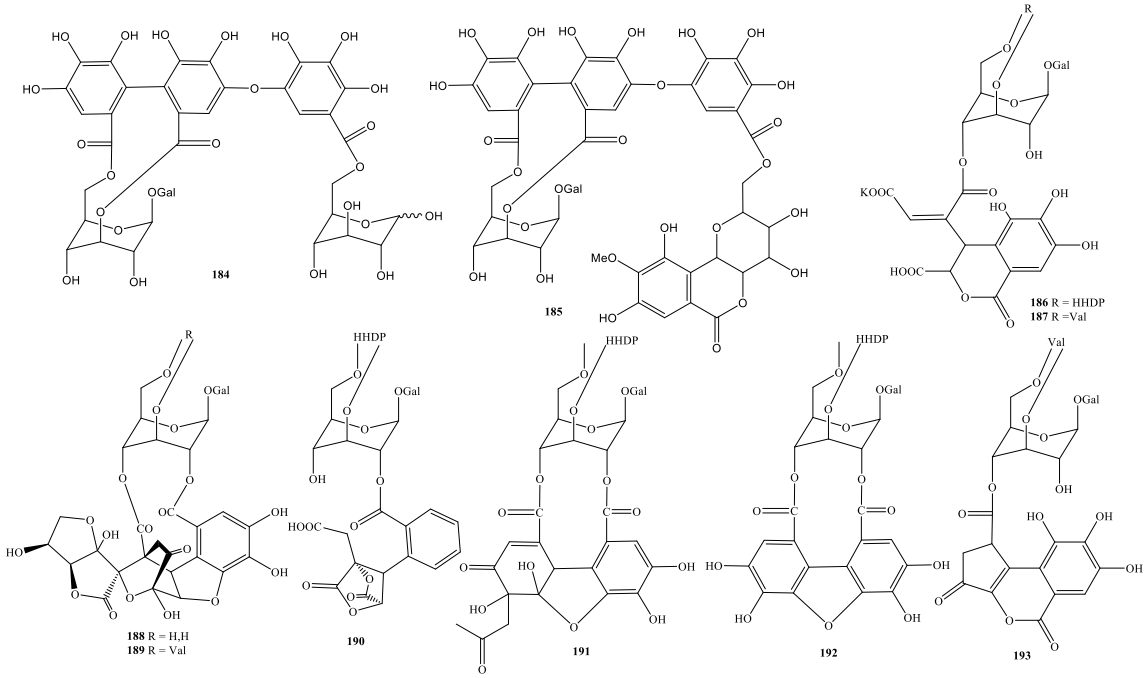


Figure 8. Chemical structures of tannins from *Mallotus* genus (**170**-**193)**.

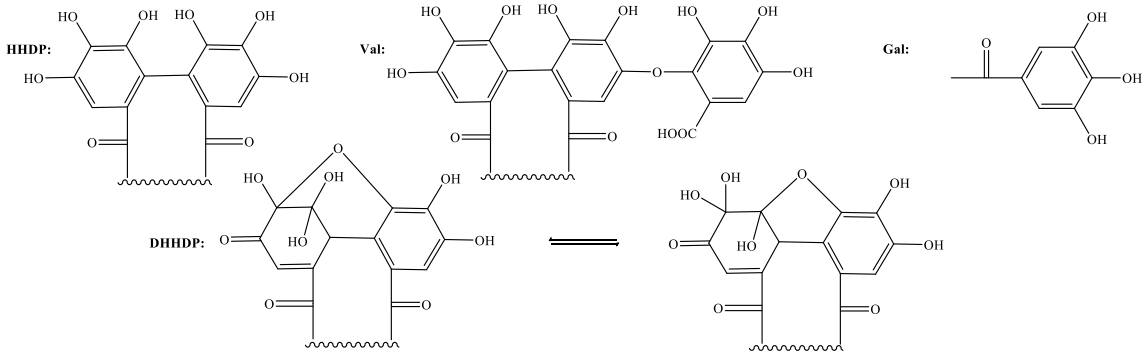


Figure 9. Chemical structures of tannins from *Mallotus* genus (**170**-**193**) *(Continue).*

Lignans (**194**-**199**) have been reported from *M. apelta* (roots), *M. furetianus* (leaves), *M. japonicus* (leaves), *M. philipinesis* (leaves), and *M. macrostachyus* (leaves) (Table 8).

Table 8. Lignans from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
194	schizandriside	*M. apelta*	roots	[76]
195	aviculin	*M. furetianus*	leaves	[8]
196	(+)-lyoniresinol-3*α*-*O*-*α*-L-rhamnopyranoside	*M. furetianus*	leaves	[8, 16]
197	bilariciresinol	*M. philippensis*	leaves	[35]
198	(+)-pinoresinol di-*O*-*β*-D-glucopyranoside	*M. macrostachyus*	leaves	[77]

199	syringaresinol di-*O*-*β*-D-glucopyranoside	*M. macrostachyus*	leaves	[77]

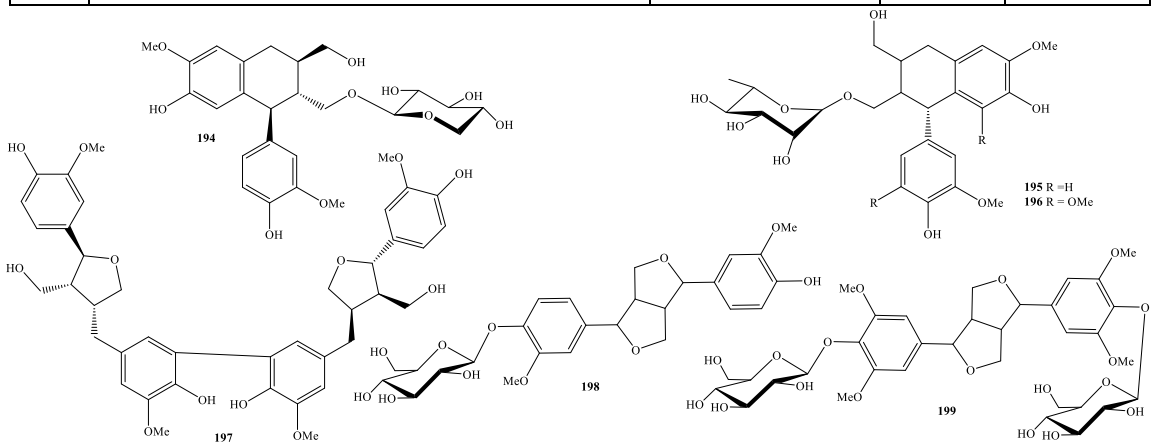


Figure 10. Chemical structures of lignans from *Mallotus* genus (**194**-**199**).

Other phenolics (**200**-**219**) have been reported from *M. anisopodus* (stems), *M. apelta* (branches), *M. conspurcatus* (roots), *M. japonicus* (fruits), *M. metcalfianus* (stems), *M. oppositifolius* (leaves), *M. pallidus* (leaves), and *M. roxburghianus* (leaves) (Table 9).

Table 9. Other phenolic compounds from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
200	(*E*)-1,2-bis(4-methoxyphenyl) ethane	*M. apelta*	branches	[20]
201	methoxy cinnamic acid	*M. apelta*	branches	[20]
202	mellein	*M. oppositifolius*	leaves	[15]
203	pallidol	*M. pallidus*	leaves	[58, 59]
204	trans-ferulic acid	*M. metcalfianus*	stems	[39]
205	2-hydroxy ferulic acid	*M. conspurcatus*	roots	[34]
206	3-(1-C-*β*-D-glucopyranosyl)-2,6-dihydroxy-5-methoxybenzoic acid	*M. roxburghianus*	leaves	[63]
207	pallidusol	*M. pallidus*	leaves	[58, 59]
208	dehydropallidusol	*M. pallidus*	leaves	[58, 59]
209	acronyculatin *S*	*M. oppositifolius*	leaves	[15]
210	acronyculatin T	*M. oppositifolius*	leaves	[15]
211	aspidinol B	*M. oppositifolius*	leaves	[17]
212	2,6-dihidroxy-3-methyl-4-methoxyacetophenone	*M. oppositifolius* *M. japonicus* *M. roxburghianus*	leaves fruits leaves	[15] [26, 27, 46-48] [63]
213	mallophenone	*M. japonicus*	fruits	[49]
214	methoxybenzoic acid	*M. apelta*	branches	[20]
215	4-hydroxybenzoic acid	*M. roxburghianus*	leaves	[63]
216	gallincin	*M. conspurcatus*	roots	[34]

217	2,4,8,9,10-pentahydroxy-3,7-dimethoxy anthracene-6-*O*-*β*-D- rhamnopyranoside	*M. roxburghianus*	leaves	[63]
218	methyl salicylate glucoside	*M. metcalfianus*	stems	[39]
219	junipetrioloside A	*M. anisopodus*	stems	[66]

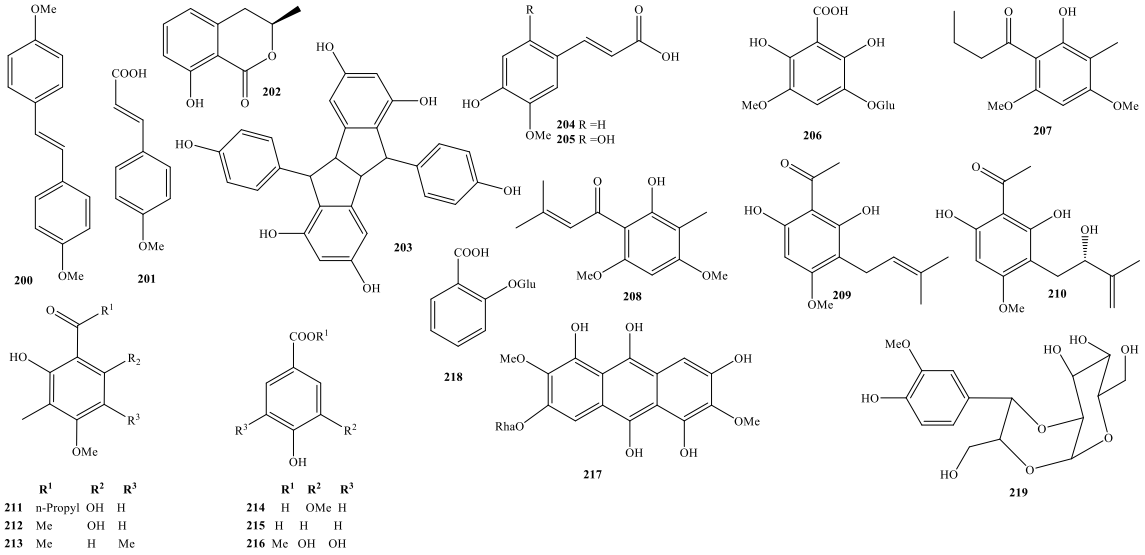


Figure 11. Chemical structures of other phenolic compounds from *Mallotus* genus (**201**-**219**).

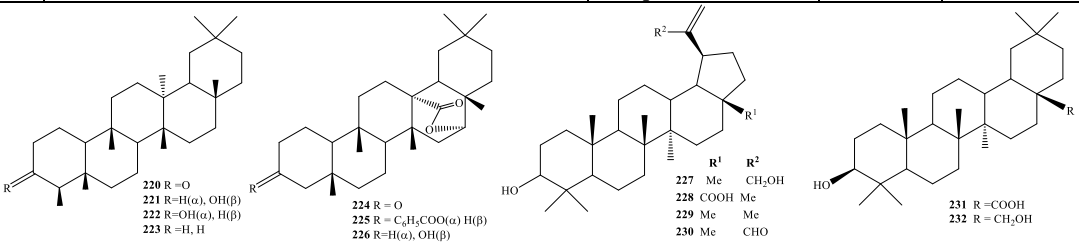
3.2.5. Triterpenoids

There are 36 triterpenoids (**220**-**255**) from the *Mallotus* genus. The compounds have been reported from *M. apelta* (leaves), *M. barbatus* (leaves), *M. conspurcatus* (leaves), *M. macrostachyus* (leaves and branches), *M. metcalfianus* (stems), *M. mollissimus* (leaves), *M. nepalensis* (leaves), *M. philippensis* (leaves), *M. philippiensis* (stems), *M. repandus* (stems), and *M. roxburghianus* (leaves) (Table 10).

Table 10. Triterpenoids from *Mallotus genus.*

No.	Compound names	Sources	Part	Ref.
220	friedelin	*M. barbatus* *M. macrostachyus* *M. conspurcatus* *M. apelta* *M. roxburghianus*	leaves branches leaves leaves leaves	[37] [77, 78] [79] [80] [81]
221	friedelanol	*M. metcalfianus* *M. macrostachyus* *M. apelta* *M. roxburghianus*	stems branches leaves leaves	[39] [78] [80] [81]
222	epifriedelanol	*M. macrostachyus* *M. roxburghianus*	branches leaves	[77, 78] [81]
223	friedelane	*M. conspurcatus*	leaves	[79]
224	3-oxo-D:A-friedo-oleanan-27,16*α*-lactone	*M. repandus*	stems	[82]
225	3*α*-benzoyloxyD:A-friedo-oleanan-27,16*α*-lactone	*M. repandus*	stems	[82]
226	3*β*-hydroxy-D:A-friedo-oleanan-27,16*α*-lactone	*M. repandus*	stems	[82]

227	hennadiol	*M. apelta*	leaves	[80]
228	betulinic acid	*M. roxburghianus*	leaves	[63]
229	lupeol	*M. oppositifolius* *M. nepalensis*	leaves leaves	[17] [83][91][89]
230	3-hydroxy-lup-20-(29)-en-30-al	*M. conspurcatus*	leaves	[79]
231	oleanolic acid	*M. mollissimus*	leaves	[30]
232	erythrodiol	*M. conspurcatus*	leaves	[79]
233	acetylaleuritolic acid	*M. macrostachyus* *M. conspurcatus*	branches leaves	[78] [79]
234	aleuritolic acid	*M. conspurcatus*	leaves	[79]
235	pachysandiol	*M. philippensis*	leaves	[35]
236	3*β*-acetoxy-28-hydroxy-12-oleanene-3-one	*M. macrostachyus*	branches	[78]
237	12-oleanene-3,11-dione	*M. macrostachyus*	branches	[78]
238	3*β*,28-dihydroxyoleana-11,13(18)-diene	*M. conspurcatus*	leaves	[79]
239	3*α*-hydroxy-13*α*-ursan-28,12*β*-olide 3-benzoate	*M. repandus*	stems	[84, 85]
240	3*α*-hydroxy-28*β*-methoxy13*α*-ursan-28,12*α*-epoxide 3-benzoate	*M. repandus*	stems	[84, 85]
241	taraxerone	*M. mollissimus* *M. apelta*	leaves leaves	[30] [80]
242	epitaraxerol	*M. macrostachyus* *M. mollissimus* *M. apelta* *M. roxburghianus*	leaves leaves leaves leaves	[77] [30] [80] [81]
243	taraxerol	*M. macrostachyus* *M. mollissimus* *M. barbatus* *M. roxburghianus*	leaves leaves leaves leaves	[77] [30] [36] [81]
244	kamaladiol-3-acetate	*M. philippiensis*	stems	[86]
245	mallomacrostin A	*M. macrostachyus*	branches	[78]
246	3*α*-hydroxy-13*α*-ursan-28-oic acid	*M. repandus*	stems	[84, 85]
247	*α*-amyrin acetate	*M. conspurcatus*	leaves	[79]
248	ursolic acid	*M. macrostachyus* *M. nepalensis*	branches leaves	[78, 83] [83]
249	mallomacrostin B	*M. macrostachyus*	branches	[78]
250	foliasalacin D2	*M. macrostachyus*	branches	[78]
251	foliasalacin D3	*M. macrostachyus*	branches	[78]
252	3*α*-hydroxyhop-22(29)-ene	*M. apelta*	leaves	[80]
253	supinenolone 2f	*M. macrostachyus*	branches	[78]
254	squalene	*M. oppositifolius*	leaves	[17]
255	carotene	*M. apelta*	leaves	[18]



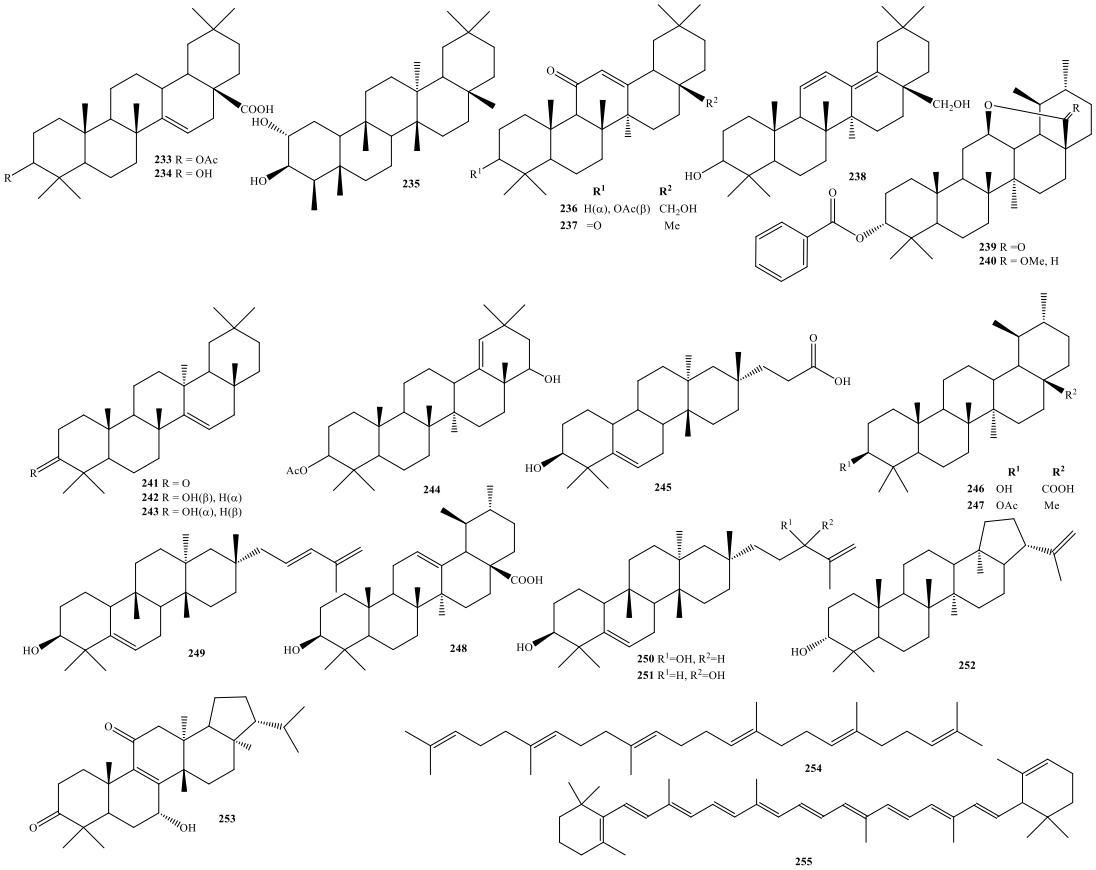


Figure 12. Chemical structures of triterpenoids from *Mallotus* genus (**220**-**255**).

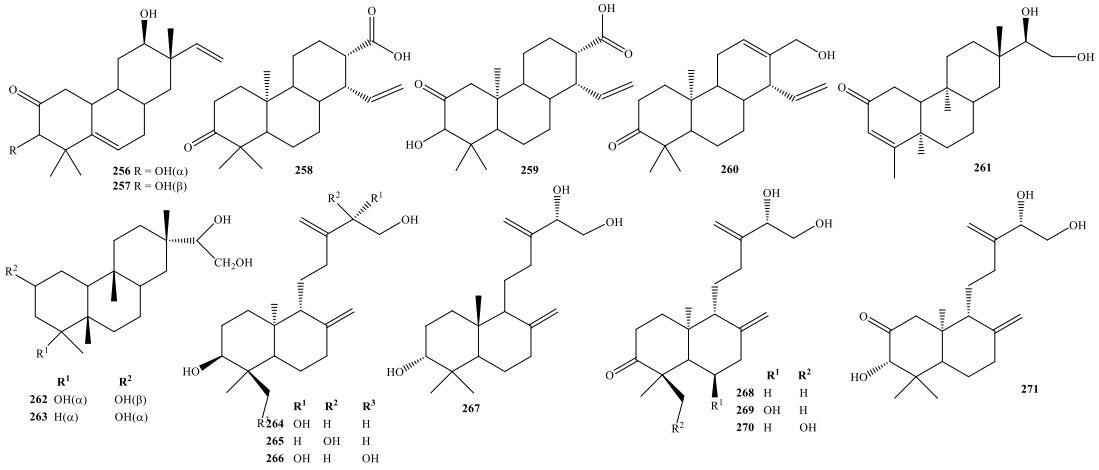
3.2.6. Diterpenoids and other terpenoids

There are 30 diterpenoids (**256**-**285**) from the *Mallotus* genus. Diterpenoids have been reported from *M. apelta* (leaves, roots, and stems), *M. anomalus* (roots), *M. conspurcatus* (leaves and roots), *M. hookerianus* (stems), *M. japonicus* (stems), *M. oppositifolius* (leaves), and *M. repandus* (stems) Table 11.

Table 11. Diterpenoids from Mallotus genus.

No.	Compound names	Sources	Part	Ref.
256	anomalusin A	*M. anomalus*	roots	[87]
257	anomalusin B	*M. anomalus*	roots	[87]
258	malloconspur A	*M. conspurcatus*	leaves	[79]
259	malloconspur B	*M. conspurcatus*	leaves	[79]
260	17-hydroxycleistantha-12,15-dien-3-one	*M. conspurcatus*	leaves	[79]
261	2-oxo-5-epi-fagonene	*M. conspurcatus*	leaves	[79]
262	2*α*,4*β*,15,16-tetrahydroxyl-dolabradane	*M. apelta*	stems	[88]
263	malloapeltin	*M. apelta*	roots	[70]
264	mallonicusin C	*M. japonicus*	stems	[89]

265	mallonicusin D	*M. japonicus*	stems	[89]
266	mallonicusin H	*M. japonicus*	stems	[89]
267	mallonicusin B	*M. conspurcatus* *M. japonicus*	leaves stems	[79] 89]
268	mallonicusin *E*	*M. japonicus*	stems	[89]
269	mallonicusin F	*M. japonicus*	stems	[89]
270	mallonicusin G	*M. japonicus*	stems	[89]
271	mallonicusin A	*M. japonicus*	stems	[89]
272	10-hydroxycembrene-5-one	*M. apelta*	stems	[88]
273	6-hydroxy-cembrene-5,10-dione	*M. apelta*	stems	[88]
274	malloapentene	*M. apelta*	stems	[90]
275	hookerianolide A	*M. hookerianus*	stems	[91]
276	hookerianolide B	*M. hookerianus*	stems	[91]
277	hookerianolide C	*M. hookerianus*	stems	[91]
278	mallotucin A	*M. repandus*	stems	[92]
279	mallotucin B	*M. repandus*	stems	[92]
280	mallotucin C	*M. repandus*	stems	[92]
281	mallotucin D	*M. repandus*	stems	[92]
282	*ent*-3*S*,16*S*,17-trihydroxy-kauran-2-one	*M. conspurcatus*	leaves	[79]
283	16-epiabbeokutone	*M. conspurcatus*	roots	[34]
284	anomaluone	*M. conspurcatus*	roots	[34]
285	*trans*-phytol	*M. oppositifolius* *M. apelta*	leaves leaves	[17][18]



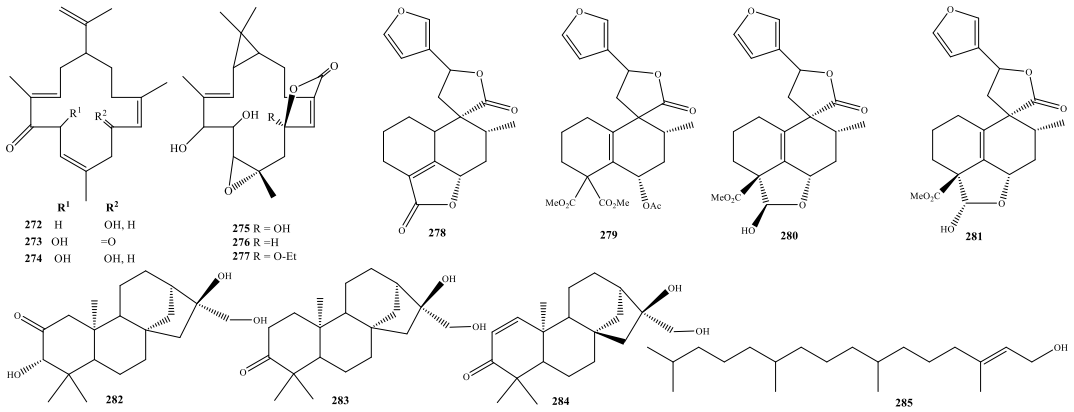


Figure 13. Chemical structures of diterpenoids from *Mallotus* genus (**256**-**285**).

There are 9 megastigmanes (**286**-**294**) from *M. anisopodus* (leaves), *M. conspurcatus* (roots), *M. macrostachyus* (leaves), *M. metcalfianus* (stems), *M. furetianus* (stems), and *M. resinosus* (leaves) (Table 12).

Table 12. Megastigmanes from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
286	corchoionoside C	*M. furetianus* *M. macrostachyus*	leaves leaves	[8] [77]
287	dihydrovomifoliol	*M. conspurcatus*	leaves	[79]
288	mallophenol B	*M. resinosus*	leaves	[8]
289	macarangioside F	*M. macrostachyus*	leaves	[77]
290	icariside B5	*M. macrostachyus*	leaves	[77]
291	vomifoliol	*M. conspurcatus*	leaves	[79]
292	blumenol C glucoside	*M. metcalfianus*	stems	[39]
293	anisoposide A	*M. anisopodus*	leaves	[66]
294	anisoposide B	*M. anisopodus*	leaves	[66]

Table 13. Other terpenoids from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
295	paeoveitol B	*M. conspurcatus*	leaves	[79]
296	malloapelin D	*M. apelta*	roots	[76]
297	curdionolide	*M. conspurcatus*	leaves	[79]

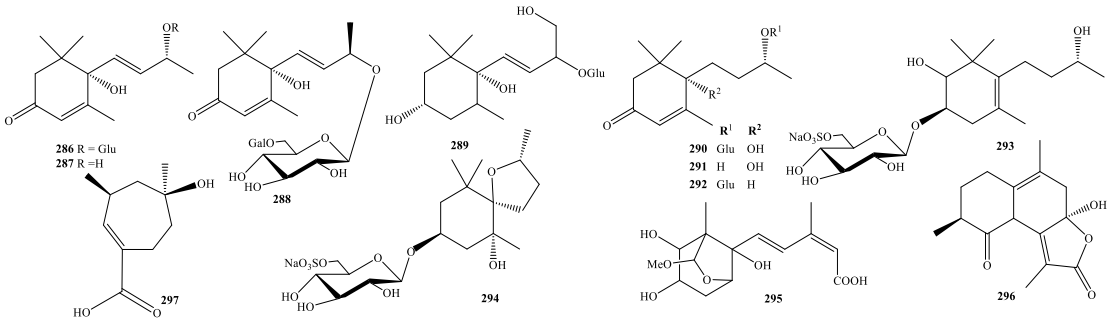


Figure 14. Chemical structures of megastigmanes and other terpenoids (**286**-**297**).

3.2.7. Steroids

Table 14. Steroids from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
298	macrostachyoside A	*M. macrostachyus*	leaves	[77]
299	25,26,27-trisnor-24-hydroxycycloartan-3-one	*M. macrostachyus*	leaves	[77]
300	25,26,27-trisnor-3-ketocycloartan-24-oic acid	*M. macrostachyus*	leaves	[77]
301	macrostachyoside B	*M. macrostachyus*	leaves	[77]
302	mallomacrostin C	*M. macrostachyus*	branches	[78]
303	cycloarta-23*E*,25-dien-3*β*-ol	*M. macrostachyus*	branches	[78]
304	(22*E*,24*S*)-3-hydroxy-24-methylcholesta-5,22-dien-7-one	*M. paniculatus*	stems	[93]
305	ergosterol	*M. paniculatus*	stems	[93]
306	polasterol A	*M. paniculatus*	stems	[93]
307	(24*R*)-3*β*-hydroxystigmast-5-en-7-one	*M. paniculatus*	stems	[93]
308	stigmasterol	*M. oppositifolius* *M. roxburghianus* *M. paniculatus*	leaves leaves stems	[17] [63] [93]
309	*β*-sitosterol	*M. paniculatus* *M. roxburghianus* *M. mollissimus* *M. nepalensis*	stems leaves leaves stems	[93] [36, 63] [30] [83]
310	daucosterol	*M. barbatus* *M. roxburghianus* *M. paniculatus* *M. nepalensis*	leaves leaves stems stems	[36] [63] [93] [83]
311	ergosterol peroxide	*M. macrostachyus*	leaves	[77]

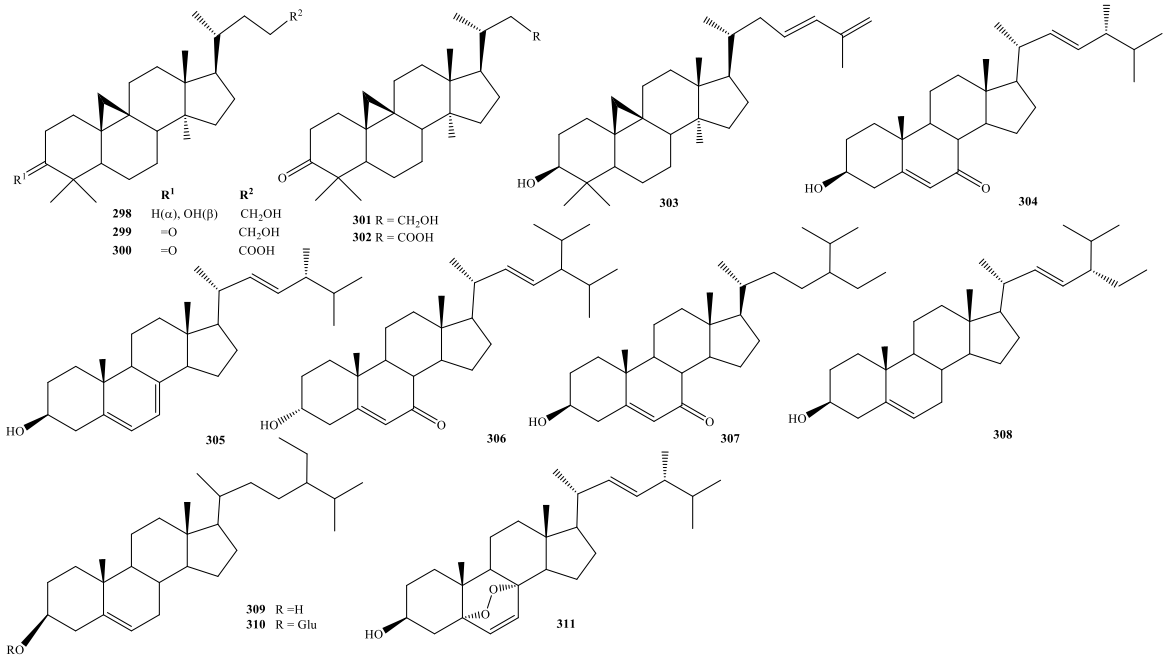


Figure 15. Chemical structures of steroids (**298**-**311**).

There are 14 steroids from the *Mallotus* genus: *M. barbatus* (leaves), *M. macrostachyus* (leaves and branches), *M. mollissimus* (leaves), *M. nepalensis* (stems), *M. oppositifolius* (leaves), *M. paniculatus* (stems), and *M. roxburghianus* (leaves) (Table 14).

3.2.8. Other compounds

Remaining compounds have been reported from *Mallotus* belonging to alkaloids and peptides. They were found in *M. barbatus, M. cuneatus, M. furetianus, M. japonicus, M. lianus, M. macrostachyus, M. nudiflorus,* and *M. repandus* (Table 15).

Table 15. Other compounds from *Mallotus* genus.

No.	Compound names	Sources	Part	Ref.
312	N-methyl-5-carboxamide-2- pyridone	*M. barbatus*, *M. macrostachyus*	leaves leaves	[37] [77]
313	*trans*-2-carboxy-4-hydroxytetrahydrofuran N,N-dimethylamide	*M. cuneatus*	leaves	[94]
314	nicotinamide	*M. japonicus*	leaves	[95]
315	mallorepine	*M. repandus*	stems	[96]
316	N-isobutyl-2*E*,4*E*,12*Z*-octadecatrienamide	*M. lianus*	roots	[97]
317	(7*Z*,10*Z*,18*Z*)-tricosa-7,10,18-trienamide	*M. lianus*	roots	[97]
318	phenazine C	*M. japonicus*	leaves	[74]
319	cyclo(L-Pro-L-Leu)	*M. nudiflorus*	stems	[98]
320	cyclo(D-*trans*-Hyp-D-Leu)	*M. nudiflorus*	stems	[98]

321	cyclo(D-Pro-L-Phe)	*M. nudiflorus*	stems	[98]
322	cyclo(D-*cis*-Hyp-L-Phe)	*M. nudiflorus*	stems	[98]
323	3-hydroxy-4,5(*R*)-dimethyl-2(5H)-furanone	*M. furetianus*	leaves	[8]
324	(*Z*)-3-hexenyl-*β*-D-glucopyranoside	*M. furetianus*	leaves	[8, 16]
325	benzyl-*O*-*β*-D-glucopyranoside	*M. macrostachyus*	leaves	[77]

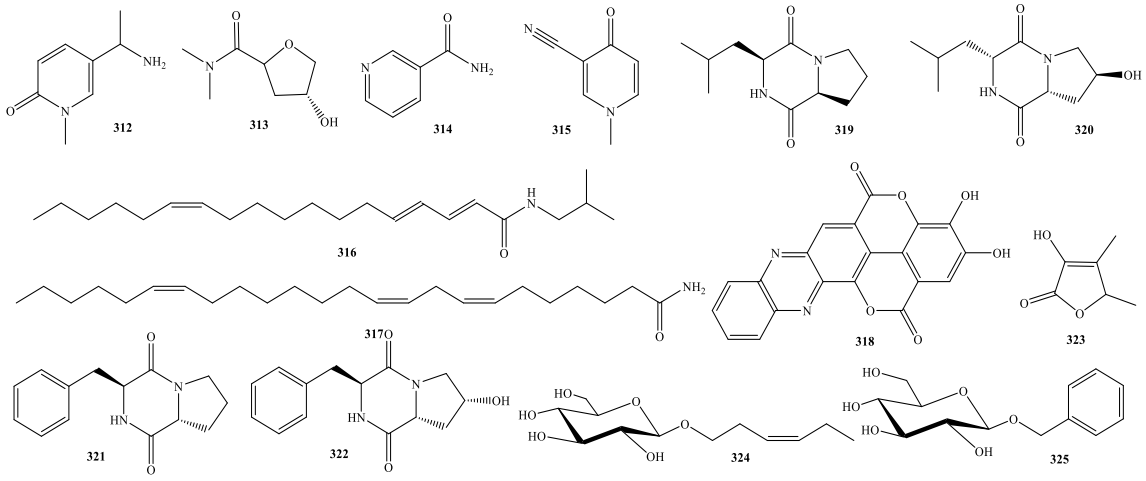


Figure 16. Chemical structures of other compounds from Mallotus genus (**312**-**325**).

3.3. Biological activities

The traditional uses and bioactive compounds from the *Mallotus* genus have led researcher's interest to study pharmacological activities and to verify the potential uses of the genus. The following discussion provides biological effects of the extracts and isolated compounds from the *Mallotus* genus. The species of *Mallotus* genus possesses a wide range of biological effects such as anti-cancer, anti-inflammatory, antioxidant, antibacterial, antifungal, immunoregulatory effects, and anti-virus effects. Below is a summary of the important biological activities of the *Mallotus* species.

3.3.1. Cytotoxic and antitumor activities

An overview of the literature on the *Mallotus* genus indicated that the components presented in the *Mallotus* genus have significant biological activities, especially anti-cancer and antitumor activities against human cancer cell lines, such as epidermoid carcinoma (KB), cervical cancer (Hela), lung adenocarcinoma (LU-1), rhabdosarcoma (RD), human hepatocellular carcinoma (Hep-2), mouse leukaemia (L5 178Y), and human ovarian cancer (A2780). Cytotoxic activity against KB and L-5 178Y cell lines has been shown in phloroglucinols. In 1985 and 1986, Arisawa isolated mallotochromene (**107**), mallotophenone (**112**), mallotolerin (**118**) and 3-(3,3-dimethylallyl)-5-(3-acetyl-2,4-dihydroxy-5-methyl-6-methoxybenzyl)-phlorobutyrophenone (**130**) from the fruits of *M. japonicus*. Compounds **107**, **112**, **118**, and **130** showed significant cytotoxic activity against the KB and L-5 178Y cancer cell lines with ED_{50} values of 4.8 and 5.2; 0.29 and 1.04; 0.95 and 0.82; and 0.26 and 1.07 μg/mL, respectively [46, 47]. Then, butyrylmallotochromene (**108**) and isobutyrylmallotochromene

(**109**) were also isolated from the cytotoxic fraction of *M. Japonicus* in 1988. These two compounds exhibited significant cytotoxic activity against KB cell line with ED_{50} values of 3.3 and 0.4 µg/mL, respectively [50]. Butyrylmallotojaponin (**128**) and isobutyrylmallotojaponin (**129**) were isolated from the leaves of *M. Japonicus* exhibited cytotoxic activity against KB cell line with ED_{50} values of 0.72 and 0.89 µg/mL, respectively [27]. Isomallotolerin (**120**) from the fruits of *M. japonicus* inhibited cytotoxic activity on KB cell line with IC_{50} value of 0.84 µg/mL [53]. In 1990, Arisawa and co-workers reported 18 phloroglucinols from the fruits of *M. japonicus*. All compounds exhibited the cytotoxic activity on Hela cells with IC_{50} values ranging from 0.28 µg/mL to 49.10 µg/mL [49]. In 2011, Nam and co-workers isolated two steroids, macrostachyoside A (**298**) and macrostachyoside B (**301**) from the leaves of *M. macrostachyus*. Compounds **298** and **301** showed significant cytotoxic effects against KB and LU-1 cell lines, with the IC_{50} values ranging from 4.31±0.09 to 7.12±0.07 µg/mL [77]. Paxiione A (**16**) was obtained from the stems of *M. paxii* also showed significant cytotoxic activity on KB cell line, with IC_{50} value of 8.62±1.31 µg/mL [9]. In 2014, a coumarine derivative, 7-hydroxy-2-hydroxymethyl-8-methoxy-4-oxo-4H-chromene-6-carboxylic acid (**20**), was found from the twigs of *M. apelta* by Lu and co-wokers. This compound demonstrated moderate cytotoxic activity against KB and HeLa cells with IC_{50} values of 9.50 and 9.23 µg/mL, respectively [20]. In 2005, Prof. Phan Van Kiem and co-wokers reported two benzopyrans, 6-[l′-oxo-3′(*R*)-hydroxy-butyl]-5,7-dimethoxy-2,2-dimethyl-2H-l-benzopyran (**7**) and 6-[l′-oxo-3′(*R*)-methoxy-butyl]-5,7-dimethoxy-2,2-dimethyl-2H-l-benzopyran (**8**), from the leaves of *M. apelta*. These compounds were evaluated for cytotoxic effects against Hep-2 and RD cell lines, compound **7** exhibited significant cytotoxic effect against two tested human cancer cell lines with IC_{50}values of 0.49 µg/mL (Hep-2) and 0.54 µg/mL (RD), while compound **8** showed moderate activity on Hep-2 cell line with IC_{50} of 4.22 µg/mL [14]. In the research of Prof. Chau Van Minh and co-authors, 22 compounds from *M. apelta* were evaluated for their cytotoxic effects against KB, FL, and Hep-2 cancer cell lines. Among them, malloapelta B (**26**) showed a strong cytotoxic effect against the three cancer cell lines, while the other compounds did not show inhibitory activities with IC_{50} values over 50 µM [99].

In addition, ten new chromene derivatives, malloapeltas C-H (**12**–**16**,**31**–**32**) and one known compound, malloapelta B (**26**) were isolated from the leaves of *M. apelta*. All compounds were evaluated for cytotoxic activity using cell counting kit-8 (CCK-8) assay against ovarian cancer cell line (TOV-21G). Compounds **12**–**16**,**26** and **31**–**32** exhibited significant growth and viability inhibitory effects with GI_{50} values ranging from 0.06 to 10.39 µM and IC_{50} values ranging from 1.62 to 10.42 µM on ovarian cancer cell line, TOV-21G. The most cytotoxic compounds **14**,**26** and **31**/**32** were chosen for studying apoptosis mechanisms. These compounds-induced apoptosis was evidenced by activated caspase 8, caspase 9, and PARP, increased Bak and Bax, and decreased Bcl-xL and survivin. Moreover, those compounds significantly inhibited the NF-κB signaling pathway [23]. Compounds **18** and **19** significantly reduced both cell viability of PC-3 cells and ANO1 channel activity. An electrophysiological study revealed that compound **19** is a potent and selective ANO1 inhibitor with an IC_{50} value of 2.64 µM. Compound **19** had minimal effect on cystic fibrosis transmembrane conductance regulator (CFTR) chloride channel activity and intracellular calcium signaling. Notably, **19** significantly reduced ANO1 protein expression levels and cell viability in an ANO1-dependent manner in PC-3 and oral squamous cell carcinoma CAL-27 cells. In addition, **19** strongly reduced cell migration and induced activation of caspase-3 and cleavage of PARP in PC-3 and CAL-27 cells [24]. In 2013, Harinantenaina *et al*. isolated three phloroglucinols, mallotophenone (**112**), mallotojaponin B (**126**), and mallotojaponin C (**140**) from the leaves of *M.oppositifolius*,

and evaluated cytotoxic activity on human ovarian cancer (A2780) cell line. Compounds **112**, **126**, and **140** showed significant cytotoxic activity against the A2780 human ovarian cancer cell line (IC_{50} 6.3±0.4, 1.10±0.05, and 1.3±0.1 μM, respectively) [15, 51]. Recently, five prenylflavonoids, 6-prenylnaringenin (**52**), 7-*O*-methyl-6-prenylnaringenin (**53**), 4′-*O*-methyl-6-prenylnaringenin (**54**), 7-*O*-methyl-8-prenylnaringenin (**55**), and 8-prenylnaringenin (**59**) obtained from *M. conspurcatus* exhibited cervical cancer (HeLa) cells with IC_{50} values ranging from 10.08 to 60.16 μM [29].

3.3.2. Anti-inflammatory and immunoregulatory activities

Besides anti-cancer effects, the anti-inflammatory properties of the extracts and compounds from the *Mallotus* genus have been reported, suggesting their potential to be developed as anti-inflammatory drugs or drug-lead compounds. In 2001, compounds **107**, **112-114**, **117**, **124**, and **127** significantly inhibited NO production on a murine macrophage-like cell line, RAW 264.7, stimulated by lipopolysaccharide (LPS) and interferon-Q (IFN-Q)

An aqueous acetone extract of the pericarps of *M. japonicus* inhibited NO production by a murine macrophage-like cell line, RAW 264.7, which was activated by LPS and interferon-γ (IFN-γ). Seven phloroglucinol derivatives were isolated by Ishii *et al*. from the fruits of *M. japonicus*: 2,6-dihydroxy-3-methyl-4-methoxyacetophenone (**212**), mallotophenone (**112**), mallotojaponin (**127**), butyrylmallotolerin (**117**), mallotochromene (**107**), mallotochromanol (**113**), isobutyrylmallotochromanol (**114**), and isomallotochromanol (**124**). Among these phloroglucinol derivatives, **124** exhibited strong inhibitory activity on NO production with IC_{50} value of 10.7 μM. The phloroglucinol derivatives significantly reduced both the induction of inducible nitric oxide synthase (iNOS) protein and iNOS mRNA expression. NO production by macrophages preactivated with LPS and IFN-gamma for 16 h was also inhibited by the phloroglucinol derivatives [48]. Isomallotochromanol (**124**) and isomallotochromene (**123**) were the most potent in inhibiting cytokine production. The phloroglucinol derivatives significantly reduced these cytokine mRNA expressions [100].

In 2004, three new chalcones from the fruits of *M. philippinensis*, mallotophilippens C (**97**), D (**98**), and E (**99**) inhibited NO production and inducible NO synthase (iNOS) gene expression by a murine macrophage-like cell line (RAW 264.7), which was activated by LPS and recombinant mouse interferon-γ (IFN-γ). Furthermore, they downregulated cyclooxygenase-2 (COX-2) gene, interleukin-6 (IL-6) gene and interleukin-1β (IL-1β) gene expressions. These results suggest that they have anti-inflammatory and immunoregulatory effects [43].

Analgesic and anti-inflammatory activities of *M. repandus* were evaluated using acetic acid induced writhing test, xylene induced ear edema, cotton pellet induced granuloma, and tail immersion methods at doses of 500, 1000, and 2000 mg/kg body weight. The extract of *M. repandus* exhibited considerable antinociceptive and anti-inflammatory activities against four classical models of pain. In acetic acid induced writhing, xylene induced ear edema, and cotton pellet granuloma models, the extract revealed dose dependent activity. These findings suggest that this plant can be used as a potential source of new antinociceptive and anti-inflammatory candidates. [101]. In 2016, Gangwar *et al*. evaluated the anti-inflammatory, analgesic, and hypnotic activity of fruit extract *M. philippinensis* in different rat experimental models. The study revealed that the extract of *M. Philippinensis* was effective in reducing acute and subacute inflammation and showed effective and similar analgesic activity [102]. In 2019, two new diterpenoids, malloconspur A (**258**) and malloconspur B (**259**), and sixteen known terpenoids were isolated from the ethanol extract of *M. conspurcatus*. Malloconspur B (**259**) and 17-hydroxycleistantha-12,15-dien-3-one (**250**) substantially inhibited NO production with IC_{50}

values of 10.47 µM and 9.32 µM, respectively. Compounds **258**, **259**, and **260** markedly reduced the secretion of PGE2 and TNF-α, LPS-induced in RAW264.7 cells. Compounds **249** and **250** significantly decreased iNOS, NF-κB/p65, and COX-2 protein expressions [79].

3.3.3. Antioxidant and hepatoprotective activities

Betulinic (**228**), 3-(1-C-*β*-D-glucopyranosyl)-2,6-dihydroxy-5-methoxybenzoic acid (**151**), 2,4,8,9,10-pentahydroxy-3,7-dimethoxyanthracene-6-*O*-*β*-D-rhamnopyranoside (**217**), and bergenin (**155**) were isolated from the leaves of *M. roxburglzimms*. Compounds **228**, **151, 217**, and **155** inhibited encouraging antioxidant activities [63]. In 2008, from the leaves of *M. japonicus* some compounds have been isolated and evaluated for radical-scavenging activity. Mallotinic acid (**174**) , corilagin (**170**), geraniin (**173**), and especially mallotusinic acid (**176**) showed strong DPPH radical-scavenging activities [72]. Bergenin (**155**), a major constituent of the water extract of *M. japonicus* cortex, exerted hepatoprotective activity against CCl4-, GalN- and D-galactosamine induced in primary cultured rat hepatocytes [103-105]. In 2015, two new chalcone derivatives, mallotoate A (**100**) and mallotoate B (**97**), were obtained from ethyl acetate fraction of *M.philippensis*. Compounds **97** and **100** were evaluated for their antioxidant activities in DPPH radical scavenging activity, of which, compound **97** showed maximum and competitive activity (91.43±0.82 %) against control drugs [44].

In 2018, eight compounds, 3,4,8,9,10-pentahydroxydibenzo[b,d]pyran-6-one (**15**), gallic acid (**141**), methyl gallate (**142**), corilagin (**170**), repandinin B (**183**), mallophenol A (**149**), (+)-lyoniresinol-3α-*O*-α-L-rhamnopyranoside (**196**), and (*Z*)-3-hexenyl-β-D-glucopyranoside (**324**) were isolated from the active fractions of *M. furetianus*. Compounds **149**, **196**, and **324** revealed potent anti-steatosis activities in the oleic acid (OA)-induced steatosis cell model, with the minimum effective concentration of 0.05, 0.0005 and 0.0005 µg/mL, respectively, which were much lower than the positive control, fibrate (72.4 µg/mL). In 2008, the hepatoprotective activities of malloapelins A–C (**27**, **43**, and **44**) from *M. apelta* [16] were assessed by measuring their effects on the cell survival rate. Those compounds showed inhibitory activity at 10^{-4} M *in vitro* without any cytotoxic effects. Compared with the positive control, bicyclol and other natural products such as silybin (45.5 % at 50 µM), which is well-known to show potent hepatoprotective activity, malloapelin C (**44**) showed promising activity against D-galactosamine-induced toxicity in WB-F344 rat hepatic epithelial stem-like cells [21].

3.3.4. Antibacterial and antifungal activities

In 2014, kamalachalcone E (**86**), 1-(5,7-dihydroxy-2,2,6-trimethyl-2H-1-benzopyran-8-yl)-3-phenyl-2-propen-1-one (**87**), 4′-hydroxyrottlerin (**89**) and rottlerin (**101**) were reported from the fruits of *M. philippinensis*. Compounds **86**–**87**,**89** and **101** were evaluated for antifungal activity against different human pathogenic yeasts and filamentous fungi. The antiproliferative activity of the compounds was also evaluated against Thp-1 cell lines. As a result, both compounds **86** and **87** exhibited antifungal activity against *Cryptococcus neoformans* PRL518, *C. neoformans* ATCC32045, and *Aspergillus fumigatus* with IC_{50} values of 8, 4, and 16 µg/mL, respectively. Compound **89** showed 54 % growth inhibition of Thp-1 cell lines at a concentration of 100 µg/mL [40]. Besides antioxidant activity, both compounds **100** and **101** from *M. philippinensis* showed significant fungicidal activity against *Cladosporium cladosporioides* [44]. In 2019, compounds **88** and **89** from the fruits of *M. philippinensis* showed significant antibacterial activities against *M. luteus*, *S. mutans*, *B. cereus*, *S. aureus*, and *E. coli*, with MIC values ranging from 3.8 to 15.5 µM [19].

In 2020, acronyculatin S (**110**), acronyculatin T (**210**), mallotojaponin C (**140**), and bergenin (**155**) were reported from the leaves of *M. oppositifolius* and showed inhibitory activity against the bacterial strains *E. coli*, *S. aureus*, *S. typhi*, *P. aeruginosa* with MIC values ranging from 3.125 to 50 µg/mL [15].

3.3.5. Antiviral activity

The extract from *M. apelta* was evaluated for inhibitory activities of murine retroviral reverse transcriptase and human DNA polymerases and shown by its low IC_{50} values for reverse transcriptase (0.4–0.5 µg/mL) and DNA polymerase-α (0.9–1.4 µg/mL) [106]. In 2006, Xu *et al*. evaluated the inhibitory effect of the root of *M. apelta* on duck hepatitis B virus (D-HBV) *in vivo*. The root of *M. apelta* was found to exhibit therapeutic effects on D-HBV. It can restrain the duplication of D-HBV *in vivo*. Thus, *M. apelta* is an effective, safe and economical drug for hepatitis B [107]. In 2010, malloapeltic acid (**48**) from the roots of *M. apelta,* which showed strong anti-HIV activity *in vitro* [33]. Nineteen phloroglucinol derivatives from *M. japonicus* were isolated and evaluated for their capacity to inhibit the replication of herpes simplex virus type 1 (HSV-1). All compounds inhibited the replication of HSV-1 with ED_{50}values ranging from0.088to 48.1 µg/mL. Butyrylmallotochromanol (**116**) and isomallotochroman (**125**) were found *in vitro* therapeutic index with 10.9 and 9.1, respectively. This study indicated that compounds **116** and **125** could be an antiviral drug [49]. In 2005, five phloroglucinol derivatives, mallopallidol (**132**), homomallopallidol (**133**), pallidusol (**189**), pallidol (**203**), and dehydropallidusol (**208**) from *M. pallidus* were evaluated for inhibitory effects against herpes simplex virus HSV-1, HSV-2, and human immunodeficiency virus HIV-1. Among them, compounds **132** and **133** showed significant activity against both HSV and HIV viruses. However, their antiviral activity seemed to be accompanied by toxicity, as indicated by their IC_{50} values in Vero cells and PBMCs [58].

3.3.6. Other activities

Compounds **126** and **140** from *M. oppositifolius* showed potent antimalarial activity against chloroquine-resistant *Plasmodium falciparum* with IC_{50} values of 0.75±0.30 and 0.14±0.04 µM [51]. Benzopyrans were reported from the leaves of *M. apela*. All compounds were tested for their antibacterial activity against *Staphylococcus aureus, Micrococcus lutens, Pseudomonas aeruginosa,* and *Escherichia coli*. 4-Hydroxy-2,6-dimethyl-6-(3,7-dimethyl-2,6-octadienyl)-8-(3-methyl-2-butenyl)-2H-1-benzopyran-5,7(3H,6H)-dione (**9**) showed antibacterial activity with an MIC value of 7.34 µg/mL [12]. In 2015, twelve compounds were reported from the leaves of *M. oppositifolius*. *In vitro* trypanocidal and antileishmanial activities of all above compounds were evaluated. Among them, allopposinol (**122**) and aspidinol B (**211**) showed weak antileishmanial activities against *Leishmania donovani* promastigotes, with EC_{50} values of 21.3 and 38.8 µM, respectively. Methylene-bis-aspidinol (**111**) exhibited trypanocidal activity against *Trypanosoma brucei* trypomastigotes with LC_{100} value of 0.8 µM, similar to the positive control, pentamidine (LC_{100} of 0.4 µM). Hosokawa *et al.* reported kaempferol-3-*O*-rutinoside (**58**), quercetin (**72**), isoquercitrin (**80**), rutin (**81**), quercitrin (**83**)[17], and phyllanthusiin D (**191**) from the leaves of *M.japonicus*. These compounds were found to suppress AhR transformation in a concentration-dependent manner, with IC_{50} values of 0.12 µM (**191**), 0.45 µM (**72**), 0.97 µM (**80**), and 16 µM (**81**) against 1 nM 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced AhR transformation [75].

4. CONCLUSION

All the above-mentioned researches have shown that *Mallotus* is an important genus in the Euphorbiaceae family, but chemical and biological studies are still limited, representing an opportunity to find new bioactive substances. The chemical constituent features of benzopyrans, coumarins, flavonoids, and phloroglucinols have led them to be considered markers of the genus. However, the pre-clinical pharmacological studies found in this review exhibited low methodological quality, which hinders the unambiguous interpretation of the results. It is still noteworthy that several gaps need to be addressed for better applying of the genus *Mallotus*. This review provides the medicinal potential and basic understanding of the genus *Mallotus* for further research on the application of medicinal plants. The review is a compilation of information about the *Mallotus* genus that should be investigated by cytotoxic assays to develop new drugs for the treatment of cancer diseases and symptoms.

CRediT authorship contribution statement. Author 1: Conceptualization, Methodology, Writing-Original Draft, Data analysis. Authors 2-8: Review and Editing. Author 9: Supervision, Methodology, Review.

Declaration of competing interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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