Review article

Traditional uses and pharmacological properties of *Clerodendrum* phytochemicals

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ABSTRACT

Clerodendrum is a genus of *ca.* 500 species in the family Lamiaceae and widely distributed throughout the whole world. Up to now, many species of this genus have been described in various indigenous systems of medicine and are used in preparation of folklore medicines for the treatment of various life-threatening diseases, and more than eleven species of the *Clerodendrum* genus have been very well studied for their chemical constituents and biological activities, and 283 compounds, including mono-terpene and its derivatives, sesquiterpene, diterpenoids, triterpenoids, flavonoid and flavonoid glycosides, phenylethanoid glycosides, steroids and steroid glycosides, cyclohexylethanoids, anthraquinones, cyanogenic glycosides, and others have been isolated and identified. Pharmacological studies have shown that these compounds and extracts from the *Clerodendrum* genus have extensive activities, such as anti-inflammatory and anti-nociceptive, anti-oxidant, anti-hypertensive, anticancer, antimicrobial, anti-diarrheal, hepatoprotective, hypoglycemic and hypolipidemic, memory enhancing and neuro-protective, and other activities. In this review, we attempt to highlight over phytochemical progress and list the phytoconstituents isolated from the genus *Clerodendrum* reported so far. The biological activities of this genus are also covered.

1. Introduction

Clerodendrum is a genus of flowering plants in the family Lamiaceae (Verbenaceae).[1] Its common names include glorybower, bagflower, and bleeding-heart. Estimates of the number of species in *Clerodendrum* vary widely, from about 150[2] to about 500,[1] and is native to tropical and warm temperate regions of the world, with most of the species occurring in tropical Africa and southern Asia, but with a few in the tropical Americas and northern Australasia, and a few extending north into the temperate zone in eastern Asia.[3] *Clerodendrum* is a genus of small trees, shrubs, lianas, and sub herbaceousperennials. There are 40 species in mainland China, mainly spread in southern and southwest regions, including *Clerodendrum serratum*, *Clerodendrum inerme*, *Clerodendrum bungei*, *Clerodendrum phlomidis*, *C. serratum* var. amplexifolium, *Clerodendron infortunatum*, *Clerodendrum trichotomum*, *Clerodendrum chinense*, *Clerodendrum petasites*, *Clerodendrum grayi*, *Clerodendrum indicum*, and so on. *C. trichotomum* is a common ornamental in warmer parts of the world.[3] Eight other species are also grown in the tropics for their abundant and attractive flowers.[4] Both butterflies and hummingbirds are often attracted by blooming *Clerodendrum*.

Plants belonging to genus *Clerodendrum* are well known for their pesticidal properties,[5] and various *Clerodendrum* species like *C. indicum*, *C. phlomidis*, *C. serratum* var. amplexifolium, *C. trichotomum*, *C. chinense*, *C. petasites*, etc. have been historically used as folk and traditional medicine to treat many kinds of diseases, such as cold, hyperpyrexia, asthma, furunculosis, hypertension, rheumatism, dysentery, mammitis, toothache, anorexia, leucoderma, leprosy, arthrophlogosis, and other inflammatory disease in various parts of the world such as India, China, Korea,

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Japan, Thailand, and Africa.[6–9] The traditional or ethnomedical claims of the species have also been evaluated. The biological activities of these species described in ancient literature have been reported to be associated with the chemical constituents present in the species.

A variety of constituents have been isolated and characterized from this genus, including: monoterpene and its derivatives,[10] sesquiterpene,[11] diterpenoids,[12,13] triterpenoids,[14,15] flavonoid and flavonoid glycosides,[16] phenylethanoid glycosides,[17,18] steroids and steroid glycosides,[19] cyclohexylethanoids,[20] anthraquinones,[21] cyanogenic glycosides,[22] and others. Some of these constituents have been evaluated with a number of biological properties, mainly including anti-inflammatory and anti-nociceptive, anti-oxidant, anti-hypertensive, anticancer, antimicrobial, anti-diarrheal, hepatoprotective, hypoglycemic and hypolipidemic, memory enhancing and neuroprotective, and other activities.

In this review, we will summary all identified chemical constituents and biological activities from the genus *Clerodendrum* over the past few decades. It will provide a basis for the development of therapeutic agents and utilization of these plants in forthcoming studies.

2. Phytochemistry

To the best of our knowledge, over 280 chemical constituents have been isolated and identified from different species of the genus *Clerodendrum*, These compounds could be divided into: **27** monoterpene and its derivatives, **3** sesquiterpene, **58** diterpenoids, **31** triterpenoids, **43** flavonoid and flavonoid glycosides, **40** phenylethanoid glycosides, **43** steroids and steroid glycosides, **13** cyclohexylethanoids, **4** anthraquinones, **2** cyanogenic glycosides, and **19** others (Table 1). With respect to isolated phytochemicals of the genus, aerial parts, roots and leaves were the most common targets of investigation for bioactive principles and most of these compounds were reported from *C. serratum*, *C. inerme*, *C. bungei*, *Clerodendrum incisum*, *C. infortunatum*, and *C. trichotomum*. Diterpenoids, flavonoids, phenylethanoid glycosides, and steroids are abundant and major bioactive principles of this genus.

2.1. Monoterpene and its derivatives

Monoterpenes are a class of terpenes that consist of two isoprene units and have the molecular formula $C_{10}H_{16}$. Monoterpenes may be linear (acyclic) or contain rings. Most monoterpenes are fragrant and the main composition of essential oil. **Twenty-seven** monoterpenes and derivatives (**1**–**27**) were isolated from the roots, leaves, aerial parts of *C. serratum*, *C. inerme*, *C. incisum*, *C. trichotomum*, *Clerodendrum ugandense*, and *C. chinense*.

2.2. Sesquiterpenes

Sesquiterpenes are bitter substances and a class of terpenes that consist of three isoprene units and have the molecular formula $C_{15}H_{24}$. They often contain α, β-unsaturated-γ-lactone as a major structural feature. In recent studies, sesquiterpenes have been associated with anti-tumor, cytotoxic, and anti-microbial activities. But, only **three** sesquiterpenes (**28**–**30**) were obtained from the aerial parts and roots of *C. inerme* and *C. bungei*, respectively.

2.3. Diterpenoids

To date, **fifty-eight** diterpene compounds (**31**–**88**) have been isolated and identified from this genus, and all of them are labdane diterpenoids. These compounds can be sorted to five types based

Table 1
The phytochemicals obtained from the *Clerodendrum* genus plants.

No.	Phytochemicals	Plant parts	Source	Ref.
Monoterpene and its derivatives				
1	Serratumin A	Aerial parts	*C. serratum*	23
2	Serratoside A	Aerial parts	*C. serratum*	24
3	Serratoside B	Aerial parts	*C. serratum*	24
4	7-*O*-p-couma-royloxyugandoside	Aerial parts	*C. serratum*	25
5	Monomelittoside	Aerial parts	*C. inerme*	26
6	Melittoside	Aerial parts	*C. inerme*	27
7	Sammangaoside C	Aerial parts	*C. inerme*	28
8	Inerminosides A	Leaves	*C. inerme*	10
9	Inerminosides C	Leaves	*C. inerme*	10
10	Inerminosides D	Leaves	*C. inerme*	10
11	Inerminoside C heptaacetate	Aerial parts	*C. inerme*	29
12	Inerminoside A	Aerial parts	*C. inerme*	29
13	Inerminoside A hexaacetate	Aerial parts	*C. inerme*	29
14	Inerminoside B	Aerial parts	*C. inerme*	29
15	Inerminoside B heptaacetate	Aerial parts	*C. inerme*	29
16	8-*O*-foliamenthoyleuphroside	Roots	*C. incisum*	30
17	2′-*O*,8-*O*-difoliamenthoyleuphroside	Roots	*C. incisum*	30
18	Euphroside	Roots	*C. incisum*	30
19	Plantarenaloside	Roots	*C. incisum*	30
20	Aucubin	Whole plants	*C. thomsonae*	27
21	8-*O*-acetylharpagide	Whole plants	*C. thomsonae*	27
22	Harpagide	Whole plants	*C. thomsonae*	27
23	Ajugoside	Leaves	*C. thomsonae*	27
24	8-*O*-acetylmioporoside	Whole plants	*C. thomsonae*	27
25	Reptoside	Whole plants	*C. thomsonae*	27
26	Ugandoside	Whole plants	*C. ugandense*	27
27	5-*O*-β-glucopyranosyl-harpagide	Aerial parts	*C. chinense*	31
Sesquiterpene				
28	Sammangaoside A	Aerial parts	*C. inerme*	28
29	Sammangaoside B	Aerial parts	*C. inerme*	28
30	2-{(2S,5R)-5-[(1E)-4-hydroxy-4-methylhexa-1,5-dien-1-yl]-5-methyltetrahydrofuran-2-yl}propan-2-yl-β-D-glucopyranoside	Roots	*C. bungei*	32
Diterpenoids				
31	Mandarone A	Stems	*C. mandarinorum*	33
32	Mandarone B	Stems	*C. mandarinorum*	33
33	Mandarone C	Stems	*C. mandarinorum*	33
34	Crolerodendrum A	Whole plants	*C. philippinum*	25
35	Bungone A	Stems	*C. bungei*	34
36	Bungone B	Stems	*C. bungei*	34
37	Inerme A	Leaves	*C. inerme*	35
38	Inerme B	Leaves	*C. inerme*	35
39	14,15-dihydro-15β-methoxy-3-epicaryoptin	Leaves	*C. inerme*	35
40	14,15-dihydro-15-hydroxy-3-epicaryoptin	Leaves	*C. inerme*	35
41	Clerodermic acid	Whole plants	*C. inerme*	36
42	Cleroinermin	Whole plants	*C. inerme*	37
43	3-epicaryoptin	Whole plants	*C. paniculatum*	38
44	Clerodin	Whole plants	*C. paniculatum*	38
45	Uncinatone	Stems	*C. trichotomum*	39
		Roots	*C. bungei*	40
		Roots	*C. trichotomum*	41
		Aerial parts	*C. inerme*	42
46	2-acetoxyclerodendrin B	Whole plants	*C. infortunatum*	25
47	Clerodendrin A	Whole plants	*C. trichotomum*	38
48	Clerodendrin B	Whole plants	*C. trichotomum*	38
49	Clerodendrin C	Whole plants	*C. trichotomum*	38
50	Clerodendrin D	Whole plants	*C. trichotomum*	38
51	Clerodendrin E	Whole plants	*C. trichotomum*	38
52	Clerodendrin F	Whole plants	*C. trichotomum*	38
53	Clerodendrin G	Whole plants	*C. trichotomum*	38
54	Clerodendrin H	Whole plants	*C. trichotomum*	38

Table 1 (*continued*)

No.	Phytochemicals	Plant parts	Source	Ref.
55	Trichotomone	Roots	*C. trichotomum*	43
56	Sugiol	Stems	*C. trichotomum*	39
57	Teuvincenone A	Stems	*C. trichotomum*	39
58	Teuvincenone B	Stems	*C. trichotomum*	39
59	Teuvincenone F	Stems	*C. trichotomum*	39
		Roots	*C. bungei*	40
		Roots	*C. trichotomum*	41
60	Teuvincenone H	Stems	*C. trichotomum*	39
61	Cyrtophyllone B	Stems	*C. trichotomum*	39
62	Bungnate A	Roots	*C. bungei*	40
63	Bungnate B	Roots	*C. bungei*	40
64	15-dehydrocyrtophyllone A	Roots	*C. bungei*	40
65	15-dehydro-17-hydroxycyrtophyllone A	Roots	*C. bungei*	40
66	12,16-epoxy-11,14,17-trihydroxy-6-methoxy-17(15→16)-abeo-abieta-5,8,11,13-tetraene-7-one	Roots	*C. bungei*	40
67	Cyrtophyllone A	Roots	*C. bungei*	40
68	Villosin C	Roots	*C. bungei*	40
		Roots	*C. trichotomum*	41
69	19-hydroxyteuvincenone F	Roots	*C. bungei*	40
70	Mandarone E	Roots	*C. bungei*	40
		Roots	*C. trichotomum*	41
71	12,16-epoxy-11,14-dihydroxy-6-methoxy-17(15→16)-abeo-abieta-5,8,11,13,15-pentaene-3,7-dione	Roots	*C. bungei*	40
		Roots	*C. trichotomum*	41
72	12-*O*-β-ᴅ-glucopyranosyl-3,11,16-trihydroxyabieta-8,11,13-triene	Roots	*C. bungei*	40
73	6-methoxyvillosin C	Roots	*C. trichotomum*	41
74	18-hydroxy-6-methoxyvillosin C	Roots	*C. trichotomum*	41
75	(10*R*,16*S*)-12,16-epoxy-11,14-dihydroxy-6-methoxy-17(15→16)-abeo-abieta-5,8,11,13-tetraene-3,7-dione	Roots	*C. trichotomum*	41
76	(10*R*,16*S*)-12,16-epoxy-11,14-dihydroxy-18-oxo-17(15→16),18(4→3)-diabeo-abieta-3,5,8,11,13-pentaene-7-one	Roots	*C. trichotomum*	41
77	(10*R*,16*R*)-12,16-epoxy-11,14,17-trihydroxy-17(15→16),18(4→3)-diabeo-abieta-3,5,8,11,13-pentaene-2,7-dione	Roots	*C. trichotomum*	41
78	(3*S*,4*R*,10*R*,16*S*)-3,4:12,16-diepoxy-11,14-dihydroxy-17(15→16),18(4→3)-diabeo-abieta-5,8,11,13-tetraene-7-one	Roots	*C. trichotomum*	41
79	12,16-epoxy-11,14-dihydroxy-6-methoxy-17(15→16)-abeo-abieta-5,8,11,13,15-pentaene-3,7-dione	Roots	*C. trichotomum*	41
80	Formidiol	Roots	*C. trichotomum*	41
81	Teuvincenone E	Roots	*C. trichotomum*	41
82	12,16-epoxy-17(15→16),18(4→3)-diabeo-abieta-3,5,8,12,15-pentaene-7,11,14-trione	Roots	*C. trichotomum*	41
83	3β-(β-ᴅ-glucopyranosyl)isopimara-7,15-diene-11α,12α-diol	Roots	*C. bungei*	44
84	16-O-β-ᴅ-glucopyranosyl-3β-20-epoxy-3-hydroxyabieta-8,11,13-triene	Roots	*C. bungei*	44
85	Coleon U	Whole plants	*C. canescens*	45
86	Coleon U-12-methyl ether	Whole plants	*C. canescens*	45

Table 1 (*continued*)

No.	Phytochemicals	Plant parts	Source	Ref.
87	Cleroserroside A	Aerial parts	*C. serrartum*	46
88	Cleroserroside B	Aerial parts	*C. serrartum*	46
Triterpenoids				
89	3-*O*-acetyloleanolicacid	Aerial parts	*C. inerme*	42
90	3-*O*-acetyloleanolicaldehyde	Aerial parts	*C. inerme*	42
91	Glutinol	Aerial parts	*C. inerme*	42
92	Friedelin	Leaves	*C. trichotomum*	47
		Aerial parts	*C. inerme*	48
93	Taraxerol	Roots	*C. indicum*	49
		Whole plants	*C. bungei*	50
		Leaves	*C. trichotomum*	47
94	Clerodone	Whole plants	*C. bungei*	51
95	α-amyrin	Whole plants	*C. bungei*	51
96	Glochidone	Whole plants	*C. bungei*	50
97	Glochidonol	Whole plants	*C. bungei*	50
98	Glochidiol	Whole plants	*C. bungei*	50
99	Lupeol	Roots	*C. indicum,* *C. villosum*	49,52
		Leaves	*C. trichotomum*	47
		Whole plants	*C. canescens*	51
		Aerial parts	*C. inerme*	42
100	α-amyrin 3-undecanotate	Whole plants	*C. canescens*	51
101	Lupeol acetate	Whole plants	*C. canescens*	51
102	Lupeol 3-palmitate	Whole plants	*C. canescens*	51,52
103	Melastomic acid	Whole plants	*C. canescens*	51
104	β-amyrin acetate	Whole plants	*C. canescens*	51
105	Betulinic acid	Roots	*C. villosum*	49,52
		Aerial parts	*C. inerme*	53
		Leaves	*C. trichotomum*	47
		Whole plants	*C. canescens*	51
106	Magnificol	Aerial parts	*C. inerme*	42
107	Glutinone	Aerial parts	*C. inerme*	42
108	Mi-saponin	Roots	*C. wildii*	54
109	Basic acid	Roots	*C. wildii*	54
110	Protobassic	Roots	*C. wildii*	54
111	Mi-glycoside I	Roots	*C. wildii*	54
112	Ursolic acid	Roots	*C. japonicum*	55
113	3β-hydroxy-D:B-friedo-olean-5-ene	Roots	*C. indicum,* *C. villosum*	49
114	Oleanolic acid	Whole plants	*C. serratum*	56
115	Oleanolic acid-3-acetate	Roots	*C. indicum*	49
116	Taraxerol-3β-yloctacosanoate	Roots, stems	*C. philippinum*	57
117	Se-saponin	Aerial parts	*C. serratum*	58
118	Lup-1,5,20(29)-trien-3-*O*-ᴅ-glucopyranoside	Leaves	*C. inerme*	59
119	Clerodendrumic acid	Leaves	*C. glabrum*	60
Flavonoid and flavonoid glycosides				
120	5,7,8,4′-tetrahydroxy-6-methoxy-flavone	Aerial parts	*C. serratum*	23
121	5,6,7-trihydroxy-4′-methoxyflavone 7-glucopyranoside	Aerial parts	*C. serratum*	23
122	5, 7, 4′-trihydroxy-3′-methoxyflavone	Whole plants	*C. serratum*	25
123	Astragalin	Whole plants	*C. philippinum*	61
124	Apigenin	Aerial parts	*C. inerme*	48
125	Tricin	Whole plants	*C. japonicum*	25
126	Hispidulin	Roots	*C. indicum*	62
127	Hispidulin-glucuronide	Whole plants	*C. infortunatum*	63
128	Eupafolin	Whole plants	*C. infortunatum*	63
129	Scutellarin	Whole plants	*C. infortunatum*	63
130	Scutellarein	Whole plants	*C. serratum*	64
131	Pectolinarigenin	Aerial parts	*C. inerme*	65
132	7-hydroxyflavone	Flowers	*C. phlomidis*	66
133	7-hydroxyflavanone 7-*O*-glucoside	Flowers	*C. phlomidis*	66
134	Luteolin	Whole plants	*C. serratum*	64
135	Chalcone glycoside	Flowers	*C. phlomidis*	66
136	α-ʟ-Rhamnopyranosyl-(1→2)-α-D-Glucopyranosyl-7-*O*-naringin-4-ᴅ-glucopyranoside-5-methylether	Whole plants	*C. phlomidis*	25

Table 1 (continued)

No.	Phytochemicals	Plant parts	Source	Ref.
137	4,2′,4′-trihydroxy-6′-methoxy ehalcone-4,4′-α-D-diglucoside	Whole plants	C. phlomidis	25
138	7-hydroxyflavonone	Flowers	C. phlomidis	66
139	Kaempferol	Whole plants	C. fragrans	67
140	5,4′-dihydroxy-kaempferol-7-O-β-rutinoside	Whole plants	C. fragrans	67
141	6-hydroxyflavone	Flowers	C. phlomidis	66
142	4′-methyl scutellarein	Aerial parts	C. inerme	65
143	Apigenin-7-O-glucuronide	Roots	C. serratum	68
144	5-hydroxy-4′, 7-dimethoxymethyl flavone	Whole plants	C. inerme	25
145	Salvigenin	Aerial parts	C. inerme	65
146	Acacetin	Leaves	C. inerme	69
		Aerial parts	C. inerme	48
147	Cynaroside	Aerial parts	C. inerme	13
148	2′,4,4′-trihydroxy-6′-methylchalcone	Flowers	C. phlomidis	66
149	Cirsimaritin	Aerial parts	C. petasites	70
150	Cirsimaritin-4′-glucoside	Aerial parts	C. mandarinorum	71
151	Quercetin-3′-methyl	Aerial parts	C. mandarinorum	71
152	Pectolinarigenin	Roots	C. indicum	49
153	5-hydroxy-6,7,4′-trimethoxyflavone	Aerial parts	C. inerme	53
154	5,7,4′-trihydroxy-flavone	Leaves	C. trichotomum	72
		Whole plants	C .serratum	56
155	5,7,4′-trihydroxy-3′-methoxyflavone	Whole plants	c. serratum	73
156	3,2′,3′-trihydroxy-4′-methoxychalcone	Seeds	C. phlomidis	74
157	3,2′-dihydroxy-4′,6′-dimethoxychalcone	Seeds	C. phlomidis	74
158	5-hydroxy-7-methoxyflavanone	Seeds	C. phlomidis	74
159	5-hydroxy-7-methoxyflavone	Seeds	C. phlomidis	74
160	Kaempferol-3-O-α-L-rhamnopyranoside	Seeds	C. phlomidis	74
161	Hispidulin7-O-glucuronide	Aerial parts	C. infortunatum	63
162	Naringin-4′- O-α-glucopyranoside	Flowers	C. phlomidis	66
Phenylethanoid glycosides				
163	Decaffeoylverbascoside	Aerial parts	C. inerme	75
164	Darendoside B	Roots	C. bungei	40
165	Salidroside	Aerial parts	C. inerme	25
166	Verbascoside	Roots	C. bungei	40
		Roots	C. villosum	49
		Aerial parts	C. inerme	75
167	Isoverbascoside	Aerial parts	C. inerme	75
168	Campneoside I	Aerial parts	C. bungei	76
		Aerial parts	C. inerme	75
169	Cistanoside E	Aerial parts	C. inerme	75
170	Purpureaside B	Aerial parts	C. inerme	75
171	2-phenylethyl-3-O-(6-dexoy-α-L-mannopyranosyl)-β-D-glucopyranoside	Roots	C. bungei	32
172	Campneoside II	Aerial parts	C. bungei	76
173	Martynoside	Whole plants	C. japonicum	55
174	Jionoside D	Aerial parts	C. trichotomum	77
175	Clerodendronoside	Aerial parts	C. bungei	76
176	Cistanoside C	Aerial parts	C. bungei	76
177	Jionoside C	Aerial parts	C. bungei	76
178	Leucosceptoside A	Roots	C. bungei	40
		Aerial parts	C. bungei	76
179	Cistanoside D	Aerial parts	C. bungei	76
180	Cistanoside F	Aerial parts	C. bungei	76
181	Bungein A	Aerial parts	C. bungei	78
182	Monoacetylmartinoside	Whole plants	C. japonicum	55
183	Clerodenoside A	Whole plants	C. japonicum	55
184	3,4-dihydroxyphenylethanol	Whole plants	C. indicum	25
185	Isomartynoside	Roots	C. bungei	40
186	Serratumoside A	Aerial parts	C. serratum	79

Table 1 (continued)

No.	Phytochemicals	Plant parts	Source	Ref.
187	Bunginoside A	Roots	C. bungei	40
188	3″,4″-di-O-acetylmartynoside	Roots	C. bungei	40
189	Acetylmartynoside A	Roots	C. bungei	40
190	Acetylmartynoside B	Roots	C. bungei	40
191	3″-O-acetylmartynoside	Roots	C. bungei	40
192	2″-O-acetylmartynoside	Roots	C. bungei	40
193	Martynoside	Roots	C. bungei	40
194	Trichotomoside	Roots	C. bungei	40
195	O-2-(3-hydroxy-4-methoxyphenyl)-ethyl O-2,3-di-O-acetyl-α-L-rhamnopyranosyl-(1→3)-(4-O-cis-feruloyl)-β-D-glucopyranoside	Roots	C. bungei	40
196	Isoacteoside	Roots	C. bungei	40
		Aerial parts	C. bungei	76
197	Darendoside A	Roots	C. bungei	40
198	Phlomisethanoside	Roots	C. bungei	40
199	Acteoside	Aerial parts	C. bungei	76
		Whole plants	C. serratum	56
200	Markhamioside F	Aerial parts	C. inerme	75
201	Benzylglucoside	Aerial parts	C. inerme	75
202	Myricoside	Aerial parts	C. serratum	79
Steroids and steroid glycosides				
203	Stigmasterol	Roots	C. indicum	49
		Leaves	C. trichotomum	47
		Whole plants	C. serratum	56
204	α-spinasterol	Whole plants	C. serratum	64
205	Stigmasterol-3-O-β-D-glucopyranoside	Roots	C. indicum	49
		Whole plants	C. serratum	73
206	Serratin	Whole plants	C. serratum	80
207	Clerosterol	Roots	C. indicum, C. villosum	49
		Leaves	C. quadriloculare	81
		Leaves	C. trichotomum	47
208	Bungesterol	Whole plants	C. bungei	51
209	4α-methyl-24β-ethyl-5α-cholesta-14,25-dien-3β-ol	Aerial parts	C. inerme	36
210	4α,24,24-trimethyl-5α-cholesta-7,25-dien-3β-ol	Whole plants	C. inerme	62
211	4α-methyl-24β-ethyl-5α-cholesta-7,25-dien-3β-ol	Whole plants	C. inerme	62
212	Gramisterol	Whole plants	C. inerme	62
213	4α-methyl-24α-ethyl-5α-cholest-7-en-3β-ol	Whole plants	C. inerme	62
214	Obtusifoliol	Whole plants	C. inerme	62
215	24,24-dimethyl-5α-cholesta-7,25-dien-3β-ol	Whole plants	C. inerme	62
216	22,23-dihydrostigmasterol	Whole plants	C. japonicum	55
217	25,26-dehydrostigmasterol	Whole plants	C. japonicum	55
218	22-dehydroclerosterol 3β-O-β-D-(6′-O-margaroyl)-glucopyranoside	Leaves	C. trichotomum	82
		Whole plants	C. quadriloculare	81
219	Sitosterol	Leaves	C. trichotomum	47
220	Stigmasterol	Aerial parts	C. inerme	48
221	24β-methylcholesta-5,22E,25-trien-3β-ol	Whole plants	C. fragrans	83
222	24α-ethyl-5α-cholest-22E-en-3β-ol	Whole plants	C. fragrans	83
223	Colebrin A	Aerial parts	C. colebrookianum	84
224	Colebrin B	Aerial parts	C. colebrookianum	84
225	Colebrin C	Aerial parts	C. colebrookianum	84
226	Colebrin D	Aerial parts	C. colebrookianum	84
227	Colebrin E	Aerial parts	C. colebrookianum	84
228	Dehydropo-riferasterol	Aerial parts	C. splendens	25
229	Campesterol	Stems	C. phlomidis	85
230	Cholestanol	Stems	C. phlomidis	85
231	(22E)-stigmasta-4,22,25-trien-3-one	Roots	C. indicum	49
232	Stigmasta-4,25-dien-3-one	Roots	C. indicum	49
233	Stigmasta-4,22-dien-3-one	Roots	C. indicum	49
234	22-dehydroclerosterol	Roots	C. indicum, C. villosum,	49

Table 1 (*continued*)

No.	Phytochemicals	Plant parts	Source	Ref.
		Leaves	*C. quadriloculare*	81
		Leaves	*C. trichotomum*	47
235	β-sitosterol	Roots	*C. villosum*	49
		Aerial parts	*C. inerme*	53
		Whole plants	*C. bungei*	50
236	22-dehydroclerosterol-3-*O*-β-D-glucopyranoside	Roots	*C. indicum*, *C. villosum*	49
237	Clerosterol-3-*O*-β-D-glucopyranoside	Roots	*C. indicum*, *C. villosum*	49
238	β-sitosterol-3-*O*-β-D-glucopyranoside	Roots	*C. villosum*	49
239	(22E,24R)-stigmasta-4,22,25-trien-3-one	Leaves	*C. trichotomum*	82
240	(20R,22E,24R)-3β-hydroxy-Stigmasta-5,22,25-trien-7-one	Leaves	*C. trichotomum*	82
241	(20R,22E,24R)-stigmasta-22,25-dien-3,6-dione	Leaves	*C. trichotomum*	82
242	(20R,22E,24R)-6β-hydroxy-Stigmasta-4,22,25-trien-3-one	Leaves	*C. trichotomum*	82
243	(20R,22E,24R)-stigmasta-5,22,25-trien-3β,7β-diol	Leaves	*C. trichotomum*	82
244	(20R,22E,24R)-stigmasta-22,25-dien-3β,6β,9α-triol	Leaves	*C. trichotomum*	82
245	Bis(2-ethylhexyl)phthalate	Whole plants	*C. serratum*	56
Cyclohexylethanoids				
246	1-hydroxy-1-(8-palmitoyloxyethyl)cyclohexanone	Leaves	*C. trichotomum*	20
247	5-*O*-butyl cleroindin D	Leaves	*C. trichotomum*	20
248	Rengyolone	Leaves	*C. trichotomum*	20
		Aerial parts	*C. bungei*	86
249	Cleroindin C	Leaves	*C. trichotomum*	20
250	Cleroindin B	Leaves	*C. trichotomum*	20
251	Rengyol	Leaves	*C. trichotomum*	20
252	Clerobungin A(**1a**)	Aerial parts	*C. bungei*	86
253	Clerobungin A(**1b**)	Aerial parts	*C. bungei*	86
254	(+)-rengyolone	Aerial parts	*C. bungei*	86
255	Cleroindicin	Aerial parts	*C. bungei*	86
256	5-*O*-ethylcleroindicin D	Aerial parts	*C. bungei*	78
257	6″-*O*-[(E)-caffeoyl]rengyoside B	Roots	*C. bungei*	32
258	Clerodenone A	Roots	*C. bungei*	32
Anthraquinones				
259	Aloe-emodin	Stems	*C. trichotomum*	39
260	Emodin	Stems	*C. trichotomum*	39
261	Chrysophanol	Stems	*C. trichotomum*	39
262	2,5-dimethoxybenzoquinone	Whole plants	*C. serratum*	73
Cyanogenic glycosides				
263	(R)-lucumin	Leaves	*C. grayi*	87
264	(R)-prunasin	Leaves	*C. grayi*	87
Others				
265	B-friedoolean-5-ene-3-β-ol	Aerial parts	*C. inerme*	53
266	Stigmasta-5,22,25-trien-3-β-ol (**3**)	Aerial parts	*C. inerme*	53
267	Spicatolignan B	Stems	*C. trichotomum*	39
268	*Trans*-phytol	Leaves	*C. trichotomum*	47
269	1H-indole-3-carboxylic acid	Leaves	*C. trichotomum*	47
270	Palmitic acid	Leaves	*C. trichotomum*	72
271	Octadecanoic acid	Leaves	*C. trichotomum*	72
272	*Cis*-cinnamic acid	Aerial parts	*C. serratum*	23
273	*Trans*-cinnamic acid	Aerial parts	*C. serratum*	23
274	*P*-coumaric acid	Aerial parts	*C. serratum*	23
275	Syringic acid	Aerial parts	*C. inerme*	48
276	*P*-methoxybenzoic acid	Aerial parts	*C. inerme*	48
277	Daucosterol	Aerial parts	*C. inerme*	48
278	2-({6-O-[(4-hydroxy-3-methoxyphenyl)carbonyl]-β-D-glucopyranosyl}oxy)-2-methylbutanoic acid	Roots	*C. bungei*	32
279	24β-ethylcholesta-5,22E,25-triene-3β-ol	Aerial parts	*C. phlomidis*	88

Table 1 (*continued*)

No.	Phytochemicals	Plant parts	Source	Ref.
280	Pentadecanoic acid β-D-glucoside	Aerial parts	*C. inerme*	66
281	Cryptojaponol	Aerial parts	*C. kiangsiense*	89
282	Fortuning E	Aerial parts	*C. kiangsiense*	89
283	12-methoxy-6,11,14,16-tetrahydroxy-17(15→16)-abeo-5,8,11,13-abietatetraen-3,7-dione	Aerial parts	*C. kiangsiense*	89

on the pentacyclic ring on C_{12}: a furan ring, dihydrofuran ring, lactone ring, α,β-undersaturated lactone ring, and tetrahydrofuran ring. Many of these chemical compounds have shown remarkable bioactivities *in vivo* or *in vitro* study.

2.4. Triterpenoids

So far, a total of **thirty-one** triterpenoids (**89**–**119**), including 3-*O*-acetyloleanolicacid (**89**), 3-*O*-acetyloleanolicaldehyde (**90**), glutinol (**91**), friedelin (**92**), taraxerol (**93**), clerodone (**94**), α-amyrin (**95**), glochidone (**96**), glochidonol (**97**), glochidiol (**98**), lupeol (**99**), α-amyrin 3-undecanotate (**100**), lupeol acetate (**101**), lupeol 3-palmitate (**102**), melastomic acid (**103**), β-amyrin acetate (**104**), betulinic acid (**105**), magnificol (**106**), glutinone (**107**), etc. have been purified and characterized from the whole plants, roots, leaves, or aerial parts of *C. inerme*, *C. trichotomum*, *C. indicum*, *C. bungei*, *Clerodendrum canescens*, *Clerodendrum villosum*, *Clerodendrum wildii*, *Clerodendrum japonicum*, *C. serratum*, *Clerodendrum philippinum*, or *Clerodendrum glabrum*.

2.5. Flavonoid and flavonoid glycosides

Flavonoids, important secondary metabolites, are widespread throughout the plant kingdom. Flavonoids and their derivatives are the main bioactive components of this genus, and receiving extreme attention. Up to now, **forty-three** flavonoid and flavonoid glycosides (**120**–**162**), including astragalin (**123**), apigenin (**124**), and tricin (**125**), hispidulin (**126**), hispidulin-glucuronide (**127**), eupafolin (**128**), scutellarin (**129**), scutellarein (**130**), pectolinarigenin (**131**), 7-hydroxyflavone (**132**), 7-hydroxyflavanone 7-*O*-glucoside (**133**), luteolin (**134**), chalcone glycoside (**135**), etc. have been isolated and identified from the roots, leaves, aerial parts of different *Clerodendrum* species.

2.6. Phenylethanoid glycosides

Phenylethanoid glycosides are another kind of characteristic compounds of the *Clerodendrum* species with antioxidant activity. To date, **forty** phenylethanoid glycosides (**163**–**202**) have been obtained from this genus and the structure contains three parts: sugar chain, phenylacetyl, and coffee-acyl or ferulic-acyl. The sugar chain is often composed of glucose, rhamnose, xylose or arabinose. The phenylacetyl is linked to C_1-glucopyranose, and coffee-acyl or ferulic-acyl is often connected with the C_4 or C_6 of glucose.

2.7. Steroids and steroid glycosides

Steroids are terpenes based on the cyclopentane perhydroxy phenanthrene ring, but they are considered separately because of their chemical, biological and medicinal importance. Steroids are found in nature in free as well as in glycosidic form. There are many steroids reported from plants and they are termed phytosteroids.

Total **forty-three** steroids and steroid glycosides (**203**–**245**) have been obtained and identified from *Clerodendrum* species, mainly from *C. trichotomum*, *Clerodendrum colebrookianum*, and *C. bungei*.

2.8. Cyclohexylethanoids

A series of cyclohexylethanoids (**246**–**258**), including two new compounds 1-hydroxy-1-(8-palmitoyloxyethyl) cyclohexanone (**246**) and 5-*O*-butyl cleroindin D (**247**), together with four known ones, rengyolone (**248**), cleroindin C (**249**), cleroindin B (**250**), rengyol (**251**), were isolated from the leaves of *C. trichotomum*, and the others (**252**–**258**) were obtained and identified from the aerial parts and roots of *C. bungei*.

2.9. Anthraquinones

Only **four** anthraquinones (**259**–**262**), aloe-emodin (**259**), emodin (**260**), chrysophanol (**261**) and 2,5-dimethoxybenzoquinone (**262**), have been isolated and identified from the stem of *C. trichotomum* and *C. serratum*.

2.10. Cyanogenic glycosides

Two cyanogenic glycosides (**263**–**264**), including (*R*)-lucumin (**263**) and (*R*)-prunasin (**264**) have been obtained and identified from the leaves of *C. grayi*.

2.11. Others

A range of other compounds (**265**–**283**) were isolated and identified from the aerial parts, stems, leaves and roots of *C. inerme*, *C. trichotomum*, *C. serratum*, *C. bungei*, *C. phlomidis*, and *Clerodendrum kiangsiense*.

3. Pharmacological properties

Wide clinical uses of traditional Chinese medicine of the genus *Clerodendrum* have inspired researchers to investigate its pharmacological properties and to validate the uses of different species as therapeutic remedy. More and more studies showed that extracts or active compounds isolated from *Clerodendrum* species exhibited a wide range of pharmacological activities (Table 2).

3.1. Anti-inflammatory and anti-nociceptive activities

Many studies have provided data on anti-inflammatory effects of *C. phlomidis*, *C. petasites*, *Clerodendrum laevifolium*, *C. inerme*, *C. bungei*, and *C. serratum* extracts of aerial parts, roots, leaves and stems. Of these, lots of studies have provided data on anti-inflammatory effects of *C. serratum* (Bharangi) extracts of aerial parts, roots and stems. An aqueous extract of roots reported significant anti-inflammatory effects at high dose (180 mg/kg, p.o.) in granuloma pouch model in rats. Roots in low dose (90 mg/kg, p.o.) and stems in high dose (180 mg/kg, p.o.) showed significant preventive effects in comparison with dexamethasone (a standard anti-inflammatory agent). Thus, it can be postulated that roots are more effective than stems and it would be useful as antiallergic and antiinflammatory drug for disease like asthma.[95,96] The methanolic extract of the aerial parts of *C. serratum* was demonstrated dual inhibitory effects on arachidonic acid metabolism or an inhibitor of phospholipase A_2 when studied in ethyl phenylpropiolate-induced ear edema and in carrageenan and arachidonic acid induced hind paw edema in rats, and the extract exerted an inhibitory activity on the acute phase of inflammation due to an inhibition of synthesis and inflammatory mediators release through cyclooxygenase and lipoxygenase pathways.[97] In contrast, the alcoholic root extract of *C. serratum* showed a potent antiinflammatory effect by reducing paw edema (acute) and cotton-pellet granuloma (chronic) in inflammation models.[98] Apigenin-7-glucoside isolated from *C. serratum* roots has been demonstrated for anti-inflammatory effects in rats.[99] The hydro-alcoholic extract (50, 200 and 500 mg/kg dose) of Bharangyadi preparation showed inhibition of carrageenan induced inflammation due to the inhibition of the enzyme cyclooxygenase and subsequent inhibition of prostaglandin synthesis which rationalizes traditional use of this plant in bronchial asthma and related inflammatory conditions.[100] This anti-inflammatory effect of *C. serratum* might be observed due to flavonoids and saponins, but other active substances might also be responsible leading to synergistic effects.

Prakash et al reported that the monomer compound 3-hydroxy, 2-methoxy-sodium butanoate (HMSB, at doses of 25, 50, 100 mg/kg, i.g.) isolated from the leaves of *C. phlomidis* displayed anti-inflammatory and anti-arthritic effects on carrageenan-induced inflammation and freund complete adjuvant (FCA)-induced arthritic rat models. The results showed that HMSB could significantly reduce the paw edema response, decrease lysosomal enzymes, protein-bound carbohydrates, and acute phase protein levels. In addition, HMSB could significantly down-regulate pro-inflammatory cytokines TNF, IL-1 and IL-6 protein levels and mRNA expression in the joints with a dose-dependent manner.[90] These results indicated that the HMSB possess considerable potency in anti-inflammatory action and has a prominent anti-arthritic effect. *Panthong* et al evaluated the anti-inflammatory and antipyretic activities of the methanol extract (at doses of 1.0, 2.0, 4.0 mg/ear, i.g.) from *C. petasites*. The results proved that the extract possessed moderate inhibitory activity on acute phase of inflammation in a dose-related manner on ethyl phenylpropiolate-induced ear edema ($ED_{50} = 2.34$ mg/ear) as well as carrageenan-induced paw edema ($ED_{30} = 420.41$ mg/kg) in rats, and also reduced the alkaline phosphatase activity in serum. Moreover, the extract exhibited an excellent antipyretic effect in yeast-induced hyperthermic rats.[91] The anti-inflammatory and antipyretic effects of the methanol extract may be caused by the inhibition of the prostaglandin synthesis. The ethanol extract from the leaves of *C. laevifolium* exhibited the greatest anti-inflammatory activity against lipoxygenase with the IC_{50} of 14.12 µg/ml *in vitro* study.[92] In addition, the methanolic extract from the aerial parts of *C. inerme* exhibited anti-inflammatory activity at doses of 50, 100 and 200 mg/kg in formalin induced hind paw edema animals.[53] The anti-inflammatory activity of petroleum ether, chloroform, ethyl acetate, alcohol, and aqueous extracts of fresh leaves from *Clerodendrum paniculatum* Linn was evaluated by *in vitro* (human red blood cell membrane stabilization method) and *in vivo* methods (0.1 ml of 1% w/v carrageenan-induced rat paw edema model). Petroleum ether and chloroform extracts which showed, best in vitro anti-inflammatory activity also showed a dose dependent (200 and 400 mg/kg) significant reduction in paw edema when compared to the control (indomethacin, 10 mg/kg).[93]

Srisook et al found that two flavones, hispidulin (**126**) and acacetin (**146**) isolated from the ethyl acetate (EA) extracts from the leaves of *C. inerme* exhibit the most potent inhibitory activity on nitric oxide (NO) production in RAW 264.7 macrophage stimulated with lipopolysaccharide (LPS). Furthermore, IC_{50} values of hispidulin and acacetin were 43.7 ± 4.0 and 43.5 ± 6.4 µM, respectively. Hispidulin also inhibited prostaglandin E_2 (PGE_2) production as well as inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 expressions via the blockade of nuclear factor kappa B (NF-κB) DNA binding activity and the c-Jun NH2-terminal protein kinase (JNK) way.[94]

Table 2
The pharmacological activities of extracts and compounds from the genus *Clerodendrum*.

Pharmacological activities	Extract/Compound	Types	Testing subjects	Dose	Effects	Ref.
Anti-inflammatory and anti-nociceptive activity	3-Hydroxy, 2-methoxy-sodium butanoate	*In vivo*	Carrageenan-induced inflammation and freund complete adjuvant (FCA)-induced arthritic rat models	25, 50, 100 mg/kg, i.g.	Reduced the paw edema response, decrease lysosomal enzymes, protein-bound carbohydrates, and acute phase protein levels	90
	Methanol extract from *C. petasites*	*In vivo*	Ethyl phenylpropiolate-induced ear edema and carrageenan-induced paw edema in rats	1, 2, 4 mg/ear, i.g.	Inhibited prostaglandin synthesis	91
	Ethanol extract from *C. laevifolium*	*in vitro*	lipoxygenase	10—1000 μg/ml	Displayed the greatest inhibition capacity with the IC_{50} value of 14.12 μg/ml	92
	Methanolic extract from *C. inerme*	*In vivo*	Formalin induced hind paw edema animals	50, 100, 200 mg/kg, i.g.	Inhibited main inflammatory mediators	53
	Petroleum ether and chloroform extracts from *C. paniculatum*	*In vitro*	Human red blood cell membrane stabilization method	1000 μg/ml	Showed 57.15% protection and 48.98% protection of HRBC in hypotonic solution, respectively	93
	Petroleum ether and chloroform extracts from *C. paniculatum*	*in vivo*	Carrageenan-induced rat paw edema model	200 400 mg/kg, i.g.	Inhibited of the cyclooxygenase leading to inhibition of prostaglandin synthesis	93
	Hispidulin	*In vitro*	RAW 264.7 macrophage stimulated with LPS	12.5, 25, 50, 100, and 200 μM	inhibited PGE_2 production as well as iNOS and cyclooxygenase-2 expressions	94
	Methanolic extract from *C. serratum*	*In vivo*	Carrageenan and arachidonic acid induced hind paw edema in rats	50, 100, 200 mg/kg, i.g.	Inhibition of synthesis and inflammatory mediators release	97
	n-Butyl extract from *C. bungei*	*In vivo*	acetic acid-induced writhing model	1.0 g/kg, i.p.	prolonged the latency reaction, suppressed the prostaglandin production	102
	Aqueous extracts from *C. bungei*	*In vivo*	DNFB-induced hypersensitivity	10 and 20 g/kg, i.p.	Restrained the phlogistic infiltration, improved the ear edema, reduced the writhes of abdominal cavity and the ear edema	103
	Methanolic extract of *C. indicum*	*In vivo*	Carrageenan and arachidonic acid induced hind paw edema in rats	200 and 400 mg/kg, i.g.	Reduced the number of writhes with 62.57%, inhibited the acetic acid-induced writhing test with 70.76%, respectively	104
	Aqueous extract from *C. inerme*	*In vivo*	Milk-induced hyperpyrexia in rabbits	100 and 200 mg/kg, p.o.	Raising the pain threshold at different time of observation	105
Anti-oxidant activity	Ethanol extract from *C. infortunatum*	*In vitro*	DPPH-radicals	250 μg/ml	Inhibited DPPH	106
	Phenolic extracts from *C. volubile*	*In vitro*	DPPH-radicals, OH radicals	0—100 μg/ml	Inhibited DPPH free radicals and OH radicals	107
	Monoacetylmartinoside	*In vitro*	DPPH-radicals	25 μmol/l	Inhibited DPPH	108
	3″,4″-O-acetylmartynoside	*In vitro*	DPPH-radicals	37 μmol/l	Inhibited DPPH	108
	Acteoside	*In vitro*	DPPH-radicals	60 μmol/l	Inhibited DPPH	108
	Methanolic extract from *C. inerme*	*In vitro*	DPPH-radicals	100 μg/ml	Inhibited DPPH	53
	5-Hydroxy-6,7,4′-trimethoxyflavone	*In vitro*	DPPH-radicals	20 μM	Inhibited DPPH	53
	Ethanolic extract from *C. serratum*	*In vitro*	DPPH-radicals, FRAP, hydrogen peroxide radical	50—250 μg/ml	Inhibited DPPH, FRAP, hydrogen peroxide radical	109
	Methanolic extract from *C. serratum*	*In vitro*	DPPH-radicals, ABTS-radicals	0.125—1.0 mg/ml	Inhibited DPPH	110
	Methanolic extract from *C. serratum*	*In vitro*	DPPH-radicals	200—1000 μg/ml	Inhibited DPPH	111
	Phenolic extracts from *C. volubile*	*In vitro, in vivo*	DPPH-radicals, lipid peroxidation assay	0—312.60 μg/ml	Reduced the MDA content	107
	Methanolic extract from *C. umbellatum*	*In vivo*	*Schistosoma* mansoni-infected mice	100, 200, and 400 mg/kg, i.g.	Decreased MDA level, increase CAT activity and GSH level	113
	Methanolic extracts from *C. siphonanthus*	*In vitro*	Thiocyanate method, DPPH-radicals	0—120 mg/ml	Scavenging lipid peroxide (IC_{50} = 8 mg/ml) and DPPH radicals (IC_{50} = 7 mg/ml)	114
Anti-cancer activity		*In vivo*				115,116

Table 2 (*continued*)

Pharmacological activities	Extract/Compound	Types	Testing subjects	Dose	Effects	Ref.
	Methanolic extract from *C. serratum*	*In vivo*	DMBA-induced skin tumorigenesis in male mice	300, 600 and 900 mg/kg, i.g.	Curtailed tumor development	
	Methanolic extract from *C. serratum*	*In vivo*	DLA cell model	100 and 200 mg/kg	Reduced skin papilloma incidence and multiplicity	117
	Cryptojaponol, fortunin E, 12-methoxy-6,11,14,16-tetrahydroxy-17(15→16)-abeo-5,8,11,13-abietatetraen-3,7-dione	*In vitro*	HL-60, SMMC-7721, lA-549, MCF-7 cell lines	1.8–5.0 μM	Exhibited cytotoxicity	89
	Compounds 45, 70, 76, 78, 81, and 82	*In vitro*	BGC-823, Huh-7, KB, KE-97, and Jurkat	0.83–50.99 μM	Exhibited cytotoxicity	41
	Total flavonoids from *C. Bungei*	*In vitro*	HepG$_2$	0.025–250 μg/ml	Inhibited HepG$_2$ cells proliferation	119
	Trichotomone	*In vitro*	A549, Jurkat, BGC-823 and 293T WT	7.51–19.38 μM	Exhibited cytotoxicity	43
	Compounds 240 and 243	*In vitro*	Hela cell	28.92–35.67 μg/ml	Exhibited moderate cytotoxicity	82
Anti-bacterial activity	Methanolic extract from *C. siphonanthus*	*In vitro*	*Klebsiella pneumoniae*, *Proteus mirabilis*, *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis*	5 mg/disc	The inhibition zones were 30, 16, 16, 12, 11.5 and 10 mm, respectively	114
	n-Butyl extract from *C. bungei*	*In vitro*	*Staphylococcus aureus* and *Micrococcus pyogenes*	50 mg/ml	The MIC values were 50 mg/ml and 25 mg/ml, respectively	120
	Aqueous extract from *C. bungei*	*In vitro*	*Rhizoctonia cerealis*, *Fusarium graminearum*, *Rhizoctonia solani*, and *Setosphaeria turrum*	50–400 mg/ml	Displayed the strong antibacterial action on *Fusarium graminearum*, and the MIC values 10 mg/ml	121
Anti-fungal activity	Ethyl acetate extract from *C. inerme*	*In vitro*	*Alternaria*, *Lasiodiplodia*, *Pestalotiopsis*, *Nigrospora*, *Diaporthe*, and *Phomopsis*	50 μg/disc	Inhibited the growth of most fungi	122
	Ethyl acetate and chloroform extracts from *C. infortunatum*	*In vitro*	*B. megaterium*, *S. typhi*, *K. pneumoniae* and to fungi against *A. niger* and *C. albicans*	1–512 μg/ml	Inhibited *B. subtilis*, *K. pneumonia*, *S. aureus* and *E. coli* growth	123
Anti-plasmodial activity	Ethyl acetate, methanol and aqueous extracts from *C. rotundifolium*	*In vitro*	NF54 chloroquine sensitive and FCR3 chloroquine-resistant strains of *Plasmodium falciparum*	5 μg/ml	Inhibited the growth of NF54 and FCR3 strains of *Plasmodium falciparum*	124
Insecticidal activity	Aqueous extract from *C. chinense*	*In vitro*	*A. subpictus*, *A. albopictus*, and *C. tritaeniorhynchus*	647.05–6877.28 μg/ml	Reduced populations of vector mosquitoes without detrimental effects on predation rates of non-target aquatic organisms, such as *D. indicus*, *A. bouvieri* and *G. affinis*	125
Anti-hypertensive activity	Aqueous extract from *C. colebrookianum*	*In vivo, in vitro*	Fructose-induced hypertension model in rats and in isolated frog heart.	50–100 mg/ml	The 100 mg/ml test samples were showed calcium antagonism in rat ileum and at 50 mg/ml and 75 mg/ml doses exhibited ROCK-II and PDE-5 inhibition respectively	126
	Compounds 64, 166, 178, 196	*In vitro*	ACE and a-glucosidase inhibitory activity assay	0.1–0.7 mM	Inhibited ACE and a-glucosidase.	123
Anti-obesity activity	Methanolic extract from *C. phlomidis*	*In vivo*	High fat diet induced obesity in female mice	200–400 mg/kg, i.g.	Decreased food consumption, body weight, adiposity index, pancreatic lipase activity, adiposity diameter, glucose, insulin, SGOT, SGPT, TG, TC and LDL-c levels	40
	Aqueous extract from *C. glandulosum*	*In vivo*	High fat diet induced obesity in C57BL/6J mice	0–200 μg/ml	Decreased adipogenesis, TG accumulation, leptin release and G3PDH activity	130
Anti-diarrheal activity	Methanolic extract and chloroform fraction from the *C. indicum*	*In vitro*	Castor oil-induced diarrhea testing	400 mg/kg	Inhibited defecation	104
	Methanolic extract from *C. phlomidis*	*In vivo*	castor oil induced diarrhea and PGE$_2$ induced enteropooling in rats	600–800 mg/kg, p.o.	Exhibited significant inhibitory activity	131

Table 2 (*continued*)

Pharmacological activities	Extract/Compound	Types	Testing subjects	Dose	Effects	Ref.
Hepatoprotective activity	Ethanolic extract of *C. inerme*	*In vivo*	CCl$_4$-induced liver damage in rats	200 mg/kg, i.g.	Decreased the serum ALT, AST, ALP, TGL, TC, and increased the GSH level	132
	Alcoholic extract from *C. serratum*	*In vivo*	CCl$_4$-induced wistar rats	20 mg/kg, i.g.	Reduced the level of serum bilirubin and liver function marker enzymes	133
	Alcoholic and aqueous extract from *C. serratum*	*In vivo*	CCl$_4$-induced liver damage in rats	200 mg/kg, i.g.	Restored AST, ALT, and ALP level	134
	Methanolic extract from *C. umbellatum*	*In vivo*	*Schistosoma mansoni*-infected mice	100, 200 and 400 mg/kg, i.g.	Reduced ALT activity and increase total protein level	113
Hypoglycemic and hypolipidemic activities	Aqueous extract from *C. capitatum*	*In vivo*	High fat diet fed rats	100, 400 and 800 mg/kg, i.g.	Reduced the mean fasting plasma glucose concentration, TC, VLDL-c and LDL-c	136
	Aqueous extract from *C. glandulosum*	*In vivo*	High fat diet fed rats	200, 400 and 800 mg/kg, i.g.	Suppressed the HMG CoA reductase and cholesterol ester synthase activity, increased the plasma lecithin cholesterol acyl transferase and lipoprotein lipase levels	137
Memory enhancing effects	Methanolic extract from *C. infortunatum*	*In vivo*	Rectangular maze and Y maze (interoceptive behavioral models)	100 and 200 mg/kg, i.g.		138
Neuroprotective effects	Compound 46	*In vivo*	Rat hippocampal nerve terminals (synaptosomes)	10 and 50 mg/kg, i.p.	Inhibited depolarization-evoked glutamate release and cytosolic free Ca^{2+} concentration in the hippocampal nerve terminals, inhibited glutamate release	69
Other activities	Ethanolic extract from *C. petasites*	*In vitro*	Isolated guinea-pig	2.25—9 mg/ml	Exhibited significantly tracheal smooth muscle relaxant activity	9
	Methanolic extract from *C. phlomidis*	*In vivo*	Phenobarbitone sodium-induced sleeping time	200, 400 and 600 mg/kg, i.g.	Reduced spontaneous activity, decreased exploratory behavioral profiles	139
	Ethanol extract from *C. inerme*	*In vivo*	Spontaneous locomotor activity or performance in the rotarod test	100 mg/kg, i.p.	Reduced methamphetamine-induced hyperlocomotion in mice	62

Narayanan et al (1999) studied anti-nociceptive effects of an alcoholic extract of *C. serratum* roots (50, 100 and 200 mg/kg) in acetic acid induced writhing (200 mg/kg) and hot plate method (100 and 200 mg/kg).[98] A reduction in the number of abdominal constrictions in acetic acid induced writhing in mice indicated the anti-nociceptive effect of *C. serratum* which has further been supported by the findings of hot plate method where a significant increase in area under curve was observed. However, the response was much less when compared to morphine and exact mechanism remains to be investigated in detail. The authors have also indicated significant antipyretic activity of alcoholic extract (100 and 200 mg/kg) of *C. serratum* roots in rabbit model through a dose dependent reduction in pyrexia after administration of *C. serratum*.[97] The ethanolic extract of *C. serratum* leaves has been found to produce considerable centrally acting analgesic activity in tail flick test at 250 mg/kg dose and peripherally acting analgesic activity in acetic acid induced writhing test at 500 mg/kg dose which was found comparable with diclofenac sodium. Blockade of capillary permeability or release of endogenous substances like prostaglandins might be a postulated mechanism.[101] In another study, the author has established a potent analgesic effect of methanolic extract of the aerial parts of *C. serratum* when injected subcutaneously into the right dorsal hind paw of the mice via an inhibition of peripherally and centrally mediated nociception in early as well as in late phase.[97]

The n-butyl extract (at dose of 1.0 g/kg, i.p.) from the roots of the *C. bungei* displayed a significant anti-nociceptive effect in an acetic acid-induced writhing model, prolonged the latency reaction in the hot-plate test in 15, 30, 60 and 90 min in mice. Moreover, the extracts administered in combination with naloxone significantly prolonged the latency reaction, and indicating that naloxone did not revert the action of the extract effect. Also, the extracts notably suppressed the production of prostaglandin (PG) in a dose-dependent manner.[102] The extracts from the roots of *C. bungei* significantly restrained the phlogistic infiltration, improved the ear edema and reduced the writhes of abdominal cavity and the ear edema induced by 2,4-dinitro-1-fluorobenzene (DNFB)-induced hypersensitivity.[103] The methanolic extract of *C. indicum* at doses of 200 and 400 mg/kg showed a significant (*P* < 0.001) and dose-dependent reduction in the number of writhes with 62.57% and 70.76% of inhibition in the acetic acid-induced writhing test, respectively.[104] *Thirumal* et al reported that the aqueous extract obtained from *C. inerme* leaves (at doses of 100 and 200 mg/kg, p.o.) displayed significant analgesic effect by raising the pain threshold at different time of observation (0—120 min).[105]

The combination of antiinflammatory, anti-nociceptive and antipyretic effects of the *Clerodendrum* genus indicated a prospect of intervention with prostaglandin synthesis, as prostaglandins have been established as a common mediator in all these responses. However, this possibility remains to be investigated

thoroughly. Advanced studies can be undertaken in the direction of purification of the chemical constituents of the leaves and investigation of the biochemical pathways for the development of a potent analgesic agent with a low toxicity and better therapeutic index.

3.2. Antioxidant activity

Gouthamchandra et al have demonstrated the antioxidant activity of the ethanol extract of leaves of *C. infortunatum* with the highest scavenging activity in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay (IC$_{50}$ values 250 μg/ml). Moreover, the ethanol extract at 250 μg/ml concentration displayed significantly radical scavenging activity in hydroxyl, superoxide anion, and nitric oxide radical *in vitro*, and the scavenging ratio were 68.58%, 62.06%, and 52.65%, respectively.[106] *Adefegha* et al reported that the phenolic (free and bound) extracts from the leaves of *Clerodendrum volubile* scavenging DPPH free radicals and OH radicals in a concentration dependent manner. Interestingly, the IC$_{50}$ values revealed that the free soluble phenolic extract (IC$_{50}$ = 89.18 μg/ml and 924.90 μg/ml) have a significantly higher scavenging ability against DPPH free radicals and OH radicals than the bound phenolic extracts (IC$_{50}$ = 133.40 μg/ml and 1224.0 μg/ml), respectively.[107] Three phenylethanoid glycosides monoacetylmartinoside **(182)**, 3″,4″-O-acetylmartynoside **(188)** and acteoside **(199)** isolated from the roots of *Clerodendrum lindleyi* exhibited significant *in vitro* antioxidant activity in DPPH assay, and the radical scavenging rate were 25, 37, 60 μmol/l, respectively.[108] The methanolic extract and 5-hydroxy-6,7,4′-trimethoxyflavone **(153)** isolated from the aerial parts of *C. inerme* showed notably scavenging activity with maximum inhibition of 61.84% for the methanolic extract (100 μg/ml) and 37.19% for 5-hydroxy-6,7,4′-trimethoxyflavone (20 μM), respectively, using DPPH assay.[53]

Bhujbal et al have demonstrated *in-vitro* antioxidant effects of ethanolic root extract of *C. serratum* (50–250 μg/ml) at various concentrations in the DPPH radical scavenging assay (IC$_{50}$ value 175 μg/ml); FRAP (ferric reducing antioxidant power) assay and hydrogen peroxide radical scavenging assay (IC$_{50}$ value 85 μg/ml) and suggested the role of polyphenols and flavonoids for the observed antioxidant effects in the extract.[109] The antioxidant potential of methanolic extract of leaves of *C. serratum* was found more potent (EC$_{50}$ value 0.51 μg/ml) due to higher polyphenolic content than other extracts (petroleum ether, chloroform and water) when evaluated in trolox equivalent antioxidant capacity (TEAC) in DPPH and 2,20-azinobis-(3-ethylbenzothiazoneline-6-sulfonic acid) diammonium salt (ABTS) assays.[110] Antioxidant potential of methanolic extract (200–1000 μg/ml) from the leaves of *C. serratum* was further supported by additional reports on DPPH assay, reducing power assay and total antioxidant activity assay.[111]

Feng et al reported that the flavonoid compound from *C. bungei* exhibited strong scavenging capability on nitrite, superoxide anion free radicals and hydroxyl free radicals, and also showed stronger antioxidant effect on pork fat than vitamin C.[112] Also, the phenolic extracts (free and bound) from the *C. volubile* leaf were able to significantly reduce the MDA content in a dose dependent manner (0–312.60 μg/ml). The free soluble phenolic extracts (192.30–77.90%) had a significantly higher concentration dependent inhibition of MDA compared with that of the bound phenolic extract (192.30–91.30%).[107] *Jatsa* et al reported that the methanolic extract (at doses of 100, 200, and 400 mg/kg, i.g.) of *Clerodendrum umbellatum* significantly decrease malondialdehyde (MDA) level, increase catalase (CAT) activity and glutathione level.[113] The methanolic extracts of leaves of *Clerodendrum siphonanthus* displayed extremely effective in scavenging lipid peroxide (IC$_{50}$ = 8 mg/ml) and DPPH radicals (IC$_{50}$ = 7 mg/ml).[114]

3.3. Anticancer activity

Chinchali et al reported that administration of methanolic extract of *C. serratum* leaves significantly reduced tumor development in 7,12-dimethylbenz[α] anthracene (DMBA) induced skin carcinogenicity in testis, liver and kidney of mice.[115,116] The researchers have further demonstrated that flavonoids and phenolics can effectively reduce the incidence and multiplicity of skin papilloma, many investigators have confirmed anti-cancer property of *C. serratum* by various *in vivo* and *in-vitro* studies.[117,118] The methanolic extract of roots of *C. serratum* exhibited notably *in vivo* anticancer activity using DLA cell model at the dose 100 and 200 mg/kg body weight.[117]

Xu et al reported that diterpenoids cryptojaponol **(281)**, fortunin E **(282)**, 12-methoxy-6,11,14,16-tetrahydroxy-17(15→16)-abeo-5,8,11,13-abietatetraen-3,7-dione **(283)** isolated from the hydroalcoholic extract of the herb of *C. kiangsiense* exhibited significant cytotoxicity against human myeloid leukemia (HL-60), hepatocellular carcinoma (SMMC-7721), lung cancer (A-549) and breast cancer (MCF-7) cell lines, and the range of IC$_{50}$ values was 1.8–5.0 μM.[89] The results suggested that these compounds might have promising potential to be anticancer agents.

Compounds **45**, **70**, **76**, **78**, **81**, and **82** isolated and identified from the roots of *C. trichotomum* displayed remarkable *in vitro* cytotoxicity activity against five human cancer cell lines (BGC-823, Huh-7, KB, KE-97, and Jurkat) by using the CellTiter Glo™ Luminescent cell viability assay method with the IC$_{50}$ values ranging from 0.83 to 50.99 μM. Among of them, teuvincenone E **(81)** exhibited the most potent activity against these five cell lines with the IC$_{50}$ values of 3.95, 5.37, 1.18, 1.27, and 0.83 μM, respectively.[41] The total flavonoids isolated from the *C. Bungei* significantly inhibited the human hepatoma HepG$_2$ cells proliferation at concentrations of 0.025, 0.25, 2.5, 25, 250 μg/ml *in vitro*, and the inhibition rates were 5.55%, 12.73%, 14.84%, 62.44%, and 76.81%, respectively.[119] A dimeric diterpene trichotomone **(55)** isolated from the roots of the *C. trichotomum* exhibited strong *in vitro* cytotoxicities against several human cancer cell lines (A549, Jurkat, BGC-823 and 293T WT) with IC$_{50}$ values ranged from 7.51 to 19.38 μM.[43] Two steroids, (20R,22E,24R)-3β-hydroxy-stigmasta-5,22,25-trien-7-one **(240)**, and (20R,22E,24R)-stigmasta-5,22,25-trien-3β,7β-diol **(243)** isolated from the leaves of *C. trichotomum* exhibited moderate cytotoxicity against Hela cell with IC$_{50}$ values at 35.67 and 28.92 μg/ml, respectively.[82]

3.4. Antimicrobial activity

3.4.1. Antibacterial activity

Arokiyaraj et al reported that the methanolic extract of leaves of *C. siphonanthus* exhibited significant antibacterial effect against *Klebsiella pneumoniae*, *Proteus mirabilis*, *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis*, and the inhibition zones were 30, 16, 16, 12, 11.5 and 10 mm, respectively.[114] *Liu* et al reported that the n-butyl extract from the roots of *C. bungei* displayed prominent antibacterial effect against *Staphylococcus aureus* and *Micrococcus pyogenes*, and the minimal inhibitory concentration (MIC) values were 50 mg/ml and 25 mg/ml, respectively.[120] Moreover, the aqueous extracts from the roots of *C. bungei* have notably antibacterial action on *Rhizoctonia cerealis*, *Fusarium graminearum*, *Rhizoctonia solani*, and *Setosphaeria turrum*, especially the aqueous extract exhibited strongest antibacterial action on *Fusarium graminearum*, and the MIC values 10 mg/ml.[121] The methanolic extract, and chloroform fraction of *C. indicum* showed moderate activity against the tested microorganisms in terms of both zones of inhibition (ranged from 9 to 13 mm, 10 to 13 mm and 10 to 13 mm, respectively, at a concentration of 400 μg/disc) and spectrum of activity.[104]

3.4.2. Antifungal activity

Gong et al firstly found that the crude ethyl acetate extract of endophytes from the stems of *C. inerme* exhibit broad *in vitro* antifungal activity against a number of fungal pathogens, including *Alternaria*, *Lasiodiplodia*, *Pestalotiopsis*, *Nigrospora*, *Diaporthe*, and *Phomopsis*, and inhibit the growth of most fungi.[122] The ethyl acetate and chloroform extracts of root, leaf, and stem of the *C. infortunatum* showed significant inhibitory activity over the bacteria and fungus comparable to the standard drug tetracycline and fluconazole. The maximum average diameter zone of inhibition was recorded to bacterial strains against *Bacillus megaterium*, *S. typhi*, *K. pneumoniae* and to fungi against *Anisops niger* and *Clerodendrum albicans*. The MIC values of ethyl acetate and chloroform root extract were determined as 64 μg/ml to *B. subtilis* and *K. pneumoniae*; to *S.-β-haemolyticus* and *S. typhi* for ethyl acetate extracts, 128 μg/ml to *S. aureus*, and *E. coli* for both ethyl acetate and chloroform root extracts but only *S. typhi* and *S.-β-haemolyticus* for chloroform extract.[123]

3.4.3. Antiplasmodial activity

Adia et al revealed that the ethyl acetate, methanol and aqueous extracts from the leaves of *Clerodendrum rotundifolium* exhibit significantly *in vitro* antiplasmodial activity against the chloroquine-sensitive and chloroquine resistant *Plasmodium falciparum* strains with the $IC_{50} < 5$ μg/ml for the first time.[124]

3.4.4. Insecticidal activity

Lots of pharmacological tests and clinical observations have shown that different extract and/or compound prescriptions derived from *C. chinense* have significant insecticidal effects against diseases and organisms including schistosomiasis and trichomoniasis. Govindarajan et al reported that *C. chinense*-fabricated silver nanoparticles (Ag NPs) display higher toxicity against *Anisops subpictus*, *Anisops albopictus*, and *Clerodendrum tritaeniorhynchus* with the LC_{50} values of 10.23, 11.10, and 12.38 μg/ml, respectively. Also, *C. chinense*-fabricated Ag NPs were found safer to non-target organisms *Diplonychus indicus*, *Anisops bouvieri* and *Gambusia affinis*, with respectively LC_{50} values ranging from 647.05 to 6877.28 μg/ml.[125] These results indicated that *C. chinense*-fabricated Ag NPs are a promising and eco-friendly tool against larval populations of mosquito vectors of medical and veterinary importance, with negligible toxicity against non-target aquatic organisms.

3.5. Antihypertensive activity

Lokesh et al evaluated the anti-hypertensive potential of the aqueous extract, and its aqueous, n-butanol, ethyl-acetate and chloroform fractions of *C. colebrookianum* leaves using fructose-induced hypertension model in rats and isolated frog heart. The results showed that the each fraction display negative inotropic and chronotropic effect on isolated frog heart and significant reduction in systolic blood pressure and heart rate in hypertensive rats. Moreover, each fraction at 100 mg/ml showed calcium antagonism in rat ileum and at 50 mg/ml and 75 mg/ml doses exhibited Rho-kinase (ROCK-II) and phosphodiesterase-5 (PDE-5) inhibition, respectively.[126] The antihypertensive activity of *C. colebrookianum* may mediate mainly by cholinergic action and following ROCK-II and PDE-5 inhibition. Liu et al demonstrated that four compounds 15-dehydrocyrtophyllone A **(64)**, verbascoside **(166)**, leucosceptoside A **(178)**, and isoacteoside **(196)**, isolated from dried roots of *C. bungei* showed inhibitory effects against angiotensin converting enzyme (ACE) and a-glucosidase. Among of them, 5-dehydrocyrtophyllone A exhibited an inhibitory effect against ACE with an IC_{50} value of 42.7 μM, while the three phenylethanoid glycosides, verbascoside, leucosceptoside A, and isoacteoside, exhibited stronger inhibitory effects against a-glucosidase, with IC_{50} values of 0.5 mM, 0.7 mM, and 0.1 mM, respectively.[40]

3.6. Anti-diabetic activity

Bachhawat et al reported that the methanolic extract (100 mg/ml) of *C. serratum* roots was evaluated for alpha-glucosidase inhibitory activity using enzyme assay. The extract was not found significantly effective (32.3% inhibition rate with IC_{50} value 265 μg/ml) and may require higher dose to produce the effect.[127]

3.7. Anti-obesity activity

Obesity, initially thought as a problem of the developed world, has now become a worldwide malady because of increasing prevalence in the developing countries as well as developed countries.[128] The impact of methanolic extract of *C. phlomidis* on weight reduction in feeding high fat diet induced obesity in female mice had been investigated. The studies showed that the methanolic extract of *C. phlomidis* at 200 and 400 mg/kg significantly decrease food consumption, body weight, adiposity index, pancreatic lipase activity, adiposity diameter, glucose, insulin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), triglycerides (TG), total cholesterol (TC) and low-density lipoprotein (LDL-c) levels induced by feeding high fat diet induced obesity in female mice, and the LD_{50} value was found to be more than 2000 mg/kg.[129] Jadeja et al reported that the aqueous extract from the leaves of *Clerodendron glandulosum* exhibited significant anti-adipogenic effect by decreasing adipogenesis, TG accumulation, leptin release and glyceraldehyde 3-phosphate dehydrogenase (G3PDH) activity along with higher glycerol release without significantly altering viability of 3T3L1 pre-adipocytes *in vitro*.[130] This study was a profound scrutiny of *C. glandulosum* extract and its role in preventing adipocyte differentiation and visceral adiposity by down regulation of PPARγ-2 related genes and leptin expression. This study validates the traditional therapeutic claim of use of CG extract in controlling obesity.

3.8. Anti-diarrheal activity

Pal. et al reported that the methanolic extract and chloroform fraction from the *C. indicum* at a dose of 400 mg/kg produced 21.74% and 26.96% inhibition of defecation in castor oil-induced diarrhea testing, respectively, which were found to be comparable to that of standard drug loperamide (37.39% inhibition at 50 mg/kg) with regard to the severity of diarrhea.[104] The methanolic extract (at doses of 600 and 800 mg/kg, p.o.) from the leaves of the *C. phlomidis* showed significant inhibitory activity against castor oil induced diarrhea and PGE_2 induced enteropooling in rats. Also, the extract also showed a significant reduction in gastrointestinal motility in charcoal meal test in rats.[131] Anti-diarrheal activity of the plant supported its traditional use in diarrhea by the people of Australia and India.

3.9. Hepatoprotective activity

Gopal et al reported that the ethanolic extract of *C. inerme* leaves exhibit hepatoprotective activity on CCl_4-induced (0.5 ml/kg, i.p.) liver damage in rats at a dose of 200 mg/kg. The extract significantly decreases the serum enzyme alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), triglycerides (TGL), total cholesterol (TC), and significantly increased the glutathione level.[132] Vidya et al reported that administration of an alcoholic extract from the roots of *C. serratum* (20 mg/kg) for two

weeks significantly reduced the level of serum bilirubin and liver function marker enzymes in carbon tetrachloride (CCl_4) induced wistar rats indicating its potential as a hepatoprotective agent possibly due to the radical scavenging activity of the flavonoids present in the drug.[133]

Also, *Agrawal* et al found that the alcoholic (200 mg/kg. p.o.) and aqueous extract (200 mg/kg, p.o.) from the leaves of *C. serratum* possess significant hepatoprotective effects by restoring the normal level of AST, ALT, and ALP with significant reduction in liver weight.[134] Reports on the biomarker ursolic acid, isolated from alcoholic root extract suggested restorative effects on the levels of AST, ALT and ALP towards respective normal value, to stabilize the plasma membranes as well as to repair hepatic tissue damage caused by CCl_4. Ursolic acid was found to normalize the disturbed antioxidant status by maintaining the levels of glutathione and by inhibiting the production of malondialdehyde or may be due to the inhibition of toxicant activation and the enhancement of body defense system.[99]

The ethanol extract of the polyherbal composition from the roots of *C. serratum* showed significant protection against acetaminophen-induced hepatotoxicity in rats, and the function may be through DPPH free radical scavenging activity.[135] The methanolic extract (at doses of 100, 200 and 400 mg/kg, i.g.) of *C. umbellatum* significantly reduced ALT activity and increase total protein level.[113] These findings provided scientific evidence to the ethnomedicinal reports of *C. serratum* in treating acute jaundice; however investigations are still required to fully explicate the exact mechanisms behind the protection.[133]

3.10. Hypoglycemic and hypolipidemic activities

Adeneye et al reported that the fresh leaves aqueous extract of *Clerodendrum capitatum* possess obvious hypoglycemic and hypo-lipidemic activities, the extracts (at doses of 100, 400 and 800 mg/kg, i.g.) could significantly reduce the mean fasting plasma glucose concentration in a dose-dependent lowering effects. Furthermore, the extracts also could notably decrease the total cholesterol, VLDL-c and LDL-c with a dose-related, but significant elevate the tri-glycerides and HDL-c with a dose-related in plasma.[136] *Jadeja* et al reported that the aqueous extract (200, 400 and 800 mg/kg, i.g.) of *C. glandulosum* leaves significantly prevented increment in plasma and tissue lipid profiles in high fat diet (HFD) fed rats, suppressed activity levels of HMG CoA reductase (Hepatic) and cholesterol ester synthase (Hepatic and intestinal), and increased the activity levels of plasma lecithin cholesterol acyl transferase and lipopro-tein lipase (plasma, hepatic and adipose), and increased excretion of triglycerides, cholesterol and bile acids through faeces.[137]

3.11. Memory enhancing effects

Gupta et al reported that the methanolic extract of *C. infortunatum* leaves exhibited promising memory enhancing ef-fects at dose of 200 mg/kg (i.g.), and the effects was closely approximated the results for the standard drug Brahmi, the higher dose evoking pronounced alteration behavior and better learning assessments.[138] The presence of steroids, terpenoids, fats and fla-vonoids were confirmed in this extract by TLC. The extract is likely to develop a promising nootropic to prevent dementia senilis disease.

3.12. Neuroprotective effects

One flavonoid acacetin (**146**) isolated from the *C. inerme* was investigated for neuroprotective activity. It was observed that acacetin inhibited depolarization-evoked glutamate release and cytosolic free Ca^{2+} concentration in the hippocampal nerve ter-minals. Moreover, acacetin (at doses of 10 and 50 mg/kg, i.p.) inhibited glutamate release from hippocampal synaptosomes by attenuating voltage-dependent Ca^{2+} entry and effectively prevents kainic acid (KA)-induced *in vivo* excitotoxicity.[69]

3.13. Other activities

Hazekamp et al found that the ethanolic extract of *C. petasites* leaves exhibited a dose-dependently tracheal smooth muscle relaxant activity on isolated guinea-pig at concentrations from 2.25 to 9 mg/ml, and the active principle was isolated and identified as the flavonoid hispidulin.[9] The results indicated that hispidulin may be beneficial in the treatment of asthma related diseases. In addi-tional, the methanolic extract (at doses of 200,400 and 600 mg/kg, i.g.) of *C. phlomidis* leaves was found to cause significant reduction in spontaneous activity, and decreases in exploratory behavioral profiles by the Y-maze and head dip test. Also, the extract exhibit significantly reduction in muscle relaxant activity by rotarod, 30° inclined screen and traction tests, as well as significantly potenti-ated the phenobarbitone sodium-induced sleeping time.[139] *Huang* et al demonstrated for the very first time that hispidulin isolated from the dichloromethane and the n-hexane fractions of ethanol extract of *C. inerme* significantly reduced methamphetamine-induced hyperlocomotion (MIH) in mice at dose of 100 mg/kg (i.p.) that did not affect their spontaneous locomotor activity or performance in the rotarod test, a measure for motor coordina-tion.[62] This study suggested that hispidulin may be a good thera-peutic potential in hyper-dopaminergic disorders.

4. Conclusions

In present review, more than 300 chemical constituents have been isolated and identified from the genus of *Clerodendrum*, and pharmacological studies indicated that the crude extracts and some special monomer compounds of the genus *Clerodendrum* exert various biological activities, such as anti-inflammatory and anti-nociceptive, antioxidant, anticancer, antimicrobial, anti-hypertensive, anti-obesity, anti-diarrheal, hepatoprotective, memory enhancing, and neuroprotective activities. Terpenes, including monoterpene and its derivatives, sesquiterpene, diter-penoids, triterpenoids, as the major characteristic constituents with significant biological activities, have great potential to be developed into new drugs, especially for anti-inflammatory, antioxidant, anticancer, and antimicrobial agents. In addition, important activities, such as anti-hypertensive, anti-obesity, and hepatoprotective activities indicated that *Clerodendrum* genus can be a promising source of biologically active compounds for these diseases.

The genus *Clerodendrum* has gained a wide acceptance for its pharmacological activities against various ailments. Although above 400 species of the genus *Clerodendrum* were distributed all over the world, only a few of them have been investigated and studied so far. From this review, it can be concluded that phyto-chemical and pharmacology investigations were mainly focused on *C. serratum*, *C. bungei*, *C. inerme*, *C. trichotomum*, *Clerodendrum chinense*, *C. colebrookianum*, *C. phlomidis*, *C. petasites*, *C. grayi*, and *C. indicum*. For some species, such as *C. grayi* was only studied phytochemically, no biological activity was reported up till now. Many other species are totally unknown phytochemically and biologically. Following these species may be of a great importance in discovering new bio-active compounds. On the other hand, few reports have been published concerning the toxic effects of isolated components, and quantitative informations of the genus *Cler-odendrum* were also relatively sparse.

All in all, the omnibearing study on this genus *Clerodendrum* should be performed as soon as possible, which will provide reliable theory evidence for better exploit and utilize the resources of the species in this genus.

Conflict of interest statement

The authors declare no conflict of interest.

Acknowledgments

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