REVIEW ARTICLE

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records of natural products

Naturally Occurring Diarylheptanoids - A Supplementary Version

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Abstract: Diarylheptanoids, as a class of structurally distinctive compounds with notable biological activities, have been of increasing interest in the past decades. We previously reviewed 307 such materials occur in nature. This review collected the inadvertently missing literature in our previous paper along with the lasted researches on this field, and 102 diarylheptanoids have been retrieved, in addition to their distributions, physiological activities and ^{13}C-NMR spectral data. 72 references are cited.

Keywords: diarylheptanoid; natural products; ^{13}C-NMR spectral data; physiological activity.

1. Introduction

Diarylheptanoid is a group of compounds which firmly bears the 1,7-diphenylheptane skeleton as a special characteristics in natural product estate and it is increasingly recognized as potential therapeutic agents for its numerous physiological activity such as anti-inflammatory, antioxidant, antitumor, estrogenic, leishmanicidal, melanogenesis, hepatoprotective and neuroprotective activities [1-21]. This kind of compounds is mainly isolated in the genus *Zingiber*, *Curcuma*, *Alpinia*, *Alnus* and *Myrica*. Since the first diarylheptanoid isolated in 1815, approximately 400 such materials have been obtained from natural resource. Many review articles have been published on the isolation and chemistry of diarylheptanoids [22-24] and we have previously reviewed 307 compounds concerning their structures, distributions, physiological activities and ^{13}C-NMR spectral data [25], while some of diarylheptanoids had been inadvertently left out, this article recollects the omissions and the newly investigations of 90 linear-diarylheptanoids and 12 cyclic-diarylheptanoids, as a supplementary version.

2. The structural features of diarylheptanoids

2.1 Linear-diarylheptanoids

We previously grouped linear-diarylheptanoid into 5 types, namely possessing heptane chain merely (type I), possessing oxy bridges (type II), possessing flavonoid moiety (type III), dimeric linear-diarylheptanoid (type IV) and unusual structure (type V). All the retrieved diarylheptanoids were well fitted to this role except for hirsunin (**87**), which has an ellagitannin (praecoxin A) moiety,

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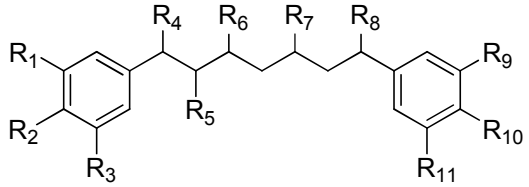

Figure 1. Structures of compounds **1-32**

Cpd.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}	R_{11}
1	H	H	H	H	H	OH (*S*)	H	H	H	OH	H
2	H	H	H	H	H	OH (*R*)	H	H	H	OH	H
3	H	H	H	OH (*S*)	H	OH (*R*)	OH (*S*)	OH (*S*)	H	H	H
4	H	OH	H	H	H	OH (*S*)	H	H	H	OH	H
5	H	OH	H	H	H	OH (*S*)	O-glc (*S*)	H	H	OH	H
6	H	OH	H	H	H	OH (*R*)	O-glc (*S*)	H	H	OH	H
7	OH	OH	H	H	H	OH (*S*)	H	H	H	OH	H
8	OH	OH	H	H	H	OH (*R*)	H	H	H	OH	H
9	OH	OH	H	H	H	$OCOCH_3$ (*S*)	H	H	H	OH	H
10	OH	OH	H	H	H	$OCOCH_3$ (*R*)	H	H	H	OH	H
11	OH	OH	OCH_3	H	H	$OCOCH_3$	$OCOCH_3$	H	OH	OH	H
12	OH	OH	OCH_3	H	H	$OCOCH_3$	$OCOCH_3$	H	OH	OH	OCH_3
13	OH	OH	OCH_3	H	H	$OCOCH_3$	$OCOCH_3$	H	OCH_3	OH	OCH_3
14	OH	OH	H	H	H	$OCOCH_3$	$OCOCH_3$	H	H	OH	H
15	OCH_3	OH	H	H	H	$OCOCH_3$	$OCOCH_3$	H	H	OH	H
16	OH	OH	H	H	H	$OCOCH_3$	OH	H	OH	OH	H
17	OH	OH	OCH_3	H	H	$OCOCH_3$	OH	H	OH	OH	OCH_3
18	OCH_3	OH	H	H	H	$OCOCH_3$	OH	H	OH	OH	OCH_3
19	OCH_3	OH	H	H	H	$OCOCH_3$	OH	H	OCH_3	OH	OCH_3
20	OCH_3	OH	OCH_3	H	H	OH	OH	H	OCH_3	OH	OCH_3
21	OCH_3	OH	H	H	OH	OH	OH	H	OCH_3	OH	H
22	OCH_3	OH	H	H	OH	H	O-xyl	H	OCH_3	OH	H
23	OCH_3	OH	H	H	H	OH (*R*)	OH (*S*)	H	OH	OH	H
24	OCH_3	OH	H	OH (*R*)	H	H	OH (*R*)	H	H	OH	H
25	H	OH	H	H	H	H	H	H	H	OCH_3	H
26	H	OH	H	H	H	SO_3Na (*S*)	H	OH	H	OH	H
27	H	OH	H	H	H	SO_3Na (*R*)	H	OH	H	OH	H
28	H	OH	H	H	H	OH (*S*)	H	H	H	OH	H
29	H	OH	H	H	H	OH (*R*)	H	H	H	OH	H
30	OH	OH	H	H	H	OH (*R*)	H	H	H	H	H
31	OH	OH	H	H	H	$OCOCH_3$ (*S*)	H	H	H	OH	H
32	OH	OH	H	H	H	$OCOCH_3$ (*R*)	H	H	H	OH	H

Cpd. **25**-**27**: $\Delta^{5,6}$; Cpd. **28**-**32**: $\Delta^{6,7}$

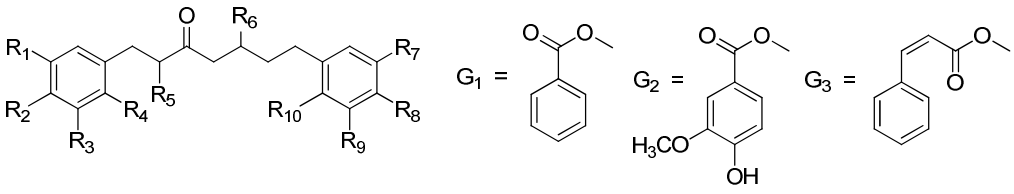

Figure 2. Structures of compounds **33-52**

Cpd.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}
33	OCH_3	OH	H	H	H	H	H	OH	H	H
34	OCH_3	OH	OCH_3	H	H	OH	OCH_3	OH	H	H
35	OH	OH	H	H	H	OH (*R*)	OH	OH	H	H
36	OH	OH	H	H	H	O-glc^{6}G$_1$ (*S*)	OH	OH	H	H
37	OH	OH	H	H	H	O-glc^{6}G$_2$ (*S*)	OH	OH	H	H

38	OH	OH	H	H	H	O-xyl^{2}G$_3$ (*S*)	OH	OH	H	H
39	H	H	H	H	H	OCH_2CH_3	OCH_3	OH	H	H
40	OH	OH	H	H	H	OH	OH	OH	H	H
41	H	H	H	H	OH (*S*)	H	H	H	H	H
42	H	OH	H	H	H	H	OH	OH	H	H
43	H	H	H	H	H	H	OH	OH	OCH_3	H
44	H	H	H	OH	H	H	H	H	H	OH
45	H	H	OH	OH	H	H	H	H	OH	OH
46	H	H	H	H	H	H	H	H	H	H
47	H	OH	H	H	H	H	H	OH	H	H
48	OH	OH	H	H	H	H	OH	OH	H	H
49	OCH_3	OH	H	H	H	H	OCH_3	OH	H	H
50	OCH_3	OH	H	H	H	H	OCH_3	OH	OCH_3	H
51	H	OH	H	H	H	H	OCH_3	OH	H	H
52	OCH_3	OH	H	H	H	H	OCH_3	OH	H	H

Cpd. **40**: $\Delta^{1,2}$; Cpd. **41**-**45**: $\Delta^{4,5}$; Cpd. **46**: $\Delta^{5,6}$; Cpd. **47**: $\Delta^{6,7}$; Cpd. **48**-**50**: $\Delta^{4,5}$, $\Delta^{6,7}$; Cpd. **51**-**52**: $\Delta^{1,2}$, $\Delta^{4,5}$, $\Delta^{6,7}$

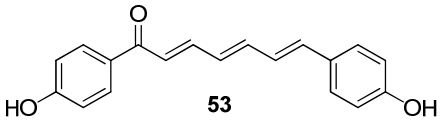

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Figure 3. Structure of compound **53**

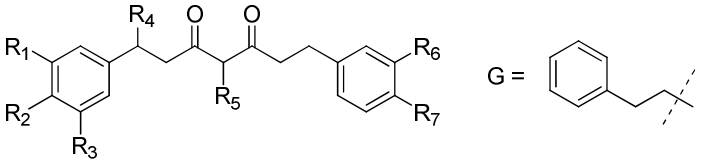

Figure 4. Structures of compounds **54-67**

Cpd.	R_1	R_2	R_3	R_4	R_5	R_6	R_7
54	H	H	H	H	H	H	H
55	H	OH	H	H	H	H	OH
56	H	H	H	H	G	H	H
57	H	OH	H	H	H	H	OH
58	H	OH	H	OH	H	H	OH
59	H	OH	H	H	H	OCH_3	OH
60	H	OH	H	OH	H	OCH_3	OH
61	OH	OH	H	OH	H	OCH_3	OH
62	OCH_3	OH	H	H	H	OCH_3	OH
63	OCH_3	OH	H	OH	H	H	OH
64	OCH_3	OH	H	H	H	H	OH
65	OCH_3	OH	H	H	H	H	H
66	OH	OH	H	H	H	H	OH
67	OCH_3	OH	OCH3	H	H	OCH_3	OH

Cpd. **56**-**65**: $\Delta^{6,7}$; Cpd. **66**-**67**: $\Delta^{1,2}$, $\Delta^{6,7}$

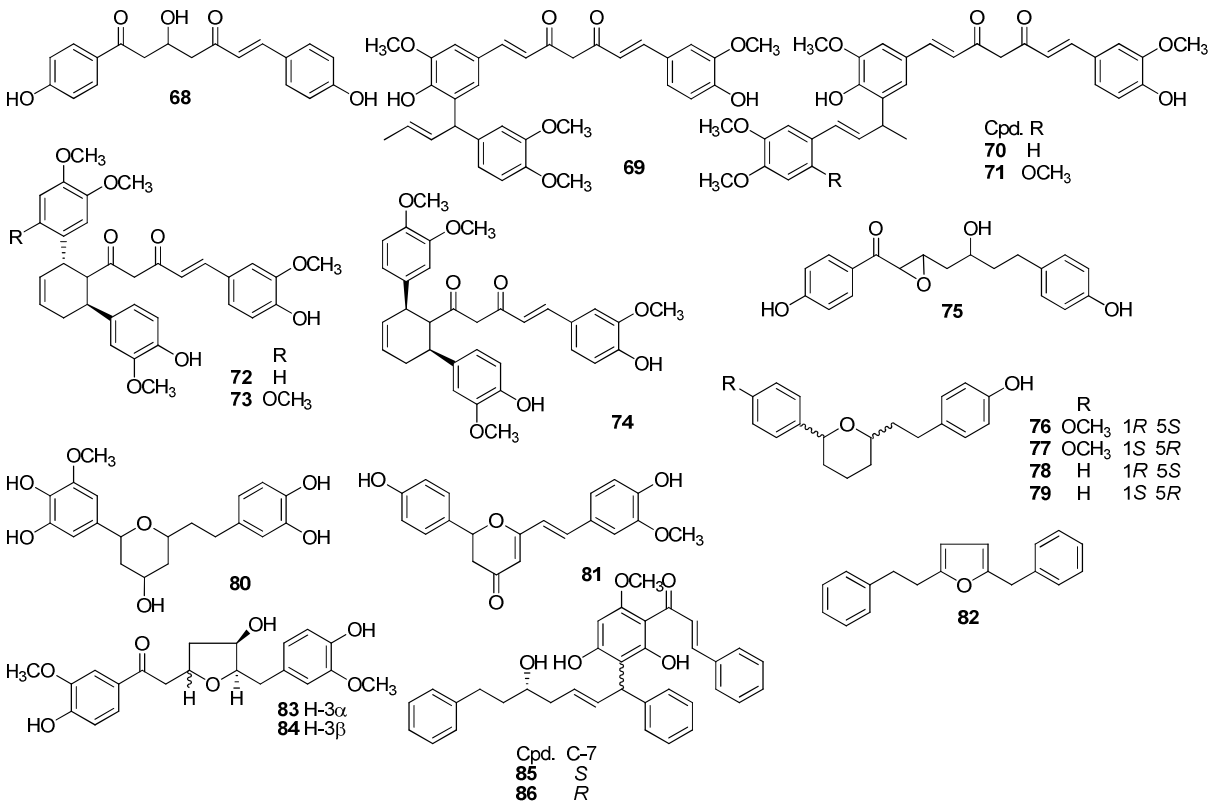

Figure 5. Structures of compounds **68-86**

and other compounds, **1-74**, **75-84**, **85-86**, **87-90** yielded to type I, II, III, V, respectively.

Compounds **1-74** belong to the type I, shown in Table 1 Figure 1-4. They are divided into two sections in the light of whether a carbonyl group attached to the aliphatic carbons. In compounds **1-32** (Figure 1), they are saturated or with one double bonds; while in **33-74** (Figures 2-5), they possess one or two carbonyl groups with several degrees of unsaturation.

Oregonosides A (**36**), B (**37**) and compound **38** are diarylheptanoid glycosides found in *Alnus* genus, and all consist of the same aglycon moiety (hirsutanonol) but a different sugar moiety and an acyl group. It is unusual that diarylheptanoids reported as acyl derivatives in the present case, however, the diarylheptanoid moiety (hirsutanonol) of these compounds is not very surprising because the majority of diarylheptanoids found in the genus *Alnus*, bears the same group. In Compound **56**, there is a phenethyl group located at the central position (C-4) in the aliphatic carbon chain with two contigeous carbonyl groups placed at C-3 and C-5 respectively, which is unusual. Cassumunin A (**70**), B (**71**), C (**69**) and cassumunarin A (**74**), B (**72**), C (**73**) are a series of complex curcuminoids isolated from *Z. cussumunar*, and they are all structurally similar to curcumin except for attaching a fused trisubstituted benzene rings, which the biosynthesis with regard to dimeric diarylheptanoid may should be responsible for. Nitidone A (**44**) and B (**46**) were obtained from *A. nitida*, and show a novel substitution pattern in linear-diarylheptanoids, since *ortho*-position substituted of the two phenyl moiety has rarely been found. While their pharmacological studies have not been reported yet, what the novel substitution pattern bring about to their biological activities need further investigation.

Compounds **75-84** (type II) in Table 1 and Figures 5, all have a 1,5- or 3,6-oxy bridge in the carbon chain except for mistletonone (**75**), forming an oxy bridge between C-2 and C-3, two adjacent carbons, which is unusual.

Katsumain A (**85**) and B (**86**) as showing in Table 1 and Figure 5, possess one flavonoid moiety located at the C-7 position, belong to the type III.

Hirsunin (**87**), present itself as a new structural grouping in the classification of diarylheptanoids, consists of diarylheptanoid glycoside (oregonin) and ellagitannin (praecoxin A) moieties. It was isolated from the genus *Alnus* in 1992, which constituted rich sources of diarylheptanoids and tannins, and it remained the unique example of a diarylheptanoid possessing an ellagitannin moiety up to now. Compounds **88**, **89** and **90**, which regard as be of unusual structure, were isolated from *A. subulatum*, *M. paradisiaca* and *A. hirsute*, respectively. They all form a new skeleton from from diarylheptanoid and the later two ones functionalized in a similar manner. The common characteristic feature of this three compounds is the occurrence of the cyclization of the aliphatic carbon atoms.
The retrieved linear-diarylheptanoids are mainly distributed in *Zingiber*, *Curcuma*, *Alpinia* and *Alnus*. Besides the 20 genus mentioned in the previous paper, there are 5 genus added including *Musa*, *Aframomum*, *Etlingera*, *Renealmia* and *Pleuranthodium*, 4 of which belong to the family of Zingiberaceae.

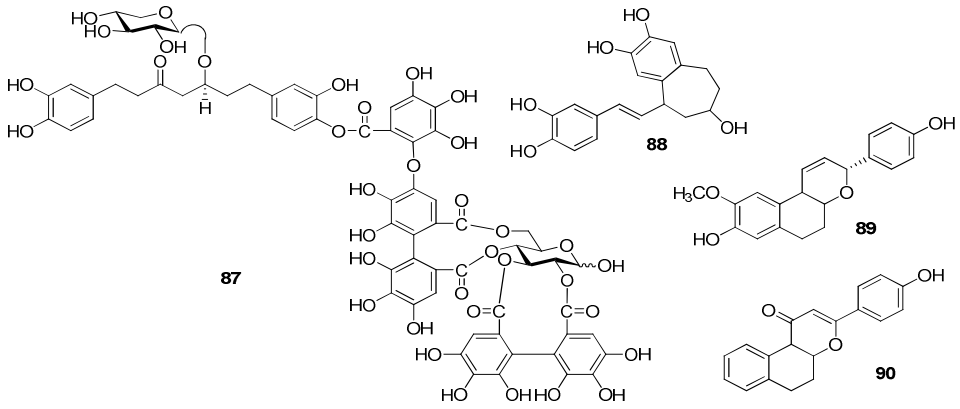

Figure 6. Structures of compounds **87-90**

2.2 Cyclic-diarylheptanoids

There were 12 cyclic-diarylheptanoids composed of 2 metaparacyclophanes and 10 metametacyclophanes and they were isolated in the genus *Myrica*, *Corylus*, *Carpinus* and *Pterocarya*.

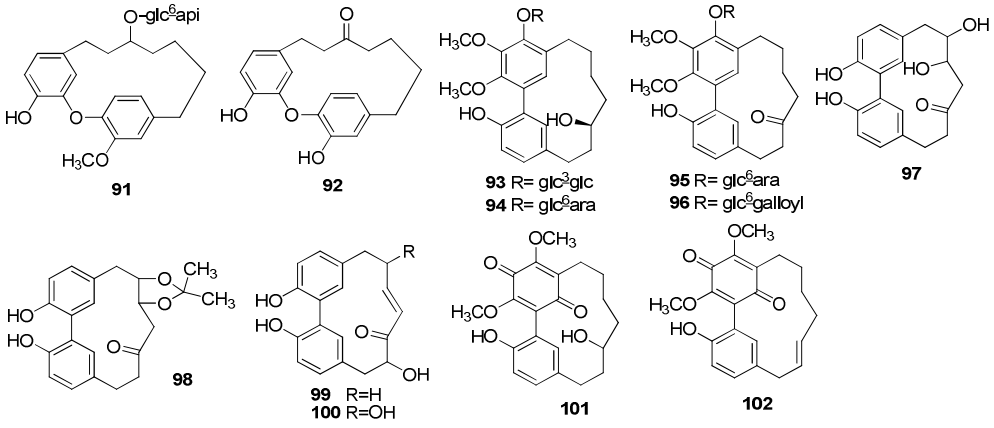

Figure 7. Structure of compounds **91-102**

Table 1. Compounds **1-102**

	Name	Resource	Ref.
1	(-)-centrolobol	*C. robustum*	26
2	(+)-centrolobol	*C. tomentosum*	26
3	diospongin C	*D. spongiosa*	27
4	(+)-centrolobol	*C. paraense* *C. sclerophyllum* *C. tomentosum* *C. robustum*	28
5	betulaplatoside Ia	*B. platyphylla*	29
6	betulaplatoside Ib	*B. platyphylla*	29
7	(3*S*)-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)heptan-3-ol	*C. kwangsiensis*	30
8	(3*R*)-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)heptan-3-ol	*C. kwangsiensis*	30
9	(3*S*)-3-acetoxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)heptanes	*C. kwangsiensis*	30
10	(3*R*)-3-acetoxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)heptanes	*C. kwangsiensis*	30
11	3,5-diacetoxy-1-(3,4-dihydroxyphenyl)-7-(3,4-dihydroxy-5-methoxyphenyl)heptane	*Z. officinale*	31
12	3,5-diacetoxy-1,7-bis(3,4-dihydroxy-5-methoxyphenyl)heptane	*Z. officinale*	31
13	3,5-diacetoxy-7-(3,4-dihydroxy-5-methoxyphenyl)-1-(4-hydroxy-3,5-dimethoxyphenyl)heptane	*Z. officinale*	31
14	3,5-diacetoxy-7-(4-hydroxyphenyl)-1-(3,4-dihydroxyphenyl)heptane	*Z. officinale*	31
15	3,5-diacetoxy-7-(4-hydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)heptane	*Z. officinale*	31
16	3-acetoxy-5-hydroxy-1,7-bis(3,4-dihydroxy-5-methoxyphenyl)-heptane	*Z. officinale*	31
17	3,5-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane	*Z. officinale*	31
18	3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxy-5-methoxyphenyl)heptane	*Z. officinale*	31
19	3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)heptane	*Z. officinale*	31
20	3,5-dihydroxy-1,7-bis(4-hydroxy-3,5-dimethoxyphenyl)	*Z. officinale*	31
21	*	*J. mandshurica,*	32
22	juglanol A 5-*O*-β-D-xylopyranoside	*J. mandshurica*	33
23	(3*R*,5*S*)-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane	*Z. ottensii*	34
24	*	*J. mandshurica,*	32
25	1-(4"-methoxyphenyl)-7-(4'-hydroxyphenyl)-(E)-hept-2-ene	*P. racemigerum*	35
26	sodium(*E*)-7-hydroxy-1,7-bis(4-hydroxyphenyl)hept-5-ene-3S-sulfonate	*Z. officinale*	36
27	sodium (*E*)-7-hydroxy-1,7-bis(4-hydroxyphenyl)hept5-ene-3R-sulfonate	*Z. officinale*	36
28	(3*S*)-1,7-bis(4-hydroxyphenyl)-(6*E*)-6-hepten-3-ol	*C. kwangsiensis*	30
29	(3*R*)-1,7-bis(4-hydroxyphenyl)-(6*E*)-6-hepten-3-ol	*C. kwangsiensis*	30
30	(3*R*)-1-(3,4-dihydroxyphenyl)-7-phenyl-(6*E*)-6-hepten-3-ol	*C. kwangsiensis*	30
31	(3*S*)-3-acetoxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)-(6*E*)-6-heptene	*C. kwangsiensis*	30
32	(3*R*)-3-acetoxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)-(6*E*)-6-heptene	*C. kwangsiensis*	30
33	5-dehydroxy-hexahydro-demethoxycurcumin	*C. kwangsiensis*	30,37
34	5-hydroxy-l-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone	*Z. officinale*	31
35	epihirsutanonol	*A. japonica*	38
36	oregonoside A	*A. rubra*	39
37	oregonoside B	*A. rubra*	39
38	2'''-cinnamoyloregonin	*A. formosana*	40
39	5-ethoxyl-7-(4-hydroxy-3-methoxy-phenyl)-1-phenyl-3-heptanone	*A. officinarum*	41
40	5-hydroxy-1,7-bis(3,4-dihydroxyphenyl)-1-hepten-3-one	*C. longa*	42
41	alpinoid E	*A. officinarum*	43
42	alusenone	*A. japonica*	44
43	7-(4",5"-dihydroxy-3"-methoxyphenyl)-1-phenyl-4-heptene-3-one	*A. officinarum*	45
44	nitidone A	*A. nitida*	46
45	1,7-diphenyl-5-heptene-3-one	*A. officinarum*	45
46	nitidone B	*A. nitida*	46
47	(*E*)-1,7-bis(4-hydroxyphenyl)-6-hepten-3-one	*C. kwangsiensis*	30
48	1,7-bis(3,4-dihydroxyphenyl)hepta-4E,6E-dien-3-one	*A. subulatum*	47
49	1,7-bis(4-hydroxy-3-methoxyphenyl)-4,6-heptadien-3-one	*C. longa*	42
50	1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)-4,6-heptadien-3-one	*C. longa*	42
51	1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one	*C. longa*	42
52	1,7-bis(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one	*C. longa*	48
53	1,7-bis(4-hydroxyphenyl)-2,4,6-heptatrienone	*E. elatior*	49
54	1,7-diphenyl-3,5-heptanedione	*A. conchigera*	50
55	letestuianin C	*A. letestuianum*	51
56	4-phenethyl-1,7-diphenyl-1-heptene-3,5-dione	*A. officinarum*	45
57	dihydrobisdemethoxycurcumin	*C. longa*	42
58	1,5-dihydroxy-1,7-bis(4-hydroxyphenyl)-4,6-heptadiene-3-one	*C. longa*	52
59	dihydrodemethoxycurcumin	*C. longa*	42
60	1-hydroxy-1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-6-hepten-3,5-dione	*C. longa*	52
61	1-(3,4-dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-6-hepten-3,5-dione	*C. longa*	42
62	letestuianin B	*A. letestuianum*	51
63	1,5-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-4,6-heptadiene-3-one	*C. longa*	52
64	letestuianin A	*A. letestuianum*	51

65	*trans,trans*-1(3'-methoxy-4'-hydroxyphenyl)-7-phenyl-5-ol-4,6-dien-3-heptanone	*A. officinarum*	53
66	4'-hydroxy-bisdemethoxycurcumin	*C. longa*	52
67	1,4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-(1E,6E)-1,6-heptadiene-3,4-dione	*C. xanthorrhiza*	54
68	3-hydroxy-1,7-bis-(4-hydroxyphenyl)-6-heptene-1,5-dione	*C. longa*	52
69	cassumunin C	*Z. cassumunar*	55
70	cassumunin A	*Z. cassumunar*	55
71	cassumunin B	*Z. cassumunar*	55
72	cassumunarin B	*Z. cassumunar*	56
73	cassumunarin C	*Z. cassumunar*	56
74	cassumunarin A	*Z. cassumunar*	56
75	mistletonone	*V. coloratum*	57
76	(-)-centrolobine	*C. robustum*	26
77	(+)-centrolobine	*C. tomentosum*	26
78	(-)-de-*O*-methylcentrolobine	*C. robustum*	26
79	(+)-de-*O*-methylcentrolobine	*C. tomentosum*	26
80	1,5-epoxy-3-hydroxy-1-(4,5-dihydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane	*Z. officinale*	58
81	3'-demethoxycyclocurcumin	*C. xanthorrhiza*	59
82	3,6-furan-1,7-diphenylheptane	*A. officinarum*	43
83	renealtin A	*R. exaltata*	60
84	renealtin B	*R. exaltata*	60
85	katsumain A	*A. katsumadai*	61
86	katsumain B	*A. katsumadai*	61
87	hirsunin	*A. hirsuta*	62
88	2,3,7-trihydroxy-5-(3,4-dihydroxy-*E*-styryl)-6,7,8,9-tetrahydro-5H-benzocycloheptene	*A. subulatum*	47
89	*rel*-(3*S*,4α*R*,10β*R*)-8-hydroxy-3-(4-hydroxyphenyl)-9-methoxy-4α,5,6,10β-tetrahydro-3H-naphtho[2,1-β]pyran	*M. paradisiaca*	63
90	*	*A. hirsuta*	64
91	16-methoxy acerogenin B 9-*O*-β-D-apiofuranosyl-6)-β-D-glucopyranoside	*M. rubra*	65
92	pterocarine	*P. tonkinesis*	66
93	myricanol 5-*O*-β-D-glycopyranosyl-(1-3)-β-D-glucopyranoside	*M. rubra*	67
94	myricanol 5-*O*-α-L-arabinofuranosyl-(l-6)-β-D-glycopyranoside	*M. rubra*	67
95	myricanone 5-*O*-α-L-arabinofuranosyl-(1-6)-β-D-glucopyranoside	*M. rubra*	65
96	myricanone 17-*O*-β-D-(6-*O*-galloyl)-glucopyranoside	*M. rubra*	65
97	11-oxo-3,8,9,17-tetrahydroxy-[7,0]-metacyclophane	*C. sieboldiana*	68
98	*	*C. cordata*	69
99	11-oxo-3,12,17-trihydroxy-9-ene-[7,0]-metacyclophane	*C. sieboldiana*	70
100	11-oxo-3,8,12,17-tetrahydroxy-9-ene-[7,0]-metacyclophane	*C. sieboldiana*	70
101	rubanol	*M. rubra*	71
102	nanaone	*M. nana*	72

3. ^{13}C-NMR data of diarylheptanoids

Table 2. ^{13}C-NMR data of linear-diarylheptanoids

Cpd.	1	2	3	4	5	6	7	1'	2'	3'	4'	5'	6'	1"	2"	3"	4"	5"	6"
3[a]	71.4	45.0	66.9	43.2	73.1	45.8	74.9	144.2	125.4	128.4	127.3	128.4	125.4	144.3	125.6	128.5	127.6	128.5	125.6
4[b]	31.5	40.0	71.7	37.6	25.7	32.3	35.3	133.6	129.6	115.5	155.4	115.5	129.6	133.6	129.6	115.5	155.4	115.5	129.6
5[c]	32.0	41.2	69.9	42.9	79.7	38.6	31.4	134.4	130.3	116.0	156.2	116.0	130.3	134.7	130.4	116.1	156.3	116.1	130.4
6[c]	32.3	41.3	68.4	43.0	78.4	39.2	31.6	134.6	130.3	116.1	156.3	116.1	130.3	134.7	130.5	116.1	156.3	116.1	130.5
7[c]	32.5	40.7	71.9	38.4	26.5	33.2	36.2	135.6	116.7	146.2	144.3	116.4	120.8	135.0	130.4	116.2	156.4	116.2	130.4
8[c]	32.5	40.7	71.9	38.4	26.5	33.2	36.2	135.6	116.7	146.2	144.3	116.4	120.8	135.0	130.4	116.2	156.4	116.2	130.4
9[c]	32.3	37.3	75.4	35.1	25.8	32.7	35.9	134.7	116.6	146.4	144.5	116.5	120.7	134.7	130.4	116.2	156.4	116.2	130.4
10[c]	32.3	37.3	75.4	35.1	25.8	32.7	35.9	134.7	116.6	146.4	144.5	116.5	120.7	134.7	130.4	116.2	156.4	116.2	130.4
21[c]	40.0	76.3	72.8	40.9	70.6	40.8	32.3	135.2	114.1	148.7	145.7	115.9	128.8	132.0	113.1	148.7	145.4	116.1	121.7
22[c]	44.7	73.8	32.7	30.8	79.9	38.1	32.2	132.0	114.2	148.8	145.9	116.1	123.0	133.5	113.3	148.8	145.4	116.1	121.9
23[a]	32.0	41.1	71.7	44.3	71.1	41.1	31.7	135.0	116.2	145.7	143.7	115.5	120.3	134.7	112.7	148.1	145.3	115.9	121.4
24[c]	81.2	34.3	25.1	32.4	78.3	39.6	31.8	136.3	110.0	148.7	146.8	115.7	119.9	134.3	130.3	116.0	156.3	116.0	130.3
25[a]	35.0	31.4	29.2	32.5	131.6	129.6	38.3	133.4	129.6	114.0	158.0	114.0	129.6	135.1	129.6	115.3	153.8	115.3	129.6
26[c]	31.9	39.9	71.3	42.0	129.8	132.5	70.6	134.4	130.3	115.9	156.2	115.9	130.3	130.3	131.4	116.0	157.7	116.0	131.4
27[c]	32.0	39.9	71.4	41.6	129.8	132.5	70.6	134.4	130.3	115.9	156.2	115.9	130.3	130.3	131.4	116.0	157.7	116.0	131.4
28[c]	32.3	40.8	71.3	38.5	30.4	128.3	131.2	134.6	130.5	116.2	156.5	116.2	130.5	131.1	128.3	116.4	157.8	116.4	128.3
29[c]	32.3	40.8	71.3	38.5	30.4	128.3	131.2	134.6	130.5	116.2	156.5	116.2	130.5	131.1	128.3	116.4	157.8	116.4	128.3
30[c]	32.6	40.7	71.4	38.2	30.4	128.0	131.5	135.4	116.7	146.2	144.3	116.4	120.8	139.4	127.1	129.6	131.5	129.6	127.1
31[c]	32.2	37.4	75.2	35.3	30.2	127.6	131.5	134.6	116.6	146.3	144.5	116.5	120.7	130.9	128.3	116.4	157.8	116.4	128.3
32[c]	32.2	37.4	75.2	35.3	30.2	127.6	131.5	134.6	116.6	146.3	144.5	116.5	120.7	130.9	128.3	116.4	157.8	116.4	128.3
33[a]	29.5	44.6	211.2	42.9	23.2	31.1	34.7	132.9	111.1	146.4	143.8	114.3	120.7	134.0	129.3	115.1	153.8	115.1	129.3
35[c]	30.1	46.3	209.3	52.2	58.2	41.3	33.0	134.0	116.6	146.4	144.7	116.5	120.7	133.9	116.8	146.4	144.7	116.5	120.9
36[c]	30.0	46.3	211.8	48.9	76.6	38.4	31.8	134.0	116.4	146.1	144.3	116.5	120.7	135.1	116.5	145.9	144.0	116.2	120.6
37[c]	30.1	46.4	211.8	48.9	76.5	38.6	31.9	134.1	116.6	146.1	144.4	116.4	120.6	135.3	116.6	146.0	144.1	116.3	120.8
38[c]	30.1	46.3	210.9	48.6	77.1	38.5	31.6	135.1	116.3	146.1	144.4	116.4	120.7	135.6	116.4	146.1	144.2	116.6	120.5
39[a]	29.4	45.4	208.7	47.9	75.1	36.6	31.2	141.0	128.3	128.4	126.0	128.4	128.3	133.8	110.9	146.4	143.7	114.3	120.8

41[a)]	40.8	75.8	199.6	125.8	148.9	34.3	34.1	136.4	129.4	128.6	126.7	128.6	129.4	140.4	128.3	128.4	126.3	128.4	128.3
42[c)]	30.8	42.9	203.0	131.7	149.5	35.8	34.9	133.3	130.5	116.3	156.8	116.3	130.5	134.0	116.7	144.7	146.4	116.5	120.7
43[a)]	30.0	41.7	199.4	130.7	146.4	34.4	34.1	132.5	110.4	147.2	141.0	124.3	122.8	141.2	128.3	128.4	126.1	128.4	128.3
44[a)]	29.3	41.9	199.8	130.7	146.6	34.3	33.5	132.8	129.5	115.2	129.4	115.3	153.9	133.3	129.6	115.5	129.4	115.4	153.8
45[a)]	29.8	45.7	210.9	30.8	127.1	147.3	35.0	141.2	128.3	128.5	126.0	128.5	128.3	141.2	128.3	128.5	126.0	128.5	128.3
45[c)]	31.6	42.7	202.8	131.7	149.2	35.8	34.5	134.8	120.6	116.2	116.5	146.3	144.6	134.2	120.5	116.3	116.4	146.4	144.1
47[c)]	30.2	45.7	212.9	43.7	28.3	126.9	131.7	133.4	130.4	116.3	156.8	116.3	130.4	130.8	128.3	116.4	157.9	116.4	128.3
48[b)]	30.3	42.7	199.5	129.1	143.9	125.0	142.3	134.0	116.2	145.6	143.9	115.9	120.3	129.5	114.3	146.1	147.5	116.3	121.3
52[b)]	143.3	123.9	188.8	129.1	143.8	125.6	142.3	128.1	111.6	148.8	150.2	116.2	124.1	129.6	111.7	148.8	149.1	116.1	122.6
53[b)]	187.9	124.9	144.1	130.8	143.1	126.5	137.6	131.3	131.5	116.1	162.5	116.1	131.5	129.5	129.3	116.5	158.9	116.5	129.3
54[a)]	31.4	39.9	202.2	99.5	193.0	39.9	31.4	140.4	128.2	128.4	126.1	128.4	128.2	140.5	128.2	128.4	126.1	128.4	128.2
55[c)]	29.7	46.4	206.5	57.4	206.5	46.4	29.7	133.0	130.4	116.3	156.7	116.3	130.4	133.0	130.4	116.3	156.7	116.3	130.4
56[a)]	31.4	31.1	199.8	100.7	176.8	122.7	139.7	129.8	128.3	128.5	126.2	128.5	128.3	135.1	127.9	128.4	128.9	128.4	127.9
58[b)]	81.3	43.5	192.9	105.8	169.5	119.5	137.5	130.6	129.0	116.1	158.7	116.1	129.0	127.8	130.3	116.6	160.0	116.6	130.3
60[b)]	81.3	43.6	192.5	105.9	169.3	119.9	137.7	130.9	129.0	116.2	158.7	116.2	129.0	128.5	111.2	148.7	149.3	116.1	122.9
62[d)]	30.4	41.3	199.2	100.2	177.9	119.7	140.2	131.6	112.5	147.4	144.7	115.3	120.3	126.3	111.0	148.0	149.2	115.7	123.0
63[b)]	81.6	43.6	192.6	105.9	169.3	119.6	137.4	131.3	111.2	148.4	147.8	115.7	120.5	128.0	130.3	116.6	159.9	116.6	130.3
64[b)]	31.7	42.7	199.5	101.0	178.5	120.8	140.6	133.4	112.9	148.3	145.9	115.8	121.6	127.8	130.9	116.9	160.5	116.9	130.9
65[b)]	31.2	42.6	201.3	101.4	177.2	123.6	139.7	132.9	112.5	147.9	145.5	115.4	121.2	135.9	128.5	129.5	130.4	129.5	128.5
66[b)]	141.4	122.4	184.9	102.1	184.9	122.4	141.8	128.1	131.3	117.2	160.9	117.2	131.3	128.7	115.6	146.7	149.1	116.8	123.0
68[b)]	198.4	46.0	66.2	48.3	199.8	125.1	144.0	130.7	131.9	116.3	163.2	116.3	131.9	127.5	131.6	117.1	161.1	117.1	131.6
75[d)]	191.8	56.4	55.8	35.2	67.7	40.2	30.8	127.7	130.9	115.8	163.3	115.8	130.9	132.5	129.2	115.4	155.5	115.4	129.2
80[d)]	72.9	40.3	62.9	37.9	70.4	38.1	30.9	133.8	101.3	148.0	132.9	145.4	106.6	132.9	118.8	115.7	143.0	114.9	115.4
81[b)]	81.4	43.5	192.7	105.8	169.4	119.8	137.7	130.7	129.0	116.2	158.8	116.2	129.0	128.4	112.3	148.8	149.5	116.2	123.0
83[c)]	198.4	48.9	75.8	41.3	73.1	86.0	34.7	130.1	110.5	147.8	152.6	114.0	123.9	131.1	112.2	147.6	144.9	114.4	121.2
84[c)]	199.8	45.1	75.6	38.5	72.9	84.8	35.6	130.1	111.6	148.8	153.8	115.3	124.6	132.7	113.7	148.5	145.9	115.5	122.1
85[e)]	33.1	39.7	72.1	41.7	128.6	135.3	44.3	144.0	129.7	128.9	126.9	128.9	129.7	145.9	128.8	129.5	126.5	129.5	128.8
86[e)]	33.0	39.7	72.0	41.9	128.6	135.4	44.3	144.0	129.6	128.9	126.8	128.9	129.6	145.9	128.8	129.5	126.5	129.5	128.8
87[f)]	29.4	46.0	211.0	47.8	76.1	38.1	31.2	—	—	—	—	—	—	—	—	—	—	—	—
88[b)]	129.9	131.2	—	43.2	69.6	—	30.2	131.0	113.3	145.9	145.3	116.0	119.0	134.3	118.0	143.3	143.3	117.0	135.8
89[c)]	130.4	128.6	73.7	69.8	27.3	27.0	130.0	116.0	145.8	147.9	112.9	129.9	38.3	133.2	130.6	116.2	158.4	116.2	130.6

70[a)]: 19.8, 35.6, 55.9, 56.0 (C×2), 121.9, 122.8, 127.0, 127.7, 128.6, 130.8, 132.0 (C×2), 140.4, 141.0, 145.3, 146.8, 146.9, 147.9, 148.5, 149.1, 183.2, 183.4. **72**[a)]: 35.8, 36.2, 44.8, 54.7, 55.8 (C×2), 56.0 (C×2), 102.0, 109.6, 110.1, 110.6, 113.2, 114.3, 114.8, 119.8, 120.4, 121.7, 122.5, 127.3, 127.7, 128.3, 132.2, 137.1, 139.5, 143.8, 146.4, 146.7, 147.6, 148.0, 148.3, 176.5, 200.5. **73**[a)]: 35.8, 36.7, 37.3, 55.1, 55.2, 56.0 (C×2), 56.0, 57.3, 95.9, 101.9, 109.3, 110.4, 114.2, 114.8, 115.9, 119.4, 120.1, 120.5, 122.4, 127.5, 127.8, 136.6, 138.5, 141.9, 143.8, 146.3, 146.8, 147.5, 148.8, 152.5, 174.8, 201.6. **74**[a)]: 33.9, 43.6, 46.6, 55.8 (C×2), 55.9, 56.0, 59.7, 103.0, 109.3, 111.0, 111.1, 111.1, 114.3, 1147, 119.7, 119.8, 120.4, 122.8, 126.9, 127.6, 130.3, 135.4, 136.2, 139.8, 144.1, 146.2, 146.7, 147.6, 147.7, 148.7, 177.1, 200.8. **82**[a)]: 34.1, 34.3, 40.8, 125.9, 126.4, 126.8, 128.3, 128.4, 128.6, 129.4, 136.5, 148.9, 199.7.

a) Measured in $CDCl_3$; b) Measured in $(CD_3)_2CO$; c) Measured in CD_3OD; d) Measured in DMSO; e) Not mentioned f) Measured in $(CD_3)_2CO+D_2O$.

Table 3. ^{13}C-NMR date of cyclic-diarylheptanoids

Cpd.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
91[a)]	144.7	145.2	150.3	117.2	123.8	134.6	29.4	36.3	81.2	37.1	23.2	30.8	35.8	141.2	115.2	153.9	122.8	125.1	114.8
92[b)]	112.5	146.8	142.9	115.6	122.8	134.0	27.3	41.1	210.5	46.4	19.0	27.2	35.6	140.6	118.0	148.8	140.6	123.4	122.9
93[a)]	126.7	128.9	149.3	145.8	150.3	129.9	27.1	26.4	23.4	40.5	67.9	35.7	27.9	131.0	130.2	117.0	153.2	135.3	130.4
94[a)]	126.7	129.0	149.9	145.9	150.3	130.2	27.3	26.5	23.6	40.5	68.0	35.8	28.0	131.0	130.2	117.0	153.1	135.1	130.3
95[a)]	126.9	128.9	149.1	146.2	150.0	130.9	28.3	22.3	25.1	45.8	212.9	42.4	28.9	132.0	129.3	117.0	153.5	134.0	129.6
96[a)]	126.8	129.1	149.2	146.3	149.4	131.1	28.0	22.3	25.0	45.4	212.7	42.1	28.6	131.9	129.1	117.0	153.4	133.9	129.7
97[c)]	126.0	125.4	151.0	116.0	128.5	130.0	25.2	40.2	209.9	48.7	68.9	72.3	36.2	130.1	128.6	116.0	151.6	133.8	133.8
98[b)]	132.0	130.1	145.4	123.0	122.9	129.1	28.2	38.5	207.0	51.9	75.9	81.2	40.8	136.7	130.3	123.0	146.6	135.4	133.4
101[b)]	120.7	141.0	144.9	184.1	144.4	146.5	34.7	24.1	26.4	26.9	72.1	33.6	39.8	133.7	130.5	117.5	150.9	131.1	184.2
102[b)]	121.3	140.2	145.0	183.8	144.5	146.2	25.6	27.1	21.3	42.0	135.8	130.2	38.9	132.4	130.2	117.5	152.5	134.2	184.1

a) Measured in C5D5N; b) Measured in $CDCl_3$; c) Measured in DMSO.

The reported ^{13}C-NMR data of diarylheptanoids carbons is showed in Table 2 and 3. For compounds **1-2**, **67**, **69, 71, 76-79**, **90**, **99** and **100**, only the ^{1}H-NMR spectroscopic data were reported and compounds **11-20**, **34**, **40**, **49-51**, **57**, **59** and **61** were identified by direct comparison their chromatographic and mass spectral data with authentic standard samples and each other, as for compounds **70**, **72-74** and **82**, a ^{13}C-NMR complete assignments were not given in the report literature and their NMR data were list below the Table 2 as footnotes.

4. The bioactivity of diarylheptanoids

4.1 Anti-oxidative activity

The anti-oxidative of compounds **48** and **88** was evaluated using DPPH radical scavenging

potential with α-tocopherol and L-ascorbic acid as a positive control. The results showed that compound **48** exhibited stronger activity than such natural antioxidants while Compound **88** were comparable to them [47]. Compound **96** also show potent scavenging activity (IC_{50} 8.7 μM) [65]. The antioxidative activities of mistletonone (**75**) were directly determined by electron spin resonance (ESR). It exhibited scavenging capability both on hydroxyl radicals and superoxide anion radicals with IC_{50} values of 0.485 mM and 0.273 mM, comparable with those of (-)-epigallocatechin gallate, the positive control (0.538 mM, 0.131 mM, respectively) [57]. Compound **53** was found to inhibit lipid peroxidation in a more potential manner than α-tocopherol [49]. The curcuminoids Cassumunin A, B, C (**70**, **71** and **69**) and cassumunarin A, B, C (**74**, **72** and **73**) are all potent antioxidants for revealing stronger or equal antioxidant activity than that of curcumin [55, 56].

4.2 Anti-cancer activity

On the evaluation of diarylheptanoids against cancer cell lines, pterocarine (**92**) revealed both cell cycle inhibitory and apoptosis inducing activities. It inhibited the proliferation of tsFT210, HCT-15 and K562 cells with the rates of 20.2±2.4, 23.8±2.4 and 50.5±1.2%, respectively (concentration 100 μg/mL); the follow-up cytometric analysis shows it inhibited the cell cycle mainly at the G_0/G_1 phase and could also induce apoptosis in HCT-15 (19%) and K562 (11%) cells [66]. Rubanol (**101**) revealed cytotoxicity against Lun-06, Neu-04, and Bre-04 cell lines with IC_{50} values of 16.03-32.58 mg/mL [71].

4.3 Hepatoprotective activity

Epihirsutanonol (**35**) was checked for their protective effects on *t*-butylhydroperoxide-induced primary rat hepatocyte injury, and found to show significant hepatoprotective activity. It exhibited effectively stronger than the positive control silibinin, a known approved hepatoprotective agent [38]. Alusenone (**42**) was found significantly hepatoprotective activity on the basis of the evaluation for its protective effects on primary rat hepatocytes pharmacologically induced by *t*-butyl hydroperoxide [44]. Betulaplatoside Ia (**5**) and Ib (**6**) shows protective effect against D-GalN-induced cytotoxicity in primary cultured rat hepatocytes and their hepatoprotective activity effected in a concentration-dependent manner [29].

4.4 Antibacterial activity

Compounds **43**, **45** and **56** were subjected to antimicrobial assessment and all proved to be potent inhibitors against *Helicobactor pylor*, with the MIC values of 9-12 μg/mL against Hp-Sydney strain 1 and the MIC values of 25-30 μg/mL against Hp-F44 [45].

4.5 Antiosteoporotic activity

The antiosteoporotic activity of diarylheptanoids was measured and diospongin B and C (**3**) were screened to exert potent inhibitory effects (completely inhibited the ^{45}Ca release) on bone resorption induced by parathyroid hormone in a bone organ culture system, and a clinical drug elcitonin was used as a positive control [27].

4.6 Melanogenesis inhibitory activity

Melanin pigmentation in skin is a major self-defense mechanism against ultraviolet ray of the sun, while hyperpigmentation may result in a serious aesthetic problem such as freckles and chloasma. The inhibitory effects on melanogenesis of compounds **91**, **95** and **96** were by measured the melanin

level in the B16 melanoma cells, and their cytotoxicity was also examined. All the test constituents exhibited inhibitory effects with 51.2%, 49.6%, and 53.9% reduction of melanin content at 25 mg/mL, respectively, and with very weak toxicity to the cells (81-90% of cell viability at 25 mg/mL) [65].

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