天然多环多异戊烯基间苯三酚衍生物研究进展

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摘 要：多环多异戊烯基间苯三酚衍生物（polycyclic polyprenylated acylphoroglucinols，PPAPs）为藤黄科植物的主要活性成分，其结构新颖，且具有抗菌、抗病毒、抗肿瘤、抗抑郁等多种生物活性，是目前天然产物研究的热点之一。对近年来从植物中分离得到的 226 个天然多环多异戊烯基间苯三酚衍生物化学结构、生物活性等方面的研究概况进行综述，以期为该类化合物的进一步研究提供参考。

关键词：藤黄科；多环多异戊烯基间苯三酚；抗菌活性；抗病毒活性；抗肿瘤活性；抗抑郁活性

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Research in progress on natural polycyclic polyprenylated acylphoroglucinols

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Abstract: As major active components of the plant of Guttiferae family, polycyclic polyprenylated acylphoroglucinols (PPAPs) have become a hot topic in natural product studies for their novel structures and varied bioactivities such as antibacterial, antiviral, antitumor, and antidepressant activities. In this paper, the chemical structures and bioactivities of 226 natural PPAPs have been summarized. It may provide the reference for the further studies of PPAPs.

Key words: Guttiferae; polycyclic polyprenylated acylphoroglucinols; antibacterial activity; antiviral activity; antitumor activity; antidepressant activity

多环多异戊烯基间苯三酚衍生物（polycyclic polyprenylated acylphoroglucinols，PPAPs）主要来源于藤黄科（Guttiferae）藤黄属 *Garcinia* Linn.、金丝桃属 *Hypericum* Linn.、猪胶树属 *Clusia* Linn.、红厚壳属 *Calophyllum* Linn. 等植物中。PPAPs 所包括的骨架种类繁多、结构奇特，且具有抗菌、抗病毒、抗肿瘤、抗抑郁等多种生物活性，这些特异的结构和良好的生物活性吸引了越来越多研究者的兴趣[1-5]。鉴于目前国内外对 PPAPs 的研究方兴未艾，本文对目前已报道的天然的 PPAPs（226 个）进行了整理，为其更深层次的开发和利用提供借鉴。

1 PPAPs 的分类

根据酰基与第 1 个成环的异戊烯取代基相对位置的不同，可将 PPAPs 分成 3 种类型，即 A、B、C 型（图 1）。将间苯三酚上与第 1 个异戊烯基的季碳相连的碳标为 C-1，则酰基在 C-1 位的为 A 型，在 C-3 位的为 B 型，在 C-5 位的为 C 型。其中的 R 常为异丙基、异丁基、仲丁基以及苯基等取代基，R_1 则多为异戊烯基或香叶基，R_3 一般为 H 或异戊烯基。目前所报道的 PPAPs 多数为 A 型或 B 型，C 型仅报道 3 个化合物。

另外，还可以根据 PPAPs 的骨架类型分类，主要包括金刚烷型、类金刚烷型、螺环型、[3.3.1] 型以及 [3.2.1] 型等（图 2）。为了更清晰更系统，在本文将 2 种方法结合起来，对化合物数量较少的金刚烷型、类金刚烷型、螺环型不再细分，而对 [3.3.1]

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型则再细分为 A、B、C 3 类。PPAPs 常见的取代基异戊烯基（isoprenyl）、香叶基（geranyl）、异香叶基（isogeranyl）和 *ω*-异香叶基（*ω*-isogeranyl）的结构见图 3。

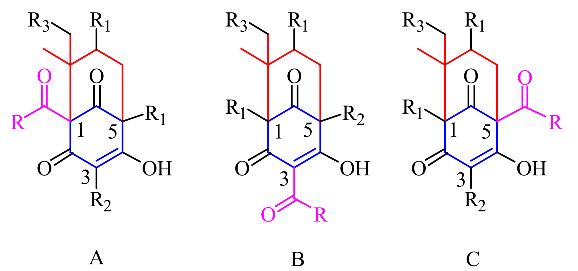


图 1　A、B、C 型 PPAPs 结构式

Fig. 1　Structures of type A, B, and C PPAPs

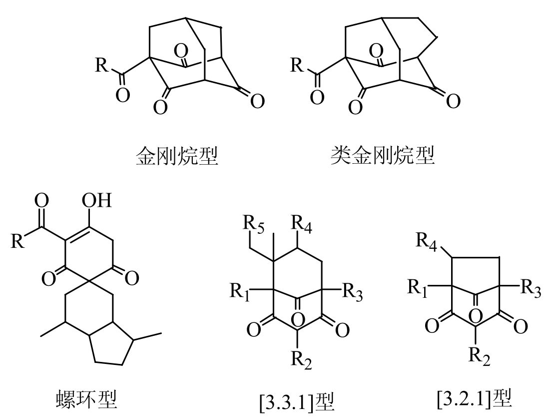


图 2　PPAPs 5 种主要骨架结构类型

Fig. 2　Structures of five main skeletons of PPAPs

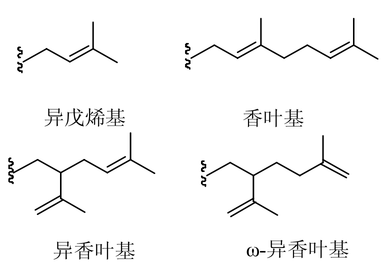


图 3　异戊烯基、香叶基、异香叶基和 ω-异香叶基结构

Fig. 3　Structures of isoprenyl, geranyl, isogeranyl, and ω-isogeranyl groups

2　金刚烷型 PPAPs

金刚烷类 PPAPs 母核骨架中包含有 1 个金刚烷碳架，从目前已发现的化合物来看，包括 [7.3.1.1.0] 和 [3.3.1.1] 2 种骨架（图 4）。这类化合物数目不多，从 1996 年第 1 个具有金刚烷骨架的 PPAPs plukenetione A（**1**）[6]自 *Clusia plukenetii* 中分离得到至今，仅有 13 个该类化合物陆续被报道。尤其是 [7.3.1.1.0] 骨架的 PPAPs，从 2000 年 sampsonione I（**3**）[7]从元宝草 *Hypericum sampsonii* 中被报道后，2005 年才又有 1 个结构相似而取代基不同的衍生物 1-苯甲酰基- 5-(1-羟基-1-甲基乙基)-6,6,13,13-四甲基四环 [7.3.1^{3,11}.0^{3,8}] 十四烷-2,12,14-三酮（**4**）[8]从 *Clusia obdeltifolia* 中被发现，之后数年再无该类骨架化合物的报道。Sampsonione I（**3**）母核为金刚烷骈合六元碳环的刚性骨架结构，对其体外细胞毒活性（P388）筛选发现其半数有效量为 6.9 μg/mL，较与其结构类似的后 1 种骨架的 sampsonione J（**5**）活性强[9]。与 sampsonione J（**5**）类似的侧链上具有三元环氧结构的化合物还有 28,29-epoxyplukenetione A（**6**）[10]和 sampsonione Q（**7**）[11]，很有可能是从侧链为双键的 plukenetione A（**1**）氧化而来。以此类推，sampsonione J（**5**）的前体极有可能是 otogirinin A（**2**）[12]，从三元环氧处次甲基的构型和化合物 **6** 和 **7** 的结构来看，可能还存在 1 个化合物 **5** 的差向异构体，只是目前尚未发现。与前面几个具有三元环氧结构的化合物不同的是，hyperandrone A（**8**）[13]的三元环氧处于 1 个香叶基上。从 *Hypericum sinaicum* 得到的 sinaicinone（**9**）[14]的取代基明显与常见的异戊烯基和香叶基不同，其碳原子数目分别是 8 个和 9 个，而且其中 1 个具有醛基。更有意思的是，B 型 PPAPs (±)-garcinialiptone A（**10** 和 **11**）[15]是以 1 对对映异构体的形式存在的，这提示在 PPAPs 的形成过程中任何 1 步反应只要有手性中心的产生，都可能会有 2 种不同构型的化合物产生，由于该类化合物结构中手性中心众多，可能存在的化合物数目十分庞大。来源于 *Garcinia oblongifolia* 的 garciniagifolone A（**12**）[16]与化合物 **10**、**11** 极为相似，具有这种 C-10 取代基的 PPAPs 十分罕见。这些金刚烷型 PPAPs 的特殊的骨架结构和良好的生物活性也吸引了有机合成化学家的注意，如 B 型结构的 hyperibone K（**13**）和 A 型的化合物 **1** 的全合成都发表在了权威杂志 *J Am Chem Soc* 上[17-19]。化合物 **1**～**3** 的结构见表 1。

3　类金刚烷型 PPAPs

类金刚烷型 PPAPs 的骨架中比金刚烷型多了 1 个碳原子（图 5）。最早报道的这类化合物是从元宝草中分离得到的 sampsonione A（**14**）和 sampsonione B（**15**）[20]，这 2 个化合物都在笼状结构旁边通过缩醛化形成了 1 个五元氧环。对 sampsonione A（**14**）进行体外细胞毒活性（P388）筛选，发现其具有一定的抗肿瘤活性，半数有效量为 13 μg/mL。之后不久，同一研究小组又得到了更多结构更为复杂的化

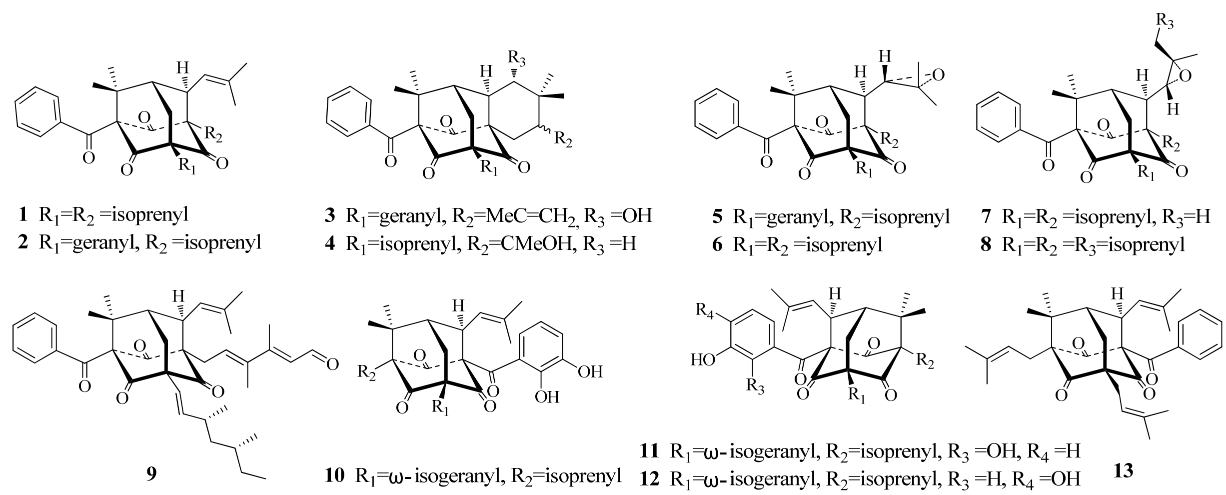


图 4 金刚烷型 PPAPs 的结构

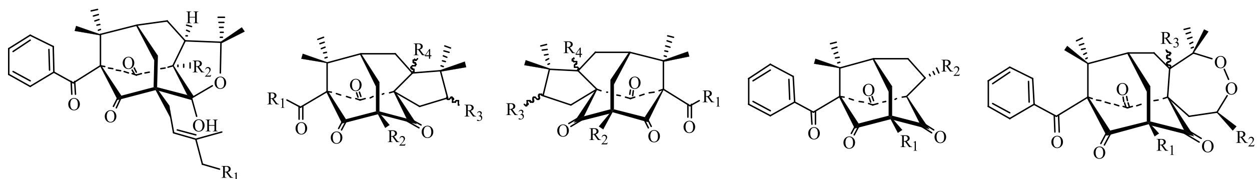
Fig. 4 Structures of adamantane type PPAPs

表 1 金刚烷型 PPAPs 的植物来源

Table 1 Plant origins of adamantane type PPAPs

编号	化合物名称	来源	文献
1	plukenetione A	*Clusia plukenetii*	6
2	otogirinin A	*Hypericum erectum*	12
3	sampsonione I	元宝草	9
4	1-苯甲酰基-5-(1-羟基-1-甲基乙基)-6,6,13,13-四甲基四环[7.3.1^{3,11}.0^{3,8}]十四烷-2,12,14-三酮	*Clusia obdeltifolia*	8
5	sampsonione J	元宝草	9
6	28,29-epoxyplukenetione A	*Clusia havetiodes* var. *stenocarpa*	10
7	sampsonione Q	元宝草	5
8	hyperandrone A	*Hypericum androsaemum*	13
9	sinaicinone	*Hypericum sinaicum*	14
10	(+)-garcinialiptone A	菲岛福木	15
11	(−)-garcinialiptone A	菲岛福木	15
12	garciniagifolone A	岭南山竹子	16
13	hyperibone K	糙枝金丝桃	17

合物 sampsoniones C～H（**17**～**22**）[21]，这些化合物在原本的笼状结构旁边形成了 1 个新的五元碳环。此后的几年，从 *H. sampsonii* 中分离鉴定了 5 个此类化合物 hypersampsone A～E（**23**～**27**）[22]。复旦大学的 1 个研究小组也从 *H. sampsonii* 中发现了一系列类似化合物 hypersampsone G（**28**）[23]、hypersampsone I、J 和 L（**29**、**30** 和 **35**）[24]。该研究小组还发现了一类特殊的有过氧七元环结构的化合物 peroxysampsone A 和 B（**37** 和 **38**）[25]，这种结构的化合物之前仅发现 2 个，即从 *Clusia plukenetii* 中获得的 plukenetione C（**39**）[26]和从 *Clusia havetiodes* 中获得的 33- hydroperoxy-isoplukenetione C（**40**）[10]。其他报道的该类化合物还有从 *Clusia obdeltifolia* 中分离鉴定的 7β-*H*-11-苯甲酰基-5α-羟基-6,6,10,10-四甲基-1-(3-甲基-2-丁烯基) 四环 [7.3.1.1^{3,1}.10^{3,7}] 十四烷- 2,12,14-三酮（**31**）、8-苯甲酰基-4α-(1-羟基-1-甲基乙基)-7,7-二甲基-1,3-二 (3-甲基-2-丁烯基) 三环 [4.3.1.1^{3,8}] 十一烷-2,9,11-三酮（**36**）和 7α-*H*-1-苯甲酰基-4-羟基-3-(3-羟基-3-甲基乙基)-6,6,13,13-四甲基- 11-(3-甲基-2-丁烯基)-5-氧杂四环 [7.3.1.0^{3,7}.0^{4,11}] 十三烷-2,12-二酮（**16**）[27]，以及从连柱金丝桃 *Hypericum cohaerens* 中分离鉴定的 hypercohones A～C（**32**～**34**）[28]。类金刚烷型 PPAPs 具体来源见表 2。



14~16　17~31　32~34　35~36　37~40

图 5　类金刚烷型 PAPs 结构

Fig. 5　Structures of *humo*-adamantane type PPAPs

表 2　类金刚烷型 PPAPs 的植物来源

Table 2　Plant origins of *humo*-adamantane type PPAPs

编号	取代基	化合物名称	来源	文献
14	R_1 = isoprenyl, R_2 = isoprenyl	sampsonione A	元宝草	20
15	R_1 = H, R_2 = isoprenyl	sampsonione B	元宝草	20
16	R_1 = H, R_2 = $CH_2CH_2CMe_2OH$	7α-*H*-1-苯甲酰基-4-羟基-3-(3-羟基-3-甲基丁基)-6,6,13,13-四甲基-11-(3-甲基-2-丁烯基)-5-氧杂四环 [7.3.1.0^{3,7}0^{4,11}] 十三烷-2,12-二酮	*Clusia obdeltifolia*	27
17	R_1 = phenyl, R_2 = geranyl, R_3 = α-CMe_2OH, R_4 = α-H	sampsonione C	元宝草	21
18	R_1 = phenyl, R_2 = geranyl, R_3 = α-CMe=CH_2, R_4 = α-H	sampsonione D	元宝草	21
19	R_1 = phenyl, R_2 = geranyl, R_3 = O (ketone), R_4 = α-H	sampsonione E	元宝草	21
20	R_1 = phenyl, R_2 = geranyl, R_3 = β-CMe_2OH, R_4 = β-H	sampsonione F	元宝草	21
21	R_1 = phenyl, R_2 = isoprenyl, R_3 = β-CMe_2OH, R_4 = β-H	sampsonione G	元宝草	21
22	R_1 = phenyl, R_2 = geranyl, R_3 = H, R_4 = β-H	sampsonione H	元宝草	21
23	R_1 = *i*-Pr, R_2 = geranyl, R_3 = α-CMe=CH_2, R_4 = α-H	hypersampsone A	元宝草	22
24	R_1 = *i*-Pr, R_2 = geranyl, R_3 = β-*i*-Pr, R_4 = β-H	hypersampsone B	元宝草	22
25	R_1 = *i*-Pr, R_2 = geranyl, R_3 = H, R_4 = β-H	hypersampsone C	元宝草	22
26	R_1 = phenyl, R_2 = geranyl, R_3 = α-*i*-Pr, R_4 = α-H	hypersampsone D	元宝草	22
27	R_1 = phenyl, R_2 = geranyl, R_3 = β-*i*-Pr, R_4 = β-H	hypersampsone E	元宝草	22
28	R_1 = phenyl, R_2 = geranyl, R_3 = β-*i*-Pr, R_4 = α-H	hypersampsone G	元宝草	23
29	R_1 = phenyl, R_2 = geranyl, R_3 = H, R_4 = α-H	hypersampsone I	元宝草	24
30	R_1 = phenyl, R_2 = geranyl, R_3 = β-CMe=CH_2, R_4 = α-H	hypersampsone J	元宝草	24
31	R_1 = phenyl, R_2 = isoprenyl, R_3 = α-OH, R_4 = β-H	7β-*H*-11-苯甲酰基-5α-羟基-6,6,10,10-四甲基-1-(3-甲基-2-丁烯基) 四环 [7.3.1.1^{3,1}10^{3,7}] 十四烷-2,12,14-三酮	*Clusia obdeltifolia*	27
32	R_1 = phenyl, R_2 = isoprenyl, R_3 = α-CMe_2OH, R_4 = β-H	hypercohone A	连柱金丝桃	28
33	R_1 = phenyl, R_2 = isoprenyl, R_3 = β-CMe=CH_2, R_4 = β-H	hypercohone B	连柱金丝桃	28
34	R_1 = phenyl, R_2 = geranyl, R_3 = β-CMe=CH_2, R_4 = β-H	hypercohone C	连柱金丝桃	28
35	R_1 = geranyl, R_2 = isoprenyl	hypersampsone L	元宝草	24
36	R_1 = isoprenyl, R_2 = CMe_2OH	8-苯甲酰基 1-4α-(1-羟基-1-甲基乙基)-7,7-二甲基-1,3-二 (3-甲基-2-丁烯基) 三环 [4.3.1.1^{3,8}] 十一烷-2,9,11-三酮	*Clusia obdeltifolia*	27
37	R_1 = isoprenyl, R_2 = β-CMe_2OOH, R_3 = α-H	peroxysampsone A	元宝草	25
38	R_1 = isoprenyl, R_2 = α-CMe_2OH, R_3 = β-H	peroxysampsone B	元宝草	25
39	R_1 = isoprenyl, R_2 = β-CMe_2OH, R_3 = α-H	plukenetione C	*Clusia plukenetii*	26
40	R_1 = CH=CHCMe_2OOH, R_2 = β-CMe_2OH, R_3 = α-H	33-hydroperoxyisoplukenetione C	*Clusia havetiodes* var. *stenocarpa*	10

4 螺环型 PPAPs

螺环型PPAPs是由酰基化的间苯三酚上的香叶基通过折叠环合，与间苯三酚的C-3位形成螺环的化合物以及相关衍生物，目前共发现23个此类型的化合物（图6和表3）。

最早的螺环型 PPAPs 是日本学者于 2008 年报道的 tomoeone A～H（**41**～**48**）[29]，其母体仍然是间苯三酚，C-1 位为酰基取代，C-5 位为 2 个异戊烯基取代，C-3 位原本是香叶基取代，但是香叶基发生了环合形成了 1 个骈合的五元环和六元环，且六元环与间苯三酚 C-3 位形成了螺环。其中，化合物 **46** 的生物活性突出，不但对 KB 细胞的半数抑制浓度达到了 6.2 μmol/L，对 KB-C2 和 K562/Adr 细胞的抑制效果也优于阿霉素。之后又陆续有类似化合物被报道，其中有 C-1 位为苯甲酰取代的 hyperbeanol A～D（**49**～**52**）[30]，乙酰基取代的 harrisotone A～E（**53**～**57**）[31]，其中化合物 **49** 是目前为止唯一通过单晶确证过结构的螺环型 PPAPs 化合物。从生物活性上来看，这些化合物大都具有一定的细胞毒活性。另外，chipericumin A～D（**58**～**61**）是罕见的 C-5 位为甲基和异戊烯基取代的螺环型 PPAPs 化合物[32]，在化合物 **58** 和 **59** 中，C-5 位异戊烯基还与 C-6 位羟基形成了 1 个新的呋喃环。Hyperielliptone HA（**62**）、HB（**63**）[33]都是以互变异构体混合的形式得到的，这也是这类化合物中唯一以混合物形式报道的化合物。

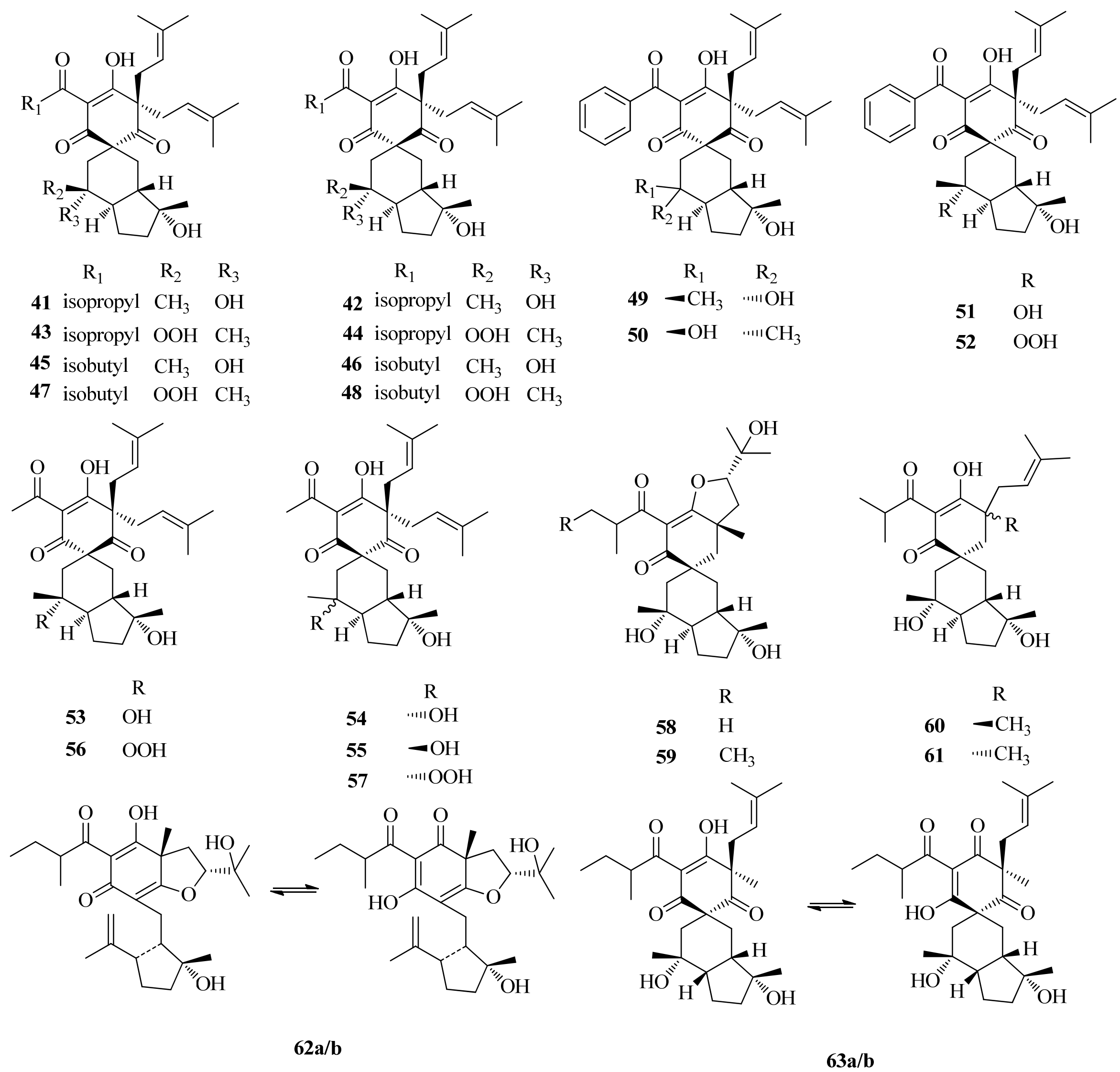


图 6 螺环型 PPAPs 结构

Fig. 6 Structures of spiro type PPAPs

表 3　螺环型 PPAPs 植物来源

Table 3　Plant origins of spiro type PPAPs

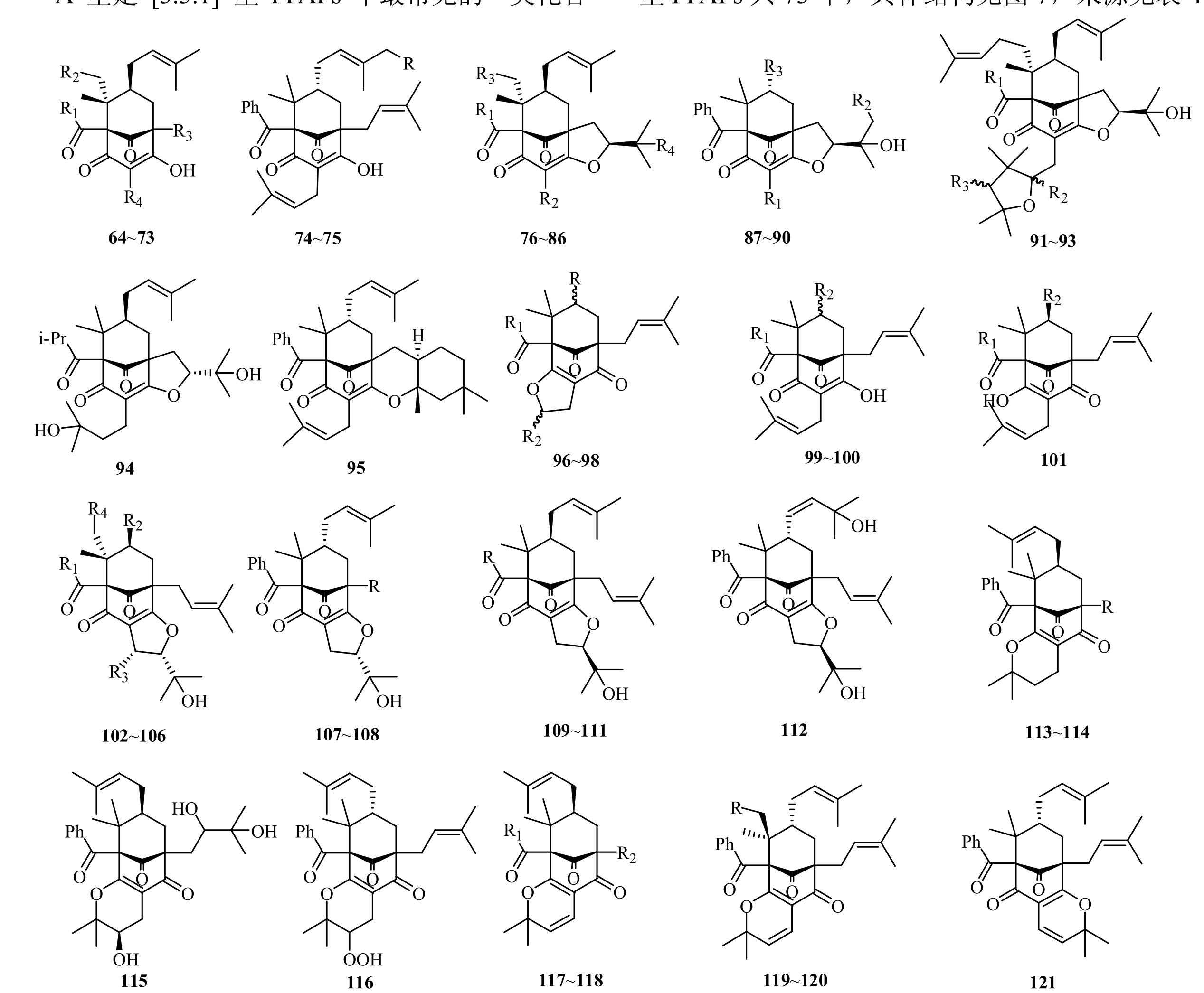
编号	化合物名称	来源	文献
41～48	tomoeone A～H	黄海棠	29
49～52	hyperbeanol A～D	栽秧花	30
53～57	harrisotone A～E	牛筋果	31
58～61	chipericumin A～D	*Hypericum chinense*	32
62a/b	hyperielliptone HA	*Hypericum geminiflorun*	33
63a/b	hyperielliptone HB	*Hypericum geminiflorun*	33

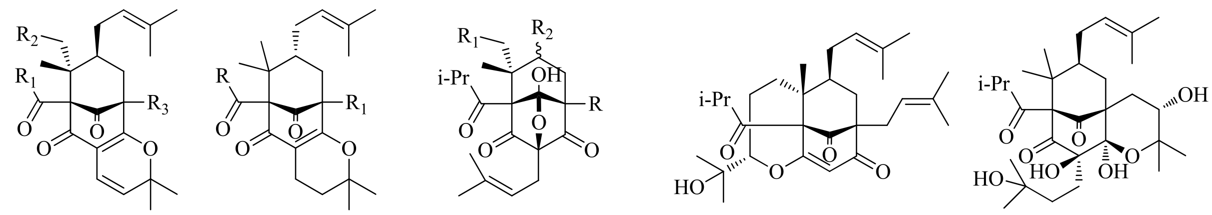
5　[3.3.1] 型 PPAPs

由于 [3.3.1] 型 PPAPs 数量较多（145 个），为了更方便综述和查阅，特将其细分为 A、B 和 C 型，其中 A、B 型 PPAPs 数量较多，C 型仅 3 种。[3.3.1] 型 PPAPs 中，A 型包括化合物 **64～136**，B 型包括化合物 **137～205**，C 型包括化合物 **206～208**。

5.1　[3.3.1] A 型 PPAPs

A 型是 [3.3.1] 型 PPAPs 中最常见的一类化合物，其特征是酰基连接在 C-1 位上（图 1）。由于酰基的吸电子诱导效应，这类化合物 C-1 的化学位移值都较大，一般在 δ 70 以上，加之其 C-2、9 位往往也是羰基，则 C-1 的化学位移可接近 δ 80，这一点很值得注意，对于不熟悉这类化合物的研究者来说，这样的化学位移极易被误认为是连接了氧原子，从而对结构的正确解析造成干扰。目前已分离鉴定的 A 型 PPAPs 共 73 个，具体结构见图 7，来源见表 4。





122~128　129~131　132~134　135　136

图 7　[3.3.1] A 型 PPAPs 结构

Fig. 7　Structures of [3.3.1] A type PPAPs

表 4　A 型 PPAPs 植物来源

Table 4　Plant origins of [3.3.1] A type PPAPs

编号	取代基	化合物名称	来源	文献
64	R_1 = *i*-Pr, R_2 = R_3 = R_4 = isoprenyl	hyperforin	贯叶连翘	34-35
65	R_1 = *s*-Bu, R_2 = R_3 = R_4 = isoprenyl	adhyperforin	贯叶连翘	36
66	R_1 = *i*-Pr, R_2 = R_3 = isoprenyl, R_4 = H	hyperevolutin A	*Hypericum revolutum*	37
67	R_1 = *s*-Bu, R_2 = R_3 = isoprenyl, R_4 = H	hyperevolutin B	*Hypericum revolutum*	37
68	R_1 = Ph, R_2 = H, R_3 = R_4 = isoprenyl	nemorosone	*Clusia insignis*	38
69	R_1 = 3-hydroxyphenyl, R_2 = H, R_3 = R_4 = isoprenyl	hydroxynemorosone	*Clusia nemorosa*	38
70	R_1 = Ph, R_2 = H, R_3 = isogeranyl, R_4 = isoprenyl	chamone I	*Clusia grandiflora*	39
71	R_1 = *i*-Pr, R_2 = H, R_3 = $CH_2CH_2CMe_2OH$, R_4 = isoprenyl	garcinielliptone A	菲岛福木	40
72	R_1 = *s*-Bu, R_2 = H, R_3 = isoprenyl, R_4 = CH_2CH_2-CMe_2OH	garcinielliptone D	菲岛福木	40
73	R_1 = *s*-Bu, R_2 = H, R_3 = isoprenyl, R_4 = (*E*)-CH=CH-CMe_2OH	garcinielliptone F	菲岛福木	41
74	R = H	plukenetione D	*Clusia nemorosa*	26,42
75	R = OAc	insignone	*Clusia insignis*	43
76	R_1 = Ph, R_2 = isoprenyl, R_3 = H, R_4 = β-CMe_2OH	hyperibone G	糙枝金丝桃	44
77	R_1 = Ph, R_2 = isoprenyl, R_3 = H, R_4 = β-CMe_2OH	propolone D	*Cuban propolis*	45
78	R_1 = Ph, R_2 = $CH_2CH(OH)CMe$=CH_2, R_3 = H, R_4 = β-CMe_2OH	hyperibone D	糙枝金丝桃	44
79	R_1 = *i*-Pr, R_2 = isoprenyl, R_3 = H, R_4 = β-CMe_2OH	garsubellin A	*Garcinia subelliptica*	46
80	R_1 = *s*-Bu, R_2 = isoprenyl, R_3 = H, R_4 = β-CMe_2OH	garsubellin B	菲岛福木	47
81	R_1 = *i*-Pr, R_2 = R_3 = isoprenyl, R_4 = β-CMe_2OH	furohyperforin	贯叶连翘	48
82	R_1 = *i*-Pr, R_2 = R_3 = isoprenyl, R_4 = β-CMe_2OOH	33-deoxy-33-hydroperoxyfurohyper-forin	贯叶连翘	49
83	R_1 = *i*-Pr, R_2 = R_3 = isoprenyl, R_4 = α-CMe_2OH	hypercohin E	连柱金丝桃	50
84	R_1 = *i*-Bu, R_2 = R_3 = isoprenyl, R_4 = α-CMe_2OH	hypercohin F	连柱金丝桃	50
85	R_1 = *i*-Pr, R_2 = R_3 = isoprenyl, R_4 = β-CMe_2OH	hypercohin G	连柱金丝桃	50
86	R_1 = Ph, R_2 = R_3 = isoprenyl, R_4 = β-CMe_2OH	hypercohin H	连柱金丝桃	50
87	R_1 = $CH_2CH(OH)CMe$=CH_2, R_2 = H, R_3 = (*E*)-CH=$CHCMe_2OH$	hyperibone E	糙枝金丝桃	44
88	R_1 = isoprenyl, R_2 = H, R_3 = (*E*)-CH=$CHCMe_2OH$	hyperibone F	糙枝金丝桃	44
89	R_1 = R_2 = R_3 = isoprenyl	sampsonione K	元宝草	7
90	R_1 = R_3= isoprenyl, R_2 = H	sampsonione L	元宝草	7
91	R_1 = *i*-Pr, R_2 = β-H, R_3 = β-CH_2OH	hypercohin A	连柱金丝桃	50
92	R_1 = Ph, R_2 = β-H, R_3 = β-CH_2OH	hypercohin B	连柱金丝桃	50

续表 4

编号	取代基	化合物名称	来源	文献
93	R_1 = *i*-Pr, R_2 = α-H, R_3 = α-CH_2OH	hypercohin C	连柱金丝桃	50
94		garcinielliptone C	菲岛福木	40
95		未命名	*Clusia obdeltifolia*	8
96	R = β-isoprenyl, R_1 = phenyl, R_2 = α-CMe_2OH	propolone C	*Cuban propolis*	45
97	R = α-isoprenyl, R_1 = phenyl, R_2 = α-CMe_2OH	sampsonione N	元宝草	5
98	R = α-(*R*)-ω-isogeranyl, R_1 = 3,4-dihydroxyphenyl, R_2 = β-CMe_2OH	garcinialiptone C	菲岛福木	15
99	R_1 = 3,4-dihydroxyphenyl, R_2 = β-(*S*)-ω-isogeranyl	garcinielliptone FC	菲岛福木	51
100	R_1 = 3,4-dihydroxyphenyl, R_2 = α-(*R*)-ω-isogeranyl	garcinialiptone D	菲岛福木	15
101	R_1 = 3,4-dihydroxyphenyl, R_2 = (*S*)-ω-isogeranyl (tautomer)	garcinielliptone FC	菲岛福木	51
102	R_1 = *i*-Pr, R_2 = isoprenyl, R_3 = R_4 = H	garsubellin D	菲岛福木	47
103	R_1 = *s*-Bu, R_2 = isoprenyl, R_3 = R_4 = H	garsubellin E	菲岛福木	47
104	R_1 = Ph, R_2 = isoprenyl, R_3 = R_4 = H	hyperibone B	糙枝金丝桃	44
105	R_1 = 3,4-dihydroxyphenyl, R_2 = (*R*)-isogeranyl, R_3 = R_4 = H	garcinielliptone FB	菲岛福木	52
106	R_1 = *s*-Bu, R_2 = R_3= isoprenyl, R_4 = OH	hypercohin I	连柱金丝桃	50
107	R = geranyl	sampsonione M	元宝草	7
108	R = isoprenyl	sampsonione O	元宝草	5
109	R = *i*-Pr	garsubellin C	菲岛福木	46
110	R = Ph	hyperibone A	糙枝金丝桃	44
111	R = Ph	garcinielliptone I	菲岛福木	41
112		garcinielliptone I	糙枝金丝桃	44
113	R = isogeranyl	chamone II	*Clusia grandiflora*	39
114	R = isogeranyl	hypersampsone H	元宝草	23
115		propolone B	*Cuban propolis*	45
116		15,16-dihydro-16-hydroperoxy-plukenetione F	*Clusia havetiodes* var. *stenocarpa*	10
117	R_1 = *i*-Pr, R_2 = methyl	papuaforin B	*Hypericum papuanum*	53
118	R_1 = Ph	scrobiculatone B	*Clusia scrobiculata*	43
119	R = H	plukenetione F	*Clusia plukenetii*	26
120	R = isoprenyl	hypersampsone F	元宝草	27
121		plukenetione G	*Clusia plukenetii*	26
122	R_1 = *i*-Pr, R_2 = R_3 = isoprenyl	pyrano [7,28-b] hyperforin	贯叶连翘	54
123	R_1 = Ph, R_2 = H, R_3 = isoprenyl	scrobiculatone A	*Clusia scrobiculata*	43
124	R_1 = *i*-Pr, R_2 = H, R_3 = CH_3	papuaforin A	*Hypericum papuanum*	53
125	R_1 = *s*-Bu, R_2 = H, R_3 = CH_3	papuaforin C	*Hypericum papuanum*	53
126	R_1 = *s*-Bu, R_2 = isoprenyl, R_3 = CH_3	papuaforin D	*Hypericum papuanum*	53
127	R_1 = *i*-Pr, R_2 = isoprenyl, R_3 = CH_3	papuaforin E	*Hypericum papuanum*	53
128	R_1 = s-Bu, R_2 = R_3 = isoprenyl	hypercohin I	连柱金丝桃	50
129	R = Ph, R_1 = isoprenyl	propolone A	*Cuban propolis*	55
130	R = *i*-Pr, R_1 = isoprenyl	garcinielliptone B	菲岛福木	40
131	R = Ph, R_1 = geranyl	hypersampsone K	元宝草	24
132	R = R_1 = isoprenyl, R_2 = β-isoprenyl	8-hydroxyhyperforin-8,1-hemiacetal	贯叶连翘	49
133	R = CH_3, R_1 = isoprenyl, R_2 = β-isoprenyl	hyperibone J	糙枝金丝桃	17
134	R = isoprenyl, R_1 = H, R_2 = α-(*E*)-CH_2CH=CMeCHO	spiranthenone A	*Spiranthera odoratissima*	56
135		oxepahyperforin	贯叶连翘	49
136		garcinielliptone H	菲岛福木	41

5.2 [3.3.1] B 型 PPAPs

[3.3.1] B 型 PPAPs 的特征是酰基连接在 C-3 位上（图 1）。C-3/C-4 或者 C-3/C-2 往往是 1 个烯醇结构，酰基的存在可使得烯醇结构更加稳定。由于存在连续的季碳，酰基的位置也无法直接通过 HMBC 确定，只能综合考虑碳原子类型、化学位移以及高分辨质谱来确定。目前，已有 69 个 B 型 PPAPs 化合物被鉴定（图 8 和表 5）。

5.3 [3.3.1] C 型 PPAPs

[3.3.1] C 型 PPAPs 目前只报道 3 个化合物（garcinielliptone K～M，**206**～**208**）。如果将其桥头上的 2 个取代基相互交换，则分别与 hyperibone B（**104**）、garsubellin C（**109**）和 garsubellin D（**102**）一致，而 garcinielliptone K（**206**）和 hyperibone B（**104**）于 $CDCl_3$ 中测试的 NMR 明显不同，这从侧面说明了 garcinielliptone K

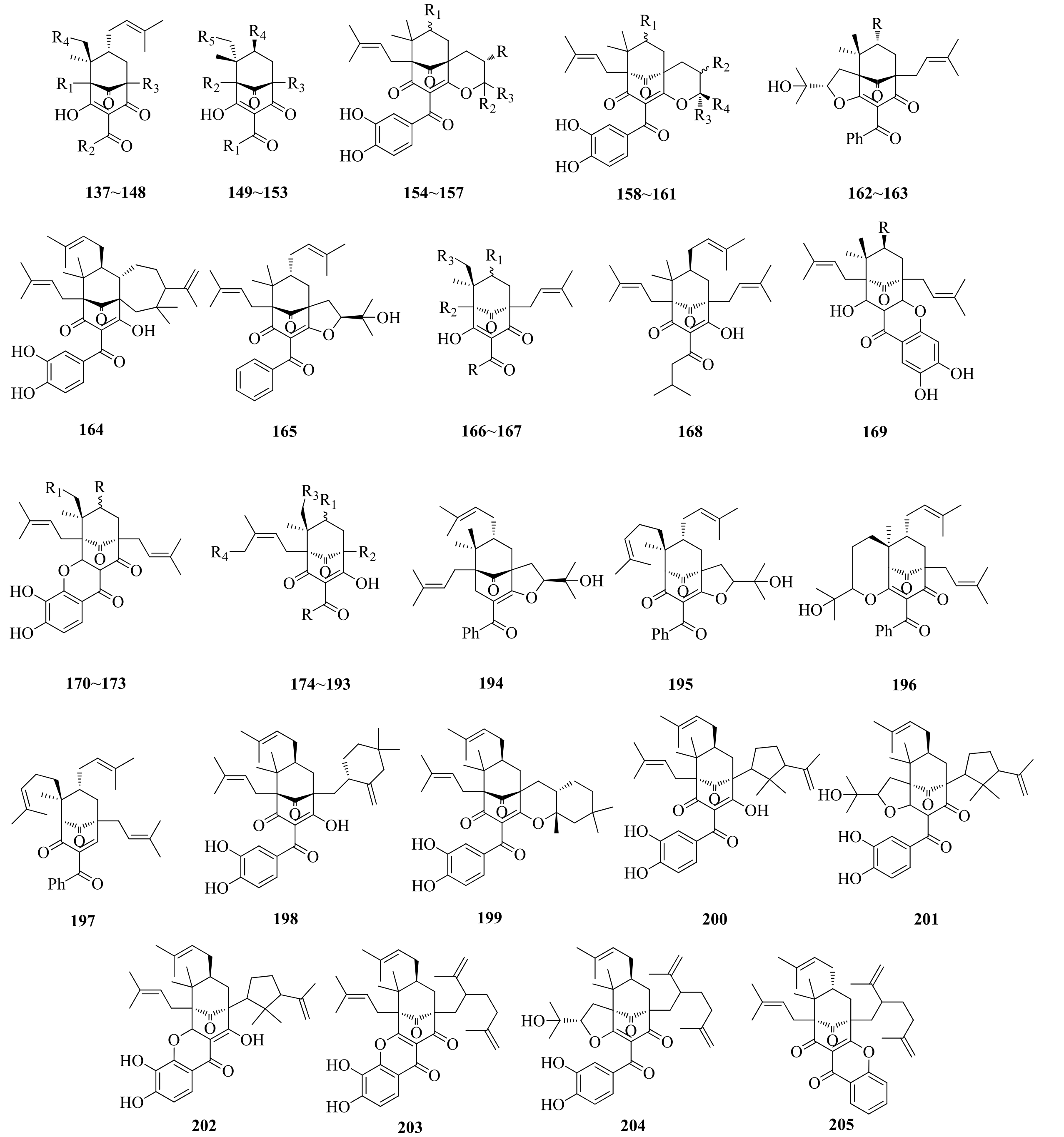


图 8 [3.3.1] B 型 PPAPs 结构

Fig. 8 Structures of [3.3.1] B type PPAPs

表 5　[3.3.1] B 型 PPAPs 植物来源

Table 5　Plant origins of [3.3.1] B type PPAPs

编号	取代基	化合物名称	来源	文献
137	R_1 = 3,4-dihydroxyphenyl, R_2 = R_3 = R_4 = isoprenyl	guttiferone A	*Symphonia globulifera*	57
138	R_1 = 3,4-dihydroxyphenyl, R_2 = R_4 = isoprenyl, R_3 = ω-isogeranyl	guttiferone C	*Symphonia globulifera*	57
139	R_1 = 3,4-dihydroxyphenyl, R_2 = R_4 = isoprenyl, R_3 = isogeranyl	guttiferone D	*Symphonia globulifera*	57
140	R_1 = 3,4-dihydroxyphenyl, R_2 = isoprenyl, R_3 = (*S*)-isogeranyl, R_4 = H	guttiferone E	*Garcinia ovalifolia*	57
141	R_1 = 3,4-dihydroxyphenyl, R_2 = isoprenyl, R_3 = (*S*)-isogeranyl, R_4 = H	garcinol	*Garcinia bancana*	58
142	R_1 = 3,4-dihydroxyphenyl, R_2 = isoprenyl, R_3 = (*R*)-isogeranyl, R_4 = H	guttiferone F	*Allanblackia stuhlmannii*	59
143	R_1 = 3,4-dihydroxyphenyl, R_2 = isoprenyl, R_3 = geranyl, R_4 = H	guttiferone I	*Garcinia griffithii*	60
144	R_1 = 3,4-dihydroxyphenyl, R_2 = isoprenyl, R_3 = (*S*)-ω-isogeranyl, R_4 = H	xanthochymol	*Clusia rosea*	61
145	R_1 = CH_3, R_2 = Ph, R_3 = isoprenyl, R_4 = H	hyperibone L	糙枝金丝桃	17
146	R_1 = CH_3, R_2 = *i*-Pr, R_3 = isoprenyl, R_4 = H	hyperpapuanone	*Hypericum papuanum*	53
147	R_1 = R_3 = isoprenyl, R_2 = Ph, R_4 = H	7-*epi*-clusianone	*Clusia sandinensis*	62
148	R_1 = $CHPhCH_2CO_2H$, R_2 = *i*-Bu, R_3 = isoprenyl, R_4 = H	laxifloranone	*Marila laxiflora*	63
149	R_1 = 3,4-dihydroxyphenyl, R_2 = R_3 = R_4 = isoprenyl, R_5 = H	aristophenone	*Garcinia aristata*	64
150	R_1 = Ph, R_2 = R_3 = R_4 = isoprenyl, R_5 = H	clusianone	*Clusia congestiflora*	65
151	R_1 = Ph, R_2 = R_4 = isoprenyl, R_3 = isogeranyl, R_5 = H	spiritone	*Clusia spiritu-sanctensis*	43
152	R_1 = 3,4-dihydroxyphenyl, R_2 = isoprenyl, R_3 = R_4 = geranyl, R_5 = H	guttiferone B	*Symphonia globulifera*	57
153	R_1 = 3,4-dihydroxyphenyl, R_2 = R_3 = R_5 = isoprenyl, R_4 = geranyl	guttiferone G	*Garcinia macrophylla*	66
154	R = isoprenyl, R_1 = α-isoprenyl, R_2 = CH_3, R_3 = CH_3	isogarcinol	*Garcinia gambogia*	67
155	R = isoprenyl, R_1 = α-isoprenyl, R_2 = CH_3, R_3 = CH_3	isoxanthochymol	*Garcinia ovalifolia*	57
156	R = $CH_2CH_2CMe{=}CH_2$, R_1 = α-isoprenyl, R_2 = R_3 = CH_3	cycloxanthochymol	*Garcinia* gambogia	67
157	R= $CMe{=}CH_2$, R_1 = β-isoprenyl, R_2 = H, R_3 = $CH{=}CMe_2$	garcinialiptone B	菲岛福木	68
158	R_1 = α-isoprenyl, R_2 = $CH_2CH_2CMe{=}CH_2$, R_3 = R_4 = CH_3	(−)-cycloxanthochymol	菲岛福木	68
159	R_1 = β-isoprenyl, R_2 = β-$CMe{=}CH_2$, R_3 = α-$CH{=}CMe_2$	garcicowin C	云树	69
160	R_1 = α-isoprenyl, R_2 = β-$CMe{=}CH_2$, R_3 = α-$CH{=}CMe_2$	garcicowin D	云树	69
161	R_1 = R_2 = α-isoprenyl, R_3 = R_4 = CH_3	isoxanthochymol	*Rheedia acuminata*	70
162	R = (*E*)-$CH{=}CHCMe_2OH$	hyperibone H	糙枝金丝桃	71
163	R = isoprenyl	hyperibone I	糙枝金丝桃	71
164		guttiferone H	大叶藤黄	72
165		sampsonione P	元宝草	5
166	R = *s*-Bu, R_1 = β-isoprenyl, R_2 = R_3 = isoprenyl	spiranthenones B (互变异构体)	*Spiranthera odoratissima*	56
167	R = phenyl, R_1 = α-isoprenyl, R_2 = isoprenyl, R_3 = H	guttiferone Q	*Garcinia chinensis*	73
168		spiranthenones B (互变异构体)	*Spiranthera odoratissima*	56
169	R = geranyl	guttiferone O	*Garcinia afzelii*	74
170	R = α-isoprenyl, R_1 = isoprenyl	oxy-guttiferone K	*Garcinia cambogia*	75
171	R = α-geranyl, R_1 = isoprenyl	garciyunnanin B	云南藤黄	76
172	R = β-geranyl, R_1 = H	oblongifolin I	岭南山竹子	68
173	R = α-geranyl, R_1 = H	oblongifolin J	岭南山竹子	68
174	R = 3,4-dihydroxyphenyl, R_1 = β-geranyl, R_2 = isoprenyl, R_3 = R_4 = H	oblongifolin A	岭南山竹子	77
175	R = 3,4-dihydroxyphenyl, R_1 = α-geranyl, R_2 = isoprenyl, R_3 = R_4 = H	oblongifolin B	岭南山竹子	77
176	R = 3,4-dihydroxyphenyl, R_1 = α-geranyl, R_2 = R_3 = isoprenyl, R_4 = H	oblongifolin C	岭南山竹子	77
177	R = 3,4-dihydroxyphenyl, R_1 = β-geranyl, R_2 = geranyl, R_3 = R_4 = H	oblongifolin D	岭南山竹子	77

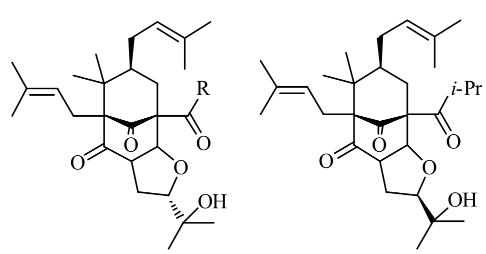
续表 5

编号	取代基	化合物名称	来源	文献
178	R = phenyl, $R_1 = R_2 = R_3$ = isoprenyl, R_4 = H	guttiferone I	*Garcinia virgata*	78
179	R = 3-hydroxyphenyl, $R_1 = R_3$ = isoprenyl, R_2 = (*E*)-CH_2CH=C-$MeCH_2OH$, R_4 =H	guttiferone J	*Garcinia virgata*	78
180	R = 3,4-dihydroxyphenyl, R_1 = α-isoprenyl, $R_2 = R_3$ = isoprenyl, R_4 = H	guttiferone K	*Rheedia calcicola*	79
181	R = 2,4,5-trihydroxyphenyl, R_1 = α-isoprenyl, $R_2 = R_3$ = isoprenyl, R_4 = H	guttiferone L	*Rheedia calcicola*	79
182	R = 3,4-dihydroxyphenyl, R_1 = β-geranyl, R_2 = isoprenyl, R_3 = H, $R_4 = CH_2CH_2CMe=CH_2$	semsinone A	*Garcinia semseii*	80
183	R = 3,4-dihydroxyphenyl, R_1 = β-geranyl, R_2 = geranyl, $R_3 = R_4$ = H	guttiferone M	*Garcinia cambogia*	75
184	R = 3-hydroxyphenyl, R_1 = β-isoprenyl, R_2 = geranyl, $R_3 = R_4$ = H	guttiferone N	*Garcinia cambogia*	75
185	R = 3-hydroxyphenyl, R_1 = α-isoprenyl, $R_2 = R_3$ = isoprenyl, R_4 = H	garciyunnanin A	云南藤黄	76
186	R = 3,4-dihydroxyphenyl, R_1 = α-isoprenyl, R_2 = geranyl, R_3 = H, R_4 = isoprenyl	guttiferone O	*Garcinia solomonensis*	81
187	R = 3,4-dihydroxyphenyl, R_1 = α-isoprenyl, R_2 = geranyl, $R_3 = R_4$ = H	guttiferone P	*Garcinia solomonensis*	81
188	R = 3-hydroxyphenyl, R_1 = β-geranyl, R_2 = isoprenyl, $R_3 = R_4$ = H	oblongifolin E	岭南山竹子	68
191	R = 3,4-dihydroxyphenyl, R_1 = α-isoprenyl, R_2 = 5-(*S*)-hydroxy-geranyl, $R_3 = R_4$ = H	32-hydroxy-*ent*-guttiferone M	*Rheedia edulis*	82
192	R = 3-hydroxyphenyl, R_1 = β-isoprenyl, $R_2 = R_3$ = isoprenyl, R_4 = H	6-*epi*-guttiferone J	*Rheedia edulis*	82
193	R = 3-hydroxyphenyl, R_1 = α-geranyl, $R_2 = R_3 = R_4$ = isoprenyl	garcicowin B	云树	69
194		sampsonione P	元宝草	5
195		guttiferone R	*Garcinia chinensis*	73
196		guttiferone S	*Garcinia chinensis*	73
197		cowanone	云树	83
198		acuminophenone	*Rheedia acuminata*	70
199		guttiferone K	*Rheedia acuminata*	70
200		thorelione A	*Calophyllum thorelii*	84
201		thorelione B	*Calophyllum thorelii*	84
202		oxy-thorelione A	*Calophyllum thorelii*	84
203		nujiangefolin A	怒江藤黄	85
204		nujiangefolin C	怒江藤黄	85
205		nujiangefolin B	怒江藤黄	85

结构的正确性。综合以上分析推测，可能是在生物合成途径中，异戊烯基与间苯三酚发生反应，形成 C 型 PPAPs 的几率极低。C 型 PPAPs 结构见图 9，来源见表 6。

6 [3.2.1] 型 PPAPs

[3.2.1] 型 PPAPs 与 [3.3.1] 型很相似，只是第 1 个异戊烯基在与间苯三酚环合时形成的是五元环。这类化合物数量十分稀少，都来自金丝桃属，其结构见图 10，来源见表 7。



206~207　　208

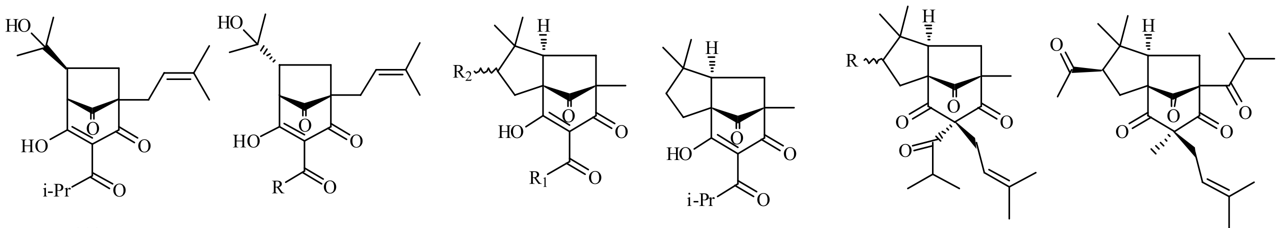
图 9 [3.3.1] C 型 PPAPs 结构

Fig. 9 Structures of [3.3.1] C type PPAPs

表 6　[3.3.1] C 型 PPAPs 植物来源

Table 6　Plant origins of [3.3.1] C type PPAPs

编号	取代基	化合物名称	来源	文献
206	R = Ph	garcinielliptone K	菲岛福木	44
207	R = *i*-Pr	garcinielliptone M	菲岛福木	44
208		garcinielliptone L	菲岛福木	44



209　**210~211**　**212~218**　**219**　**220~221**　**222**

图 10　[3.2.1] 型 PPAPs 结构

Fig. 10　Structures of [3.2.1] type PPAPs

表 7　[3.2.1] 型 PPAPs 植物来源

Table 7　Plant origins of [3.2.1] type PPAPs

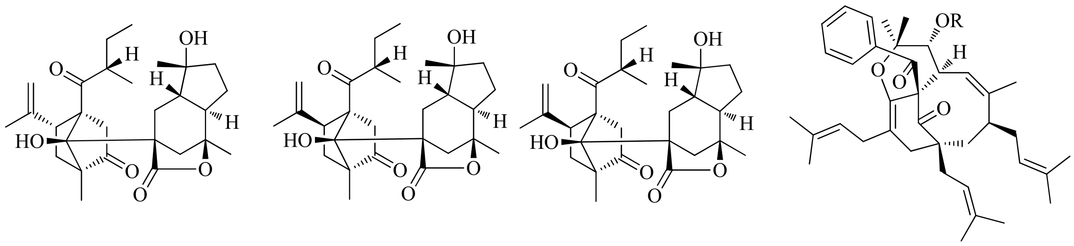
编号	取代基	化合物名称	来源	文献
209		enaimeone A	*Hypericum papuanum*	86
210	R = *i*-Pr	enaimeone B	*Hypericum papuanum*	86
211	R = *s*-Bu	enaimeone C	*Hypericum papuanum*	86
212	R_1 = *i*-Pr, R_2 = CMe=CH_2	ialibinone A	*Hypericum papuanum*	87
213	R_1 = *s*-Bu, R_2 = CMe=CH_2	ialibinone C	*Hypericum papuanum*	87
214	R_1 = *i*-Pr, R_2 = CMe_2OH	1′-hydroxyialibinone A	*Hypericum papuanum*	86
215	R_1 = *i*-Pr, R_2 = CMe=CH_2	ialibinone B	*Hypericum papuanum*	87
216	R_1 = *s*-Bu, R_2 = CMe=CH_2	ialibinone D	*Hypericum papuanum*	87
217	R_1 = *i*-Pr, R_2 = CMe_2OH	1′-hydroxyialibinone B	*Hypericum papuanum*	86
218	R_1 = *s*-Bu, R_2 = CMe_2OH	1′-hydroxyialibinone D	*Hypericum papuanum*	86
219		ialibinone E	*Hypericum papuanum*	87
220	R = α-$COCH_3$	takaneone A	*Hypericum sikokumontanum*	88
221	R = β-$COCH_3$	takaneone B	*Hypericum sikokumontanum*	88
222		takaneone C	*Hypericum sikokumontanum*	88

7　其他类型的 PPAPs

2011 年，日本学者从 *Hypericum chinense* 中得到了 3 个结构特异的 PPAPs biyoulactone A～C（**223**～**225**）[89]，这几个化合物从生源上来说应该属于螺环型 PPAPs 衍生物，但是其结构变化很大，如图 11 所示。化合物 **223**～**225** 的十碳单位没有变化，其变化主要发生在间苯三酚所在的六元环上。该环通过多次氧化断裂和重新环合，最终形成了 1 个新的碳环和 1 个内酯环。2012 年，我国研究人员从连柱金丝桃中得到了 1 个具有 [5.3.1] 全新骨架的化合物 hypercohin A（**226**）[90]，并且获得了其衍生物（**226a**）的单晶，通过单晶衍射确定了该化合物的绝对构型。体外细胞毒活性表明 hypercohin A 对多种肿瘤细胞具有较好的抑制效果，除此之外，该化合物还具有一定的胆碱酯酶抑制作用。化合物 **223**～**226** 来源见表 8。

8　结语和展望

从 PPAPs 的结构上看，其骨架结构复杂多变，取代基的变化更是丰富多样；从其活性上看，PPAPs 具有多种活性，如抗菌、抗病毒、抗氧化、细胞毒



223 224 225 226 R = H
226a R = p-BrC$_6$H$_4$CO$^-$

图 11 其他类型 PPAPs 的结构
Fig. 11 Structures of other types of PPAPs

表 8 其他类型 PPAPs 植物来源
Table 8 Plant origins of other types of PPAPs

编号	化合物名称	来源	文献
223	biyoulactone A	*Hypericum chinense*	90
224	biyoulactone B	*Hypericum chinense*	90
225	biyoulactone C	*Hypericum chinense*	90
226	hypercohin A	连柱金丝桃	90

和抗 HIV 等，其中部分还具有突出的抗抑郁活性。PPAPs 的这 2 方面的特性吸引了许多化学相关领域的研究人员，仅在过去的 8 年内发现的新天然 PPAPs 就超过了 100 个。藤黄科有约 40 属 1 000 种，资源十分丰富，而目前对其 PPAPs 成分的研究仅局限于其中几个属的植物，对其他尚无人涉足的种属展开研究也是十分必要的。PPAPs 特异的结构和良好的生物活性已经吸引了越来越多的植物化学、有机合成以及药理活性等领域的研究人员的兴趣，这些研究必将会在药物开发上取得重大突破。

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