Review

The progress in the chemical constituents of the genus *Picrasma* during 2007-2017

Jie Zhang[1], Jian Yang[1], Chuan-Xi Wang[2], Hao Gao[1,2*], Xin-Sheng Yao[1,2]

[1]College of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, Shenyang, China. [2]Institute of Traditional Chinese Medicine & Natural Products, College of Pharmacy, Jinan University, Guangzhou, China

***Correspondence to**: Hao Gao, Institute of Traditional Chinese Medicine & Natural Products, College of Pharmacy, Jinan University, Guangzhou, China. Email: tghao@jnu.edu.cn.

Highlights

The plants of the genus *Picrasma* comprise of nine species and are mainly distributed in tropical and subtropical regions of America and Asia. The bark, roots, stems, branches, or leaves of some species in the genus *Picrasma* are used as traditional herbal medicines for the treatment of anemopyretic cold, sore throat, dysentery, eczema, nausea, loss of appetite, diabetes mellitus, hypertension, and so on. The chemical constituents of the plants of this genus were carried out to isolate 157 compounds before 2007, which were reviewed by Jiao WH *et al*. From then on, some significant progresses on the plants of the genus *Picrasma* have been achieved over the last decade, and another 101 compounds with various biological activities are reported. These compounds are assigned to alkaloids, quassinoids, triterpenoids, and others. So far, the chemical investigation on the plants of the genus *Picrasma* only focus on three species (*P. quassioides*, *P. javanica* and *P. excelsa*). Among them, the most studies on chemical constituents concentrate on the plants of *P. quassioides*, followed by the plants of *P. javanica*. Little researches have been done on the plants of *P. excelsa*. The current results show that there are large differences in the chemical constituents between the species of the genus *Picrasma*. The updated overview on the chemical constituents of the plants of the genus *Picrasma* is provided herein after the systematic review by Jiao WH *et al*. in 2007.

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Abstract

The plants of the genus *Picrasma*, comprised of nine species, are mainly distributed in tropical and subtropical regions of America and Asia. Some species of this genus are used as traditional medicine resources to cure anemopyretic cold, sore throat, dysentery, eczema, nausea, loss of appetite, diabetes mellitus, hypertension, and so on. A total of 157 chemical constituents identified from *Picrasma* were reviewed by Jiao WH *et al*. in 2007. Since then, 101 compounds were reported from the plants of the genus *Picrasma*. These compounds are assigned to alkaloids, quassinoids, triterpenoids, and others. This review aims to provide an updated overview on the chemical constituents of the plants of the genus *Picrasma* during 2007-2017.

Keywords: The genus *Picrasma*, Chemical constituents, Alkaloids, Quassinoids, Triterpenoids

摘要

苦树属植物包括 9 个种，主要分布在美洲和亚洲的热带以及亚热带地区。该属某些种的植物作为重要的传统药物资源用于治疗风热感冒、咽喉肿痛、湿热痢疾、恶心晕船、食欲不振、糖尿病、高血压等疾病。2007 年，焦伟华等人对苦树属植物的化学成分进行了整理，共综述了 157 个化合物。近十年间又有 101 个化学成分从苦树属植物中被报道，包括生物碱、苦味素、三萜等。本文对 2007-2017 十年间苦树属植物化学成分的研究进展进行了综述。

关键词：苦树属；化学成分；生物碱；苦味素；三萜

Abbreviation: PDE 4: phosphodiesterase 4; NO: nitric oxide; LPS: lipopolysaccharide; NMR: nuclear magnetic resonance; HPLC: high performance liquid chromatography; CD: circular dichroism; TNF-α: tumor necrosis factor α; IL-6: interleukin 6; AI: antiangiogenic index; Vpr: viral protein R; SD: standard deviation; Glc: glucopyranosyl; Api: apiofuranosyl; Xyl: xylopyranosyl.

Competing interests: The authors declare that there is no conflict of interests regarding the publication of this paper.

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Background

The plants of the genus *Picrasma*, comprised of nine species, are mainly distributed in tropical and subtropical regions of America and Asia [1]. The bark, roots, stems, branches, or leaves of some species are used as herbal medicine resources for the treatment of some diseases, such as anemopyretic cold, sore throat, dysentery, eczema, nausea, loss of appetite, diabetes mellitus, hypertension, and so on [2-5]. In fact, the investigations on phytochemistry and pharmacology of the plants of the genus *Picrasma* are mainly focused on *Picrasma quassioides* (D. Don) Benn and *Picrasma javanica* Blume.

For the chemical constituents and bioactivities of the plants of the genus *Picrasma*, Jiao WH *et al*. made a review in 2007 [6]. Twenty-three *β*-carboline alkaloids, nine canthinone alkaloids, eleven bis *β*-carboline alkaloids, ninety-four quassinoids, eight triterpenoids, and twelve other compounds were reviewed in that report. In addition, the biological activities of those compounds and extracts were also reviewed, including anti-bacteria, anti-malaria, anti-hypertension, anti-tumor, anti-phosphodiesterase 4 (PDE 4), protect-cardiovascular, and protect-gastrointestinal mucous membrane [6]. From then on, some significant progresses on the plants of the genus *Picrasma* have been achieved over the last decade, and 101 compounds with various biological activities were reported. These compounds are assigned to alkaloids, quassinoids, triterpenoids, and others, which are described herein.

Alkaloids

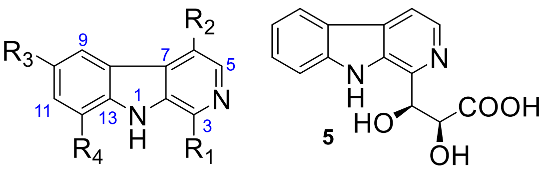
Alkaloids are the principal active components of the plants of the genus *Picrasma*. They can be divided into *β*-carboline alkaloids, canthinone alkaloids, and bis *β*-carboline alkaloids.

β-Carboline alkaloids

In 2007, four *β*-carboline alkaloids, 1-methoxy-9*H*-pyrido[3,4-*b*]indole (**1**), 4-methoxy-1-methyl-9*H*-pyrido[3,4-*b*]indole (**2**), 1-ethyl-4-methoxy-*β*-carboline (**3**), 9*H*-pyrido[3,4-*b*]indole-1-carboxylic acid (**4**), were isolated from the stems of *P. quassioides* by Chen M *et al.* [7]. At the same time, their inhibitory activities on the production of nitric oxide (NO) in mouse monocyte-macrophage RAW264.7 cells stimulated by lipopolysaccharide (LPS) were evaluated. Only compounds **1** and **2** showed weak inhibitory activities with IC_{50} values of 100.0 mM and 57.3 mM, respectively [7]. In 2010, twelve *β*-carboline alkaloids, picrasidine Y (**5**), 6-hydroxy-3-methoxycarbonyl-*β*-carboline (**6**), 6,12-dimethoxy-3-(2-hydroxyethyl)-*β*-carboline (**7**), 3,10-dihydroxy-*β*-carboline (**8**), 6,12-dimethoxy-3-(1-hydroxyethyl)-*β*-carboline (**9**), 6,12-dimethoxy-3-(1,2-dihydroxyethyl)-*β*-carboline (**10**), 6-methoxy-3-(2-hydroxyl-1-ethoxyethyl)-*β*-carboline (**11**), 6-methoxy-12-hydroxy-3-methoxycarbonyl-*β*-carboline (**12**), 3-hydroxy-*β*-carboline (**13**), 3-(2-hydroxyethyl)-*β*-carboline (**14**), 6-methoxy-3-(1,2-dihydroxyethyl)-*β*-carboline (**15**), and kumujancine (**16**), were obtained from the stems of *P. quassioides* by Jiao WH *et al.* [8]. But the absolute configuration of **5** was not be determined at that time. In 2015, its absolute configuration was firstly identified by Koike K *et al*. on basis of the comparisons of ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectral data, specific optical rotation values, High Performance Liquid Chromatography (HPLC) analysis using chiral columns, and circular dichroism (CD) spectra with the chemically synthesized stereoisomers of **5** [9]. In 2011, two *β*-carboline alkaloids, 1-(dimethoxymethyl)-9*H*-pyrido[3,4-*b*]indole (**17**), 4,8-dimethoxy-9*H*-pyrido[3,4-*b*]indole-1-carboxaldehyde (**18**), were obtained from the stems of *P. quassioides* by Jiao WH *et al.* [10]. Both of them exhibited potent inhibitory activities on the production of NO, tumor necrosis factor *α* (TNF-*α*), and interleukin 6 (IL-6) in mouse RAW264.7 cells stimulated by LPS [10]. In 2014, a *β*-carboline alkaloid, 6-hydroxy-9*H*-pyrido[3,4-*b*]indole-1-carboxylic acid (**19**), was isolated from the stems of *P. quassioides* by Lai ZQ *et al*., which showed no cytotoxic activities against four human cancer (K-562, SGC-7901, Hep G2, and A-549) and one mouse cancer (CT26.WT) cell lines [11]. In 2016, two new *β*-carboline alkaloids, 1-hydroxymethyl-8-hydroxy-*β*-carboline (**20**), 6-hydroxy-9*H*-pyrido[3,4-*b*]indole-1-carboxylic acid ethyl ester (**21**), along with **6** and **13**, were isolated from the stems of *P. quassioides* by Gong G *et al.* [12]. Meanwhile, they exhibited different potency of the anti-angiogenic activities on zebrafish *in vivo* with antiangiogenic index (AI) >1 [12]. The structures and related information of compounds **1**-**21** are shown in the Figure 1 and Table 1.

Table 1 *β*-Carboline alkaloids from the plants of the genus *Picrasma*

Number	Name	CAS number	Activity	Plant	Reference
1	1-Methoxy-9*H*-pyrido[3,4-*b*]indole	30151-92-9	NO (IC_{50} = 100.0 mM)	*P. quassioides*	[7]
2	4-Methoxy-1-methyl-9*H*-pyrido[3,4-*b*]indole	694533-71-6	NO (IC_{50} = 57.3 mM)	*P. quassioides*	[7]
3	1-Ethyl-4-methoxy-*β*-carboline	26585-14-8	-	*P. quassioides*	[7]
4	9*H*-Pyrido[3,4-*b*]indole-1-carboxylic acid	26052-96-0	-	*P. quassioides*	[7]
5	Picrasidine Y	155416-27-6	-	*P. quassioides*	[8, 9]
6	6-Hydroxy-3-methoxycarbonyl-*β*-Carboline	245662-15-1	AI = 1.5	*P. quassioides*	[8, 12]
7	6,12-Dimethoxy-3-(2-hydroxylethyl)-*β*-carboline	1131570-92-7	-	*P. quassioides*	[8]
8	3,10-Dihydroxy-*β*-carboline	1233884-59-7	-	*P. quassioides*	[8]
9	6,12-Dimethoxy-3-(1-hydroxyethyl)-*β*-carboline	1233884-60-0	-	*P. quassioides*	[8]
10	6,12-Dimethoxy-3-(1,2-dihydroxyethyl)-*β*-carboline	1131570-91-6	-	*P. quassioides*	[8]
11	6-Methoxy-3-(2-hydroxyl-1-ethoxyethyl)-*β*-carboline	77369-99-4	-	*P. quassioides*	[8]
12	6-Methoxy-12-hydroxy-3-methoxycarbonyl-*β*-carboline	245662-15-1	-	*P. quassioides*	[8]
13	3-Hydroxy-*β*-carboline	19839-52-2	AI = 2	*P. quassioides*	[8, 12]
14	3-(2-Hydroxyethyl)-*β*-carboline	1131570-92-7	-	*P. quassioides*	[8]
15	6-Methoxy-3-(1,2-dihydroxyethyl)-*β*-carboline	1131570-91-6	-	*P. quassioides*	[8]
16	Kumujancine	92631-69-1	-	*P. quassioides*	[8]
17	1-(Dimethoxymethyl)-9*H*-pyrido[3,4-*b*]indole	1205667-14-6	NO (IC_{50} = 26.9 ± 2.0 μM) TNF-*α* (IC_{50} = 35.0 ± 2.9 μM) IL-6 (IC_{50} = 50.4 ± 4.7 μM)	*P. quassioides*	[10]
18	4,8-Dimethoxy-9*H*-pyrido[3,4-*b*]indole-1-carboxaldehyde	1131570-87-0	NO (IC_{50} = 17.4 ± 1.0 μM)	*P. quassioides*	[10]
19	6-Hydroxy-9*H*-pyrido[3,4-*b*]indole-1-carboxylic acid	1402910-87-5	-	*P. quassioides*	[11]
20	1-Hydroxymethyl-8-hydroxy-*β*-carboline	-	AI = 6	*P. quassioides*	[12]
21	6-Hydroxy-9*H*-pyrido[3,4-*b*]indole-1-carboxylic acid ethyl ester	2122466-76-4	AI = 1.3	*P. quassioides*	[12]



1	$R_1 = OCH_3$	$R_2 = H$	$R_3 = H$	$R_4 = H$
2	$R_1 = CH_3$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = H$
3	$R_1 = CH_2CH_3$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = H$
4	$R_1 = COOH$	$R_2 = OH$	$R_3 = H$	$R_4 = H$
6	$R_1 = COOCH_3$	$R_2 = OH$	$R_3 = H$	$R_4 = H$
7	$R_1 = CH_2CH_2OH$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = OCH_3$
8	$R_1 = OH$	$R_2 = H$	$R_3 = OH$	$R_4 = H$
9	$R_1 = CH(OH)CH_3$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = OCH_3$
10	$R_1 = CH(OH)CH_2OH$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = OCH_3$
11	$R_1 = CH(CH_2OH)OCH_2CH_3$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = H$
12	$R_1 = COOCH_3$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = OH$
13	$R_1 = OH$	$R_2 = H$	$R_3 = H$	$R_4 = H$
14	$R_1 = CH_2CH_2OH$	$R_2 = H$	$R_3 = H$	$R_4 = H$
15	$R_1 = CH(OH)CH_2OH$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = H$
16	$R_1 = CHO$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = H$
17	$R_1 = CH(OCH_3)_2$	$R_2 = H$	$R_3 = H$	$R_4 = H$
18	$R_1 = CHO$	$R_2 = OCH_3$	$R_3 = H$	$R_4 = OCH_3$
19	$R_1 = COOH$	$R_2 = H$	$R_3 = OH$	$R_4 = H$
20	$R_1 = CH_2OH$	$R_2 = H$	$R_3 = H$	$R_4 = OH$
21	$R_1 = COOCH_2CH_3$	$R_2 = H$	$R_3 = OH$	$R_4 = H$

Figure 1 Chemical structures of **1-21**

Canthinone alkaloids

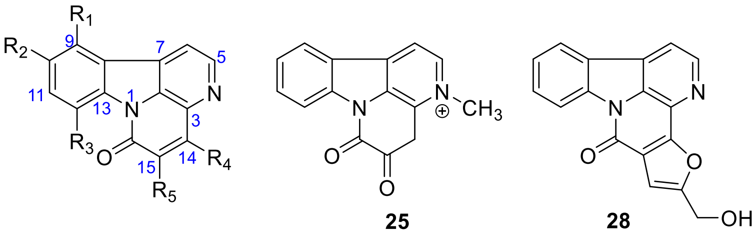
In 2007, a canthinone alkaloid, 11-hydroxycanthin-6-one (**22**), was isolated from the stems of *P. quassioides* by Chen M *et al.* [7]. It showed inhibitory activity on the NO production of mouse RAW264.7 cells stimulated by LPS with IC_{50} value of 46.3 mM [7]. In 2008, three canthinone alkaloids, 8-hydroxycanthin-6-one (**23**), 4,5-dimethoxy-10-hydroxycanthin-6-one (**24**), and 3-methyl-5,6-dioxo-4*H*-indole[3,2,1-de] [1,5] naphthyridinium (**25**), were obtained from the stems of *P. quassioides* by Jiang MX *et al.* [13]. Their cytotoxic activities were evaluated against human nasopharyngeal carcinoma (CNE2) and human liver cancer (Bel-7402) cell lines with the result that only compounds **23** and **24** exhibited significant cytotoxic activities against CNE2 cell line [13]. In 2011, a canthinone alkaloid, 6-oxo-6*H*-indole[3,2,1-de] [1,5] naphthyridine-4-butanoic acid (**26**), was isolated from the stems of *P. quassioides* by Jiao WH *et al*. [10]. Meanwhile, its inhibitory activities on the production of NO, TNF-α, or IL-6 in mouse RAW264.7 cells stimulated by LPS was evaluated. But it didn't display obvious inhibitory activities [10]. In 2016, two canthinone alkaloids, 5-methoxy-11-hydroxycanthin-6-one (**27**) and furancanthin (**28**), were isolated from the stems of *P. quassioides* by Gong G *et al.* [12]. Their biological results showed no anti-angiogenic activities on zebrafish *in vivo* [12]. The structures and related information of compounds **22-28** are shown in the Figure 2 and Table 2.

Bis *β*-carboline alkaloids

Eight bis *β*-carboline alkaloids, quassidines A-H (**29-36**) [10,14], along with two pairs of bis-*β*-carboline alkaloid enantiomers, (±)-quassidines I (**37-38**) and (±)-quassidines J (**39-40**) [15], were isolated from the stems of *P. quassioides* by Jiao WH *et al*. At the same time, their biological activities showed that compounds **29**, **33**, **34** and **35** displayed potent inhibitory activities on the production of NO, TNF-α, and IL-6 in mouse RAW 264.7 cells stimulated by LPS. Whereas, compounds **30**, **31**, **32** and **36** showed potent cytotoxicities on mouse RAW 264.7 cells at the concentration of 100 mg/ml [10,14]. In addition, **37-40** displayed potent cytotoxicities against human cervical HeLa and gastric MKN-28 cancer cell lines [15]. The structures and related information of compounds **29-40** are shown in the Figure 3 and Table 3.

Table 2 Canthinone alkaloids from the plants of the genus *Picrasma*

Number	Name	CAS number	Activity	Plant	Reference
22	11-Hydroxycanthin-6-one	75969-83-4	NO (IC_{50} = 46.3 mM)	*P. quassioides*	[7]
23	8-Hydroxycanthin-6-one	66762-19-4	CNE ((IC_{50} = 56.8 ± 9.7 μM) Bel-7402 (IC_{50} = 166.4 ± 41.2 μM)	*P. quassioides*	[13]
24	4,5-Dimethoxy-10-hydroxycanthin-6-one	1131570-94-9	CNE (IC_{50} = 39.2 ± 8.4 μM)	*P. quassioides*	[13]
25	3-Methyl-5,6-dioxo-4*H*-indole[3,2,1-*de*][1,5]naphthyridinium	1942857-74-0	CNE (IC_{50} = 94.5 ± 19.3 μM)	*P. quassioides*	[13]
26	6-Oxo-6*H*-indole[3,2,1-*de*][1,5]naphthyridine-4-butanoic acid	1131570-93-8	NO (IC_{50} = 47.9 ± 4.1 μM) TNF-α (IC_{50} = 25.5 ± 3.3 μM) IL-6 (IC_{50} = 67.0 ± 6.6 μM)	*P. quassioides*	[10]
27	5-Methoxy-11-hydroxycanthin-6-one	-	-	*P. quassioides*	[12]
28	Furancanthin	-	-	*P. quassioides*	[12]

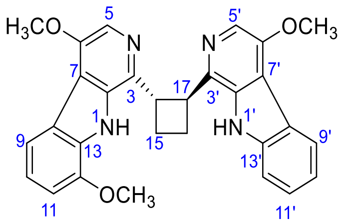


22	R_1 = H	R_2 = H	R_3 = H	R_4 = H	R_5 = H
23	R_1 = H	R_2 = H	R_3 = OH	R_4 = H	R_5 = H
24	R_1 = H	R_2 = OH	R_3 = H	R_4 = OCH_3	R_5 = OCH_3
26	R_1 = H	R_2 = H	R_3 = H	R_4 = $(CH_2)_3COOH$	R_5 = H
27	R_1 = OH	R_2 = H	R_3 = H	R_4 = H	R_5 = OCH_3

Figure 2 Chemical structures of **22-28**.

Table 3 Bis *β*-carboline alkaloids from the plants of the genus *Picrasma*

Number	Name	CAS number	Activity	Plant	Reference
29	Quassidine A	1207862-36-9	NO (IC_{50} = 89.4 μM) TNF-*α* (IC_{50} = 88.4 μM)	*P. quassioides*	[14]
30	Quassidine B	1207862-37-0	-	*P. quassioides*	[14]
31	Quassidine C	1207862-38-1	-	*P. quassioides*	[14]
32	Quassidine D	1207862-39-2	-	*P. quassioides*	[14]
33	Quassidine E	1393888-72-6	NO (IC_{50} = 20.5 ± 1.7 μM) TNF-*α* (IC_{50} = 25.6 ± 2.3 μM) IL-6 (IC_{50} = 45.4 ± 3.3 μM)	*P. quassioides*	[10]
34	Quassidine F	1131570-95-0	NO (IC_{50} = 9.9 ± 0.8 μM) IL-6 (IC_{50} = 24.3 ± 2.2 μM)	*P. quassioides*	[10]
35	Quassidine G	1131570-96-1	NO (IC_{50} = 13.1 ± 1.2 μM) TNF-*α* (IC_{50} = 12.3 ± 1.4 μM) IL-6 (IC_{50} = 17.1 ± 1.6 μM)	*P. quassioides*	[10]
36	Quassidine H	1393888-73-7	-	*P. quassioides*	[10]
37	(+)-Quassidine I	1643689-92-2	HeLa (IC_{50} = 5.8 μM) MKN-28 (IC_{50} = 6.3 μM) B-16 (IC_{50} = 10.8 μM)	*P. quassioides*	[15]
38	(-)-Quassidine I	1643689-93-3	HeLa (IC_{50} = 10.5 μM) MKN-28 (IC_{50} = 12.3 μM) B-16 (IC_{50} = 15.4 μM)	*P. quassioides*	[15]
39	(+)-Quassidine J	1643689-94-4	HeLa (IC_{50} = 4.0 μM) MKN-28 (IC_{50} = 4.9 μM) B-16 (IC_{50} = 9.3 μM)	*P. quassioides*	[15]
40	(-)-Quassidine J	1643689-95-5	HeLa (IC_{50} = 10.1 μM) MKN-28 (IC_{50} = 9.6 μM) B-16 (IC_{50} = 14.8 μM)	*P. quassioides*	[15]



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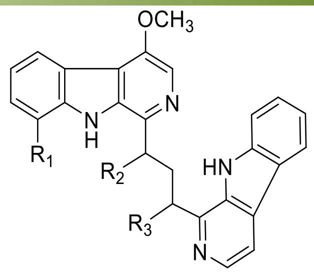
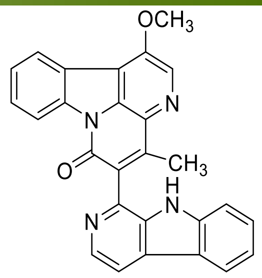


30 $R_1 = OCH_3$ $R_2 = H$ $R_3 = OH$
31 $R_1 = H$ $R_2 = H$ $R_3 = OH$
32 $R_1 = OCH_3$ $R_2 = H$ $R_3 = OCH_3$
34 $R_1 = H$ $R_2 = H$ $R_3 = {=O}$
35 $R_1 = OH$ $R_2 = H$ $R_3 = {=O}$
36 $R_1 = OCH_3$ $R_2 = OH$ $R_3 = OCH_3$



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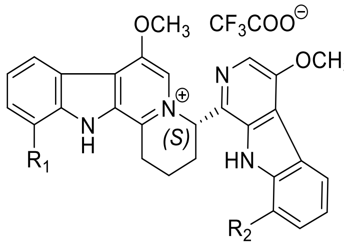
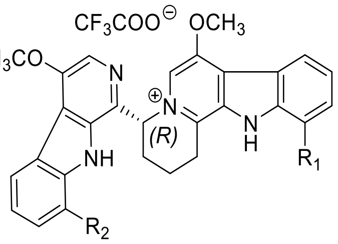


37 $R_1 = OCH_3$ $R_2 = H$
39 $R_1 = OH$ $R_2 = OCH_3$



38 $R_1 = OCH_3$ $R_2 = H$
40 $R_1 = OH$ $R_2 = OCH_3$

Figure 3 Chemical structures of **29-40**

Quassinoids

In 2011, one quassinoid, 2'-isopicrasin A (**41**), was isolated from the stems of *P. quassioides* without inhibitory activities on the production of NO, TNF-α, and IL-6 in mouse RAW 264.7 cells stimulated by LPS [16]. In 2015 and 2016, thirteen new quassinoids, picrajavanicins A−M (**42−54**), together with the compound **41**, were obtained from the bark of *P. javanica* collected in Myanmar by Nwet Nwet Win *et al.* [3, 17]. Meanwhile, **41-54** were tested for antiproliferative activities against five human cancer cell lines of A549, HeLa, PANC-1, PSN-1, and MDA-MB-231. The results showed that **41** and **49-54** displayed potent antiproliferative activities against the human pancreatic cancer PANC-1 cell line [17]. And compounds **41** and **49** exhibited antiproliferative activities against the human cervical cancer HeLa cell line [17]. After that, an assay of anti-viral protein R (Vpr) activity for picrajavanicins A–K (**42**–**52**) and M (**54**) was tested by Nwet Nwet Win *et al.* in 2016. The results revealed that **42**–**52** and **54** exhibited anti-Vpr activities against TREx-HeLa-Vpr cells at concentrations of 1.25, 2.5, and 5 μM with damnacanthal as a positive control [18]. In 2016, three quassinoids, nigakilactone P (**55**), picraqualide F (**56**) and nigakilactone Q (**57**), were identified from the stems of *P. quassioides* by Xu J *et al.* [19]. They were tested for the cytotoxicities and inhibitory activity of NO production with the result of no cytotoxic activities against three human cancer cell lines of MCF-7, A-549 and HepG-2, and no inhibitory activity on the production of NO [19]. The structures and related information of compounds **41-57** are shown in the Figure 4 and Table 4.

Triterpenoids

Thirty tirucallane-type triterpenoids, picraquassins A-D (**58-61**), 6β-hydroxypicraquassin C (**62**), picraquassins E-J (**63-68**), 21β-ethoxybourjotinolone A (**69**), 6-oxo-21β-ethoxybourjotinolone A (**70**), 9,11-dehydrotoonaciliatin K (**71**), 5,6,9,11-dehydrotoonaciliatin K (**72**), 21β-ethoxy-20α-hydroxymelianodiol (**73**), picraquassin K (**74**), xanthocerasic acid methyl ester (**75**), 11-oxobrumollisol A (**76**), picraquassin L (**77**), melianodiol (**78**), 6β-hydroxypicraquassin C (**76**), (13α,14β,17α,20*S*,21*R*,23*R*,24*S*)-21,23-epoxy-21-ethoxy-24,25-dihydroxylanost-7-en-3-one (**79**), toonaciliatin K (**80**), 21-methoxy-21,23-epoxytirucalla-7,24-dien-3α-ol (**81**), bourjotinolone A (**82**), sapelin B (**83**), 3β,29-dihydroxytirucalla-7,24-dien-21-oic acid (**84**), piscidinol A (**85**), brumollisol B (**86**), and 24*S*,25-dihydroxytirucall-7-en-3-one (**87**) were identified from the stems of *P. quassioides* by Xu J *et al.* in 2016 [20]. Cytotoxicities of the isolated compounds were evaluated using three human cancer cell lines of MKN-28, A-549, and MCF-7 with *cis*-platinum as a positive control. Among them, compounds **59**, **63**, **64**, **67**, **70**, **71**, **73**, **74**, **75**, **82**, **84**, **85** and **87** exhibited inhibitory activities against MKN-28 cells; compounds **59**, **67**, **82**, and **85** showed inhibitory activities against A-549 cells; compounds **59**, **82**, **85** exhibited inhibitory activities against MCF-7 cells [20]. The structures and related information of compounds **58-87** are shown in the Figure 5 and Table 5.

Table 4 Quassinoids from the plants of the genus *Picrasma*

Number	Name	CAS number	Activity	Plant	Reference
41	2'-Isopicrasin A	1314868-60-4	PANC-1 (IC_{50} = 3.9 μM) HeLa (IC_{50} = 4.0 μM)	*P. quassioides and P. javanica*	[16,17]
42	Picrajavanicin A	1831840-53-9	153% ± 5% (2.5 μM)*	*P. javanica*	[3,18]
43	Picrajavanicin B	1831840-54-0	156% ± 5% (2.5 μM)*	*P. javanica*	[3,18]
44	Picrajavanicin C	1831840-55-1	168% ± 2% (2.5 μM)*	*P. javanica*	[3,18]
45	Picrajavanicin D	1831840-56-2	166% ± 4% (2.5 μM)*	*P. javanica*	[3,18]
46	Picrajavanicin E	1831840-57-3	136% ± 5% (2.5 μM)*	*P. javanica*	[3,18]
47	Picrajavanicin F	1831840-58-4	138% ± 1% (2.5 μM)*	*P. javanica*	[3,18]
48	Picrajavanicin G	1831840-59-5	140% ± 6% (2.5 μM)*	*P. javanica*	[3,18]
49	Picrajavanicin H	1854048-28-4	PANC-1 (IC_{50} = 4.3 μM) HeLa (IC_{50} = 9.5 μM) 147% ± 3% (2.5 μM)*	*P. javanica*	[17,18]
50	Picrajavanicin I	1854048-29-5	PANC-1 (IC_{50} = 17.4 μM) 137% ± 5% (2.5 μM)*	*P. javanica*	[17,18]
51	Picrajavanicin J	1854048-30-8	PANC-1 (IC_{50} = 10.0 μM) 126% ± 6% (2.5 μM)*	*P. javanica*	[17,18]
52	Picrajavanicin K	1854048-31-9	PANC-1 (IC_{50} = 3.3 μM) 155% ± 4% (2.5 μM)*	*P. javanica*	[17,18]
53	Picrajavanicin L	1854048-32-0	PANC-1 (IC_{50} = 8.5 μM)	*P. javanica*	[18]
54	Picrajavanicin M	1854048-33-1	PANC-1 (IC_{50} = 7.4 μM) HeLa (IC_{50} = 37.4 μM) 138% ± 3% (2.5 μM)*	*P. javanica*	[17,18]
55	Nigakilactone P	-	-	*P. quassioides*	[19]
56	Picraqualide F	2172834-22-7	-	*P. quassioides*	[19]
57	Nigakilactone Q	-	-	*P. quassioides*	[19]

*Cell proliferation (%) ± standard deviation (SD).

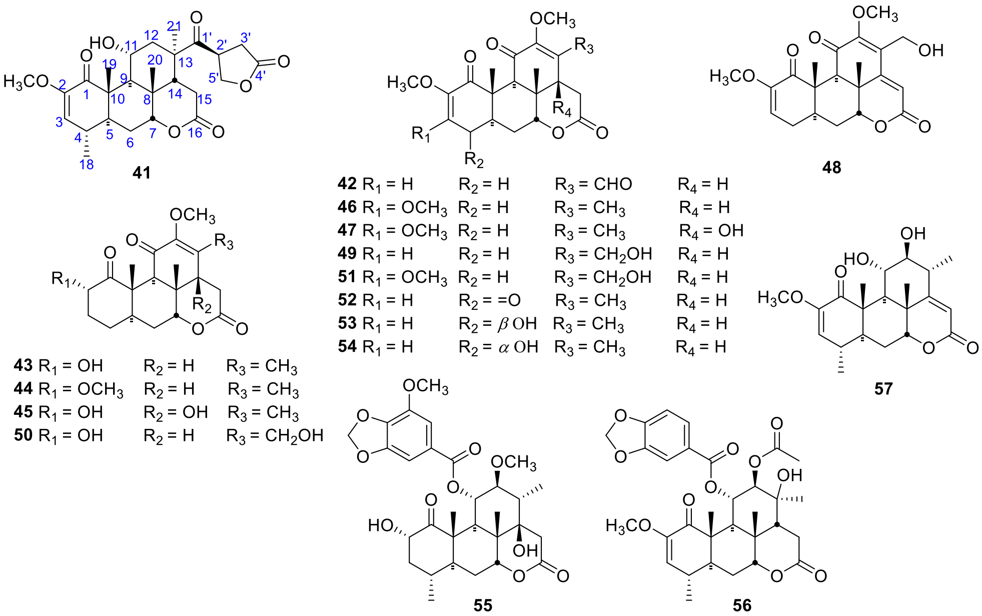


Figure 4 Chemical structures of **41-57**.

Table 5 Triterpenoids from the plants of the genus *Picrasma*

Number	Name	CAS number	Activity	Plant	Reference
58	Picraquassin A	1967020-60-5	-	*P. quassioides*	[20]
59	Picraquassin B	1973484-12-6	MKN-28 (IC_{50} = 2.5 μM) A-549 (IC_{50} = 5.6 μM) MCF-7 (IC_{50} = 9.1 μM)	*P. quassioides*	[20]
60	Picraquassin C	1973484-13-7	-	*P. quassioides*	[20]
61	Picraquassin D	1973484-15-9	-	*P. quassioides*	[20]
62	6*β*-Hydroxypicraquassin C	1973484-16-0	-	*P. quassioides*	[20]
63	Picraquassin E	1973484-16-0	MKN-28 (IC_{50} = 8.8 μM)	*P. quassioides*	[20]
64	Picraquassin F	1973484-17-1	MKN-28 (IC_{50} = 9.8 μM)	*P. quassioides*	[20]
65	Picraquassin G	1973484-18-2		*P. quassioides*	[20]
66	Picraquassin H	1973484-20-6	-	*P. quassioides*	[20]
67	Picraquassin I	1973484-21-7	MKN-28 (IC_{50} = 7.9 μM) A-549 (IC_{50} = 8.3 μM)	*P. quassioides*	[20]
68	Picraquassin J	1967020-22-8	-	*P. quassioides*	[20]
69	21*β*-Ethoxybourjotinolone A	1967020-61-6	-	*P. quassioides*	[20]
70	6-Oxo-21*β*-ethoxybourjotinolone A	1967020-62-7	MKN-28 (IC_{50} = 8.2 μM)	*P. quassioides*	[20]
71	9,11-Dehydrotoonaciliatin K	1967020-63-8	MKN-28 (IC_{50} = 8.3 μM)	*P. quassioides*	[20]
72	5,6,9,11-Dehydrotoonaciliatin K	1967020-64-9	-	*P. quassioides*	[20]
73	21*β*-Ethoxy-20*α*-hydroxymelianodiol	1967020-65-0	MKN-28 (IC_{50} = 9.0 μM)	*P. quassioides*	[20]
74	Picraquassin K	1967020-66-1	MKN-28 (IC_{50} = 9.1 μM)	*P. quassioides*	[20]
75	Xanthocerasic acid methyl ester	1967020-67-2	MKN-28 (IC_{50} = 8.3 μM)	*P. quassioides*	[20]
76	11-Oxobrumollisol A	1967023-09-1	-	*P. quassioides*	[20]
77	Picraquassin L	1973484-23-9	-	*P. quassioides*	[20]
78	Melianodiol	32764-64-0	-	*P. quassioides*	[20]
79	(13*α*,14*β*,17*α*,20*S*,21*R*,23*R*,24*S*)-21,23-Epoxy-21-ethoxy-24,25-dihydroxylanost-7-en-3-one	749849-70-5	-	*P. quassioides*	[20]
80	Toonaciliatin K	1142886-12-1	-	*P. quassioides*	[20]
81	21-Methoxy-21,23-epoxytirucalla-7,24-dien-3*α*-ol	1442419-83-1	-	*P. quassioides*	[20]
82	Bourjotinolone A	6985-35-9	MKN-28 (IC_{50} = 6.7 μM) A-549 (IC_{50} = 7.0 μM) MCF-7 (IC_{50} = 9.9 μM)	*P. quassioides*	[20]
83	Sapelin B	26790-94-3	-	*P. quassioides*	[20]
84	3*β*,29-Dihydroxytirucalla-7,24-dien-21-oic acid	262444-39-3	MKN-28 (IC_{50} = 9.1 μM)	*P. quassioides*	[20]
85	Piscidinol A	100198-09-2	MKN-28 (IC_{50} = 6.9 μM) A-549 (IC_{50} = 8.0 μM) MCF-7 (IC_{50} = 8.5 μM)	*P. quassioides*	[20]
86	Brumollisol B	1431628-61-3	-	*P. quassioides*	[20]
87	24*S*,25-Dihydroxytirucall-7-en-3-one	220864-17-5	MKN-28 (IC_{50} = 9.1 μM)	*P. quassioides*	[20]

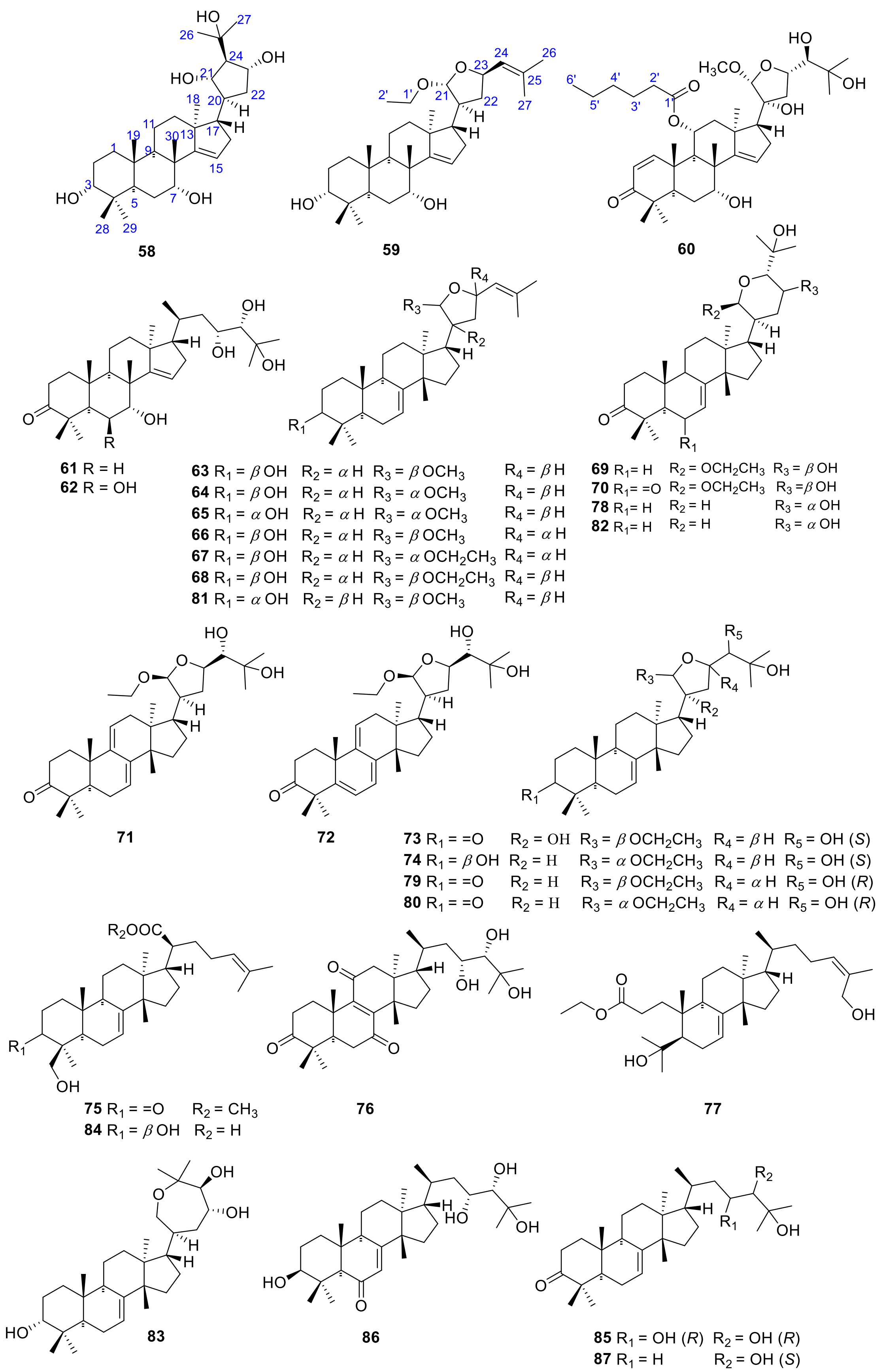


Figure 5 Chemical structures of **58-87**.

Others

In 2011, ten compounds, calycosin (**88**), ononin (**89**), formononetin 7-*O*-*β*-D-apiofuranosyl-(1→6)-*β*-D-glucopyranoside (**90**), kushenol O (**91**), umbelliferone (**92**), emodin (**93**), maackiain (**94**), trifolirhizin (**95**), stigmasterol-3-*O*-*β*-glucopyranoside (**96**), and mannitol **(97)** were obtained from branches and leaves of *P. quassioides* by Deng GH *et al.* [21] Then in 2011, three neolignans, picrasmalignan A (**98**), buddlenol A (**99**), buddlenol C (**100**), together with a flavonol, fisetin (**101**), were isolated from the stems of *P. quassioides* and they showed inhibitory activities on the production of NO, TNF-*α*, and IL-6 in mouse RAW 264.7 cells stimulated by LPS [16].The structures and related information of compounds **88-101** are shown in the Figure 6 and Table 6.

Table 6 Other compounds from the plants of the genus *Picrasma*

Number	Name	CAS number	Activity	Plant	Reference
88	Calycosin	20575-57-9	-	*P. quassioides*	[21]
89	Ononin	486-62-4	-	*P. quassioides*	[21]
90	Formononetin 7-*O*-*β*-D-apiofuranosyl-(1→6)-*β*-D-glucopyranoside	857677-78-2	-	*P. quassioides*	[21]
91	Kushenol O	19716-26-8	-	*P. quassioides*	[21]
92	Umbelliferone	93-35-6	-	*P. quassioides*	[21]
93	Emodin	518-82-1	-	*P. quassioides*	[21]
94	Maackiain	2035-15-6	-	*P. quassioides*	[21]
95	Trifolirhizin	6807-83-6	-	*P. quassioides*	[21]
96	Stigmasterol-3-O-*β*-glucopyranoside	19716-26-8	-	*P. quassioides*	[21]
97	Mannitol	87-78-5	-	*P. quassioides*	[21]
98	Picrasmalignan A	1314868-59-1	NO (IC_{50} = 6.4 ± 0.9 μM) TNF-*α* (IC_{50} = 13.4 ± 1.1 μM) IL-6 (IC_{50} = 17.3 ± 1.5 μM)	*P. quassioides*	[16]
99	Buddlenol A	97399-78-5	NO (IC_{50} = 14.6 ± 1.4 μM) TNF-*α* (IC_{50} = 19.5 ± 1.6 μM) IL-6 (IC_{50} = 24.4 ± 1.7 μM)	*P. quassioides*	[16]
100	Buddlenol C	97465-73-1	NO (IC_{50} = 5.9 ± 0.8 μM) TNF-*α* (IC_{50} = 11.4 ± 1.1 μM) IL-6 (IC_{50} = 18.8 ± 2.0 μM)	*P. quassioides*	[16]
101	Fisetin	528-48-3	NO (IC_{50} = 2.9 ± 0.4 μM) TNF-*α* (IC_{50} = 6.6 ± 0.7 μM) IL-6 (IC_{50} = 21.1 ± 1.8 μM)	*P. quassioides*	[16]

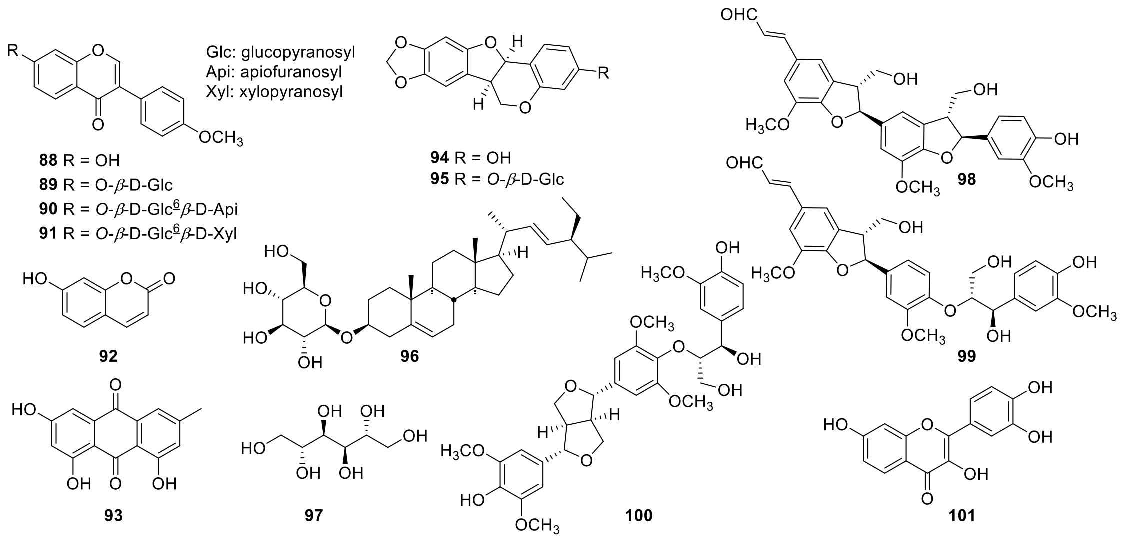


Figure 6 Chemical structures of **88-101**.

Discussion and conclusion

The plants of the genus *Picrasma* consist of nine species. In fact, chemical investigation on the plants of the genus *Picrasma* only focus on three species (*P. quassioides*, *P. javanica* and *P. excelsa*) during the last decade, which is the same as the results of a decade ago [22-28]. Among them, the most studies on chemical constituents concentrate on the plants of *P. quassioides*, followed by the plants of *P. javanica*. The branches, leaves, stems or bark of the plants of *P. quassioides* are usually used as the traditional medicine for the treatment of infectious and inflammatory diseases in China, Japan and Korea [22-23]. The bark of the plants of *P. javanica* is used in folk medicine as antimalarial drugs in Myanmar, Indonesia and Thailand [29-35]. Little researches have been done on the plants of *P. excelsa*, and the extract of which is a natural bittering agent used as a food additive in Japan, Europe and America [26, 36].

Until now, a total of 258 compounds are identified from the plants of the genus *Picrasma*, of which 195 compounds are obtained from the plants of *P. quassioides*, 71 compounds are identified from the plants of *P. javanica*, 7 compounds are isolated from the plants of *P. crenata*. And the plants of *P. quassioides* and *P. javanica* shared 15 compounds. Among the 195 components of the plants of *P. quassioides*, there are 82 alkaloids, 51 quassinoids, 36 triterpenoids, and 26 other ingredients. Seventy-one constituents from the plants of *P. javanica* include 15 alkaloids, 54 quassinoids and 2 triterpenoids. Seven compounds from the plants of *P*. crenata are all quassinoids. From the current results of chemical constituents, there are large differences in the chemical constituents between the species of the genus *Picrasma*.

The biological activities of the chemical constituents from the plants of the genus *Picrasma* are mainly focused on anti-microbial, anti-inflammatory, anti-virus activities and cytotoxicities. It is consistent with the traditional applications, such as curing anemopyretic cold, sore throat, dysentery, eczema, and so on. Alkaloids in the plant of *P. quassioides* have been proved to be the main components with anti-inflammatory activities [37-38]. Although quassinoids are the major chemical constituents in the plant of *P. javanica*., alkaloids from the stembark of the plants of *P. javanica* are proved to be the main anti-malarial active ingredients [35, 39-40].

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