Trop J Nat Prod Res, July 2025; 9(7): 2941 - 2963 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Review Article

Gnetum Genus: Review on its Traditional Uses, Phytochemistry and Pharmacological Activities

Kamsirah Jim Shamsudin[1,2], Nurulfazlina Edayah Rasol[1,2*]and Nurunajah Ab. Ghani[1,2]

[1]*Faculty of Applied Science, Universiti Teknologi MARA, 40450 Shah Alam, Selangor, Malaysia*
[2]*Atta-ur-Rahman Institute for Natural Product Discovery (AuRIns), Level 9, FF3 Building, Universiti Teknologi MARA, UiTM Selangor, Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor, Malaysia*

ARTICLE INFO

Article history:
Received 17 March 2025
Revised 24 April 2025
Accepted 14 May 2025
Published online 01 August 2025

ABSTRACT

Gnetum belongs to the family Gnetaceae and is commonly found in tropical and humid regions of Africa, South America, and Southeast Asia. Plants of this genus are used in traditional medicine to treat conditions such as arthritis, bronchitis, and asthma. *Gnetum* is recognized as a rich source of stilbenes, and numerous studies have reported the presence of stilbenes along with other bioactive constituents, including alkaloids and flavonoids. These compounds contribute to various health benefits, such as antidiabetic, anticancer, antioxidant, and anti-inflammatory effects. This review aims to provide a comprehensive overview of the traditional uses, phytochemical composition, and pharmacological activities of *Gnetum* species. Data were collected from scientific databases, including Scopus, PubMed, Web of Science, Google Scholar, ScienceDirect, and SciFinder. Phytochemical investigations have identified approximately 149 bioactive compounds in *Gnetum*, including stilbenoids, flavonoids, and alkaloids. These isolated compounds exhibit significant pharmacological properties, such as cytotoxicity, antidiabetic effects, and anti-inflammatory activity. This review highlights the traditional applications, phytochemical profiles, and pharmacological potential of *Gnetum* species. It confirms that several *Gnetum* species have been widely utilized in traditional medicine for treating various ailments. Future research in phytomedicine should focus on further exploring the phytochemistry and pharmacological mechanisms of this genus to unlock its full therapeutic potential.

Keywords: *Gnetum*, Gnetaceae, phytochemical, stilbene, pharmacological activities .

Introduction

Gnetum, the sole genus within the Gnetaceae family, belongs to the order Gnetales and represents a unique group of tropical gymnosperms. Comprising approximately 40 species, *Gnetum* is distributed across subtropical and tropical regions, including South America (particularly the Amazon), Southwest Africa, and Southeast Asia.[1] In Southeast Asia and the Indomalesian region, about 20 species have been identified, such as *Gnetum arboreum*, *G. contractum*, *G. cuspidatum*, *G. diminutum*, *G. gnemonoides*, *G. hainanense*, *G. klossii*, *G. latifolium*, *G. leptostachyum*, *G. loerzingii*, *G. macrostachyum*, *G. microcarpum*, *G. montanum*, *G. neglectum*, *G. oxycarpum*, *G. ridleyi*, *G. ula*, and *G. gnemon.* [3] Additional species, including *G. costatum*, *G. gnemonoides*, *G. klossii*, *G. latifolium*, *G. leptostachyum*, *G. loerzingii*, *G. macrostachyum*, *G. microcarpum*, *G. montanum*, and *G. ula*, have been documented in Malaysia and Southeast Asia. [2,3] Molecular-clock analyses suggest that the distribution of *Gnetum*, particularly in the Melanesian region, resulted from overland seed dispersal facilitated by low sea levels. [4] Water dispersal is also a plausible mechanism due to the unique characteristics cof *Gnetum* seeds. For instance, *G. venosum* seeds possess a specialized middle layer in the seed coat that provides buoyancy, while *G gnemonoides* features large corky diaspores. [5] Today, *G. gnemon* is widely distributed across Asia, likely due to both natural water dispersal and human intervention. *Gnetum* species are distinctive among gymnosperms due to their angiosperm-like morphological traits, such as decussate leaves, pinnate leaf venation, and the presence of vessels in their stems. [6] Traditionally, *Gnetum* plants have been used to treat various pathological conditions, including arthritis, bronchitis, joint inflammation, and asthma. [7,8] Beyond their medicinal applications, the stem bark fibers have been utilized to make bags, ropes, and fishing nets. [9] In rural areas of Africa and New Guinea, the leaves, seeds, and fruits of *Gnetum* are consumed as a nutrient-rich food source, valued for their high protein content and diverse nutritional profile. [10,11] Phytochemical studies of *Gnetum* have identified the presence of bioactive compounds such as stilbenoids, flavonoids, and alkaloids. [12,13,14] Pharmacological investigations have demonstrated that *Gnetum* extracts exhibit promising properties, including antimicrobial, antioxidant, antidiabetic, anti-inflammatory, and cytotoxic activities. [14,15,8] To further explore the potential of *Gnetum* as a source of plant-derived medicines, this review provides a comprehensive overview of the existing knowledge on its phytochemical composition and pharmacological properties. By consolidating current knowledge, this review establishes a scientific foundation for future research and highlights the therapeutic potential of *Gnetum* in modern medicine.

*Corresponding author. E mail: edayah@uitm.edu.my
Tel: +60176130594

Citation: Shamsudin KJ, Rasol NE* and Ghani NA. *Gnetum* Genus: Review on its Traditional Uses, Phytochemistry and Pharmacological Activities. Trop J Nat Prod Res. 2025; 9(7): 2941 – 2963 https://doi.org/10.26538/tjnpr/v9i7.2

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

Search Strategy

This review was conducted through searches using Dictionary of Natural Products, Science Direct, PubMed, Google Scholar, Scopus, and Web of Science. The keywords used were "*Gnetum*", “phytochemistry”, and “biological activity” articles over the period from the beginning of the database until late 2024. As a second search strategy, we included studies obtained by a manual search of the included studies' reference lists. The review was conducted using data from various scientific databases, and ChemDraw software was employed to illustrate the bioactive molecules identified in *Gnetum* species.

 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Botanical Description

Gnetaceae, a family within the order Gnetales, consists of a single genus, *Gnetum*, which comprises approximately 40 or more species. Most species are climbers with twining stems, while a few are shrubs or trees. [5]. African species are predominantly trees, whereas Asian varieties are mostly woody vines, with the exception of *G. gnemon*, a tree that can grow up to 20 meters (65 feet) tall. [16] One of the most distinctive features of *Gnetum* is its multilacunar nodes, a characteristic unique among gymnosperms, reflecting a high degree of specialization in nodal anatomy. In arborescent forms like *G. gnemon*, secondary growth follows the normal pattern. However, in climbing species such as *G. ula* and *G. africanum*, anomalous secondary growth results in successive rings, with accessory cambia originating from either the secondary phloem or cortical parenchyma. [5] *Gnetum* is a remarkable group of gymnosperms that shares several morphological features with angiosperms. For instance, the broad leaves of *Gnetum* species exhibit conspicuous, netlike venation, closely resembling that of angiosperms. Additionally, the ovules are enclosed, and the wood contains open-ended vessels, a trait typically associated with angiosperms. [17] Notably, *Gnetum* is the only gymnosperm that lacks archegonia and exhibits a tetrasporic development of the female gametophyte, a condition commonly found in many angiosperms. [5] At maturity, *Gnetum* seeds are enclosed in a fleshy outer envelope that turns red, pink, or yellow. The middle envelope forms a hard, ribbed testa, while the inner envelope is thin and silky. The small embryo is embedded in abundant endosperm, further highlighting the unique reproductive and structural adaptations of this genus. These distinctive characteristics underscore the evolutionary significance of *Gnetum*, bridging the morphological gap between gymnosperms and angiosperms, and making it a fascinating subject for botanical and evolutionary studies.

Medicinal, Nutritional, And Practical Uses of Gnetum

The *Gnetum* plant is widely recognized for its medicinal, nutritional, and practical applications. In traditional medicine, *Gnetum* has been used to treat rheumatic arthritis and bronchitis. [18] For instance, *G. montanum* is utilized in China as a remedy for arthritis and bronchitis, while its seeds are consumed fried or processed into edible oil. [9] Similarly, the seeds of *G. ula* are eaten roasted or boiled, and their oil is used by folklore practitioners to treat rheumatism. Extracts from the leaves and stems are employed to address liver enlargement and jaundice, while leaf paste is applied externally to alleviate arthritis. [19] In Karnataka's Hassan district, the fruits and oil of *Gnetum* are used as stimulants and anti-rheumatic agents. [20] In Nigeria, the leaves of *G. africanum* are used to treat an enlarged spleen, sore throat, and as a cathartic. [11] Additionally, *Gnetum* leaves serve as a remedy for nausea, act as an antidote for certain poisons, and are applied as dressings for warts, hemorrhoids, and boils. Herbal teas brewed from *Gnetum* cuttings are used to soothe labor pains. In Mozambique, the plant is valued for its high fiber content, which helps ease constipation and regulate blood sugar levels in diabetics. [11]

Beyond its medicinal uses, *G. africanum* leaves are noted for their dietary benefits. Their high fiber content contributes to weight reduction, despite their rich protein content. Older leaves, which contain longer fibers, have a stronger laxative effect. In vivo studies have shown that mice fed a *G. africanum*-based diet absorbed only 57–70% of the nitrogen they ingested, compared to those on a reference diet, resulting in a weight loss of approximately 9 grams over a 10-day interval. The fiber in *G. africanum* promotes gastric transit, water retention, and stool softening, making it beneficial for patients with hypertension and atherosclerosis, as it may help lower plasma cholesterol levels by reducing bile acid absorption. [21,22] Furthermore, the stem bark of *G. montanum* is used to make bags, fishing nets, and ropes. [9]

Gnetum species are also valued as a food source, particularly their leaves, which are consumed as a nutritious vegetable in soups, stews, sauces, or even raw. Known for their high protein and mineral content, *Gnetum* leaves are considered a vital nutrient provider. [11] They are suggested as a potential solution to combat malnutrition in rural areas with limited access to meat, as the leaves are both nutritious and palatable. [19] In West Africa, dishes featuring *Gnetum* leaves are prominently featured on restaurant menus. In Indonesia, the fruits and seeds of *Gnetum* are commonly used as vegetables. For example, in Banten, melinjo (a local name for *Gnetum*) is widely incorporated into the diet, appearing in dishes such as vegetables, side dishes, chili sauce or paste, chips, crackers, pastries, and snacks. [23] In summary, *Gnetum* is a versatile plant with significant medicinal, nutritional, and practical applications. Its widespread use in traditional medicine, its role as a nutrient-rich food source, and its utility in crafting tools and textiles underscore its importance across various cultures and regions.

Phytochemical Investigations of Gnetum Species

The first isolation of compounds from *Gnetum* species was conducted by Lins and colleagues in 1982. They successfully isolated gnetins A (46), B (47), C (48), and D (49) from the liana of *G. leyboldii* and the fruits of *G. schwackeanum.* [24] This discovery highlighted *Gnetum*'s potential as a rich source of natural products, prompting further research. In 1992, a Chinese research group isolated gnetifolin B (37), C (38), D (39), and F (40) from the liana of *G. parvifolium.* [12] Since then, over 100 oligostilbenes have been isolated from various parts of *Gnetum* species, including the liana, roots, bark, and fruits. Among these species, *Gnetum gnemon* has been the most extensively studied for its chemical constituents. *Gnetum* is particularly known for its abundance of stilbene derivatives (Table 1), along with smaller quantities of other compounds such as alkaloids and flavonoids.

Stilbenes: Structure and Classification

Stilbenes are characterized by a 1,2-diphenylethylene nucleus with hydroxyl substitutions on the aromatic rings. They exist as both monomers and complex oligomers. The monomeric stilbene skeleton consists of two aromatic rings connected by an ethylene bridge, with the trans isomer being the most common configuration. The most widely studied stilbene is trans-resveratrol, which features a trihydroxystilbene skeleton. [25,26] Oligostilbenes are formed through the oligomerization of two or more monomeric units, resulting in dimers, trimers, tetramers, or more complex structures. These oligomers arise from the oxidative coupling of monomeric stilbenes such as resveratrol (9), isorhapontigenin (7), oxyresveratrol, and piceatannol. [27]

Dimeric Stilbenes

Dimeric stilbenes, the most abundant oligostilbenes in *Gnetum*, consist of two monomeric stilbene units. Examples include parvifolol A (86), B (87), and C (88), isolated from the liana of *G. parvifolium*. Parvifolol A (86) and B (87) are dimers composed of resveratrol and oxyresveratrol units, while parvifolol C (88) consists of two oxyresveratrol units. [28] Gnetupendin A (80) and B (81) are dimers formed from an isorhapontigenin unit and a 4-hydroxybenzyl group. [29]

Table 1: Stilbenes from *Gnetum* species

No	Compounds	Molecular Formula	Species	Part	References
1	Gnetol	$C_{14}H_{12}O_4$	*G. microcarpum*	Lianas	Azmin *et al.* (2014)[48]
2	Gnetucleistol B	$C_{15}H_{14}O$	*G. cleistostachyum* C. Y. Cheng	Lianas	Yao *et al.* (2005)[31]
3	Gnetucleistol D	$C_{15}H_{14}O_4$	*G. cleistostachyum*	Lianas	Yao *et al.* (2003)[18]
4	Gnetucleistol E	$C_{16}H_{16}O$	*G. cleistostachyum*	Lianas	Yao *et al.* (2003)[18]
5	Gnetifolin E	$C_{21}H_{24}O_9$	*G. montanum* Markgr	Lianas	Wang *et al.* (2008)[49]
6	Gnetifolin K	$C_{27}H_{34}O_{14}$	*G. montanum*	Lianas	Wang *et al.* (2008)[49]

 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

7	Isorhapontigenin	$C_{15}H_{14}O_4$	*G. gnemon* L.	Fruits	Kato *et al.* (2011)[50]
8	Malaysianol E	$C_{16}H_{16}O_4$	*G. microcarpum*	Lianas	Azmin *et al.* (2014)[48]
9	Resveratrol	$C_{14}H_{12}O_3$	*G. gnemon* L.	Barks	Atun *et al.* (2007)[39]
10	Africanoside A	$C_{41}H_{44}O_{17}$	*G. africanum*	Rhizomes	Gabaston *et al.* (2020)[51]
11	Africanoside B	$C_{41}H_{44}O_{17}$	*G. africanum*	Rhizomes	Gabaston *et al.* (2020)[51]
12	Bisisorhapontigenin A	$C_{30}H_{26}O_8$	*G. cleistostachyum*	Lianas	Yao & Lin (2004)[52]
13	Bisisorhapontigenin B	$C_{30}H_{26}O_8$	*G. africanum*	Rhizomes	Gabaston *et al.* (2020)[51]
14	Cuspidan B	$C_{14}H_{10}O_4$	*G. cuspidatum*	Barks	Shimokawa *et al.* (2012)43
15	Gneafricanin A	$C_{29}H_{24}O_8$	*G. africanum*	Stems	Iliya *et al.* (2002)[53]
16	Gneafricanin B	$C_{29}H_{24}O_8$	*G. africanum*	Stems	Iliya *et al.* (2002)[53]
17	Gneafricanin C	$C_{28}H_{22}O_8$	*G. africanum*	Stems	Iliya *et al.* (2002)[53]
18	Gnemonol M	$C_{30}H_{26}O_8$	*G. cuspidatum*	Lianas	Azmin *et al.* (2016)[54]
19	Gnemonoside A	$C_{40}H_{42}O_{16}$	*G. gnemonoides*	Stems	Iliya *et al.* (2001)[55]
20	Gnemonoside B	$C_{40}H_{42}O_{16}$	*G. gnemonoides*	Stems	Iliya *et al.* (2001)[55]
21	Gnemonoside C	$C_{34}H_{32}O_{11}$	*G. gnemonoides*	Stems	Iliya *et al.* (2001)[55]
22	Gnemonoside D	$C_{34}H_{32}O_{11}$	*G. gnemonoides*	Stems	Iliya *et al.* (2001)[55]
23	Gnemonoside E	$C_{40}H_{42}O_{16}$	*G. gnemonoides*	Stems	Iliya *et al.* (2002b)[32]
24	Gnemonoside H	$C_{46}H_{52}O_{21}$	*G. gnemonoides*	Stems	Iliya *et al.* (2002c)[53]
25	Gnemonoside I	$C_{40}H_{42}O_{17}$	*G. africanum*	Stems	Iliya *et al.* (2002c)[53]
26	Gnemonoside J	$C_{40}H_{42}O_{17}$	*G. africanum*	Stems	Iliya *et al.* (2002c)[53]
27	Gnemonoside L	$C_{34}H_{31}O_{11}$	*G. gnemon*	Fruits	Kato *et al.* (2011)[50]
28	Gnemontanin A	$C_{30}H_{28}O_9$	*G. montanum*	Caulis	Zhai *et al.* (2016)[56]
29	Gnemontanin B	$C_{30}H_{28}O_9$	*G. montanum*	Caulis	Zhai *et al.* (2016)$_{56}$
30	Gnemontanin C	$C_{30}H_{26}O_8$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
31	Gnemontanin D	$C_{30}H_{25}O_8$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
32	Gnemontanin E	$C_{30}H_{27}O_9$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
33	Gnemontanin F	$C_{32}H_{32}O_9$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
34	Gnemontanin G	$C_{28}H_{22}O_7$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
35	Gnetal	$C_{21}H_{16}O_6$	*G. gnemonoides*	Stems	Iliya *et al.* (2002b)[32]
36	Gnetifolin A	$C_{16}H_{14}O_6$	*G. cleistostachyum*	Lianas	Yao *et al.* (2005)[31]
37	Gnetifolin B	$C_{16}H_{12}O_6$	*G. parvifolium*	Lianas	Lin *et al.* (1992)[12]
38	Gnetifolin C	$C_{30}H_{26}O_8$	*G. parvifolium*	Lianas	Lin *et al.* (1992)[12]
39	Gnetifolin D	$C_{30}H_{28}O_8$	*G. parvifolium*	Lianas	Lin *et al.* (1992)[12]
40	Gnetifolin F	$C_{25}H_{24}O_7$	*G. parvifolium*	Lianas	Lin *et al.* (1992)[12]
41	Gnetifolin L	$C_{30}H_{28}O_8$	*G. montanum*	Barks	Chen & Lin (1999)[57]
42	Gnetifolin M	$C_{30}H_{28}O_9$	*G. montanum*	Lianas	Chen & Lin (1999)[57]
43	Gnetifolin N	$C_{30}H_{28}O_9$	*G. montanum*	Lianas	Chen & Lin (1999)[57]
44	Gnetifolin O	$C_{30}H_{28}O_9$	*G. montanum*	Barks	Chen & Lin (1999)[57]
45	Gnetifolin P	$C_{30}H_{26}O_8$	*G. parvifolium*	Lianas	Tian *et al.* (2017) [58]
46	Gnetin A	$C_{28}H_{22}O_6$	*G. schwackeanum* Taub.	Woody	Lins *et al.* (1989)[24]
47	Gnetin B	$C_{28}H_{24}O_6$	*G. schwackeanum*	Woody	Lins *et al.* (1989)[24]
48	Gnetin C	$C_{28}H_{22}O_6$	*G. schwackeanum*	Fruits	Lins *et al.* (1989)[24]
49	Gnetin D	$C_{28}H_{22}O_7$	*G. schwackeanum*	Woody	Lins *et al.*, (1989)[24]
50	Gnetin L	$C_{29}H_{24}O_7$	*G. gnemon*	Seeds	Tani *et al.* (2020)[59]
51	Gnetofuran A	$C_{25}H_{24}O_7$	*G. klossii*	Stems	Ali *et al.* (2003)[60]
52	Gnetofuran B	$C_{16}H_{14}O_5$	*G. klossii*	Stems	Ali *et al.* (2003)[60]
53	Gnetofuran C	$C_{15}H_{12}O_5$	*G. klossii*	Stems	Ali *et al.* (2003)[60]

 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

54	Gnetucleistol A	$C_{22}H_{20}O_7$	*G. cleistostachyum*	Lianas	Yao *et al.* (2005)[31]
55	Gnetucleistol C	$C_{15}H_{12}O_4$	*G. cleistostachyum*	Lianas	Yao *et al.* (2005)[31]
56	Gnetucleistol F	$C_{26}H_{26}O_8$	*G. montanum*	Caulis	Ma *et al.* (2017)[61]
57	Gnetuhainin A	$C_{28}H_{22}O_7$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
58	Gnetuhainin B	$C_{28}H_{20}O_7$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
59	Gnetuhainin C	$C_{28}H_{22}O_7$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
60	Gnetuhainin D	$C_{28}H_{24}O_8$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
61	Gnetuhainin E	$C_{28}H_{24}O_8$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
62	Gnetuhainin F	$C_{30}H_{24}O_8$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
63	Gnetuhainin G	$C_{30}H_{22}O_9$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
64	Gnetuhainin H	$C_{30}H_{24}O_9$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
65	Gnetuhainin I	$C_{30}H_{27}O_9$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
66	Gnetuhainin J	$C_{29}H_{24}O_8$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
67	Gnetuhainin K	$C_{29}H_{24}O_8$	*G. hainanense*	Lianas	Wang *et al.* (2001)[63]
68	Gnetuhainin L	$C_{29}H_{24}O_8$	*G. hainanense*	Lianas	Wang *et al.* (2001)[63]
69	Gnetuhainin P	$C_{30}H_{28}O_9$	*G. montanum*	Caulis	Zhai *et al.* (2016)[56]
70	Gnetuhainin Q	$C_{29}H_{24}O_7$	*G. hainanense*	Lianas	Wang *et al.* (2001)[63]
71	Gnetulin	$C_{30}H_{26}O_8$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
72	Gnetumelin A	$C_{21}H_{18}O_4$	*G. montanum*	Lianas	Wang *et al.* (2008)[49]
73	Gnetumelin B	$C_{17}H_{16}O_6$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
74	Gnetumelin C	$C_{15}H_{14}O_6$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
75	Gnetumonin A	$C_{25}H_{26}O_8$	*G. montanum*	Caulis	Ma *et al.* (2017)[61]
76	Gnetumonin B	$C_{25}H_{26}O_8$	*G. montanum*	Caulis	Ma *et al.* (2017)[61]
77	Gnetumontanin A	$C_{28}H_{23}O_8$	*G. montanum*	Lianas	Li *et al.* (2004)[64]
78	Gnetumontanin C	$C_{25}H_{23}O_7$	*G. montanum*	Lianas	Li *et al.* (2004)[64]
79	Gnetumontanin D	$C_{31}H_{33}O_{12}$	*G. montanum*	Lianas	Li *et al.* (2004)[64]
80	Gnetupendin A	$C_{22}H_{20}O_5$	*G. pendulum* C.Y. Cheng	Lianas	Li *et al.* (2001a)[13]
81	Gnetupendin B	$C_{22}H_{20}O_6$	*G. pendulum*	Lianas	Li *et al.* (2001a)[13]
82	Gnetupendin C	$C_{28}H_{22}O_7$	*G. pendulum*	Lianas	Li *et al.* (2001b)[29]
83	Gnetupendin D	$C_{36}H_{36}O_{13}$	*G. pendulum*	Lianas	Li *et al.* (2003)[65]
84	Macrostachyol C	$C_{29}H_{26}O_8$	*G. macrostachyum*	Roots	Sri-in *et al.* (2011)[33]
85	Macrostachyol D	$C_{29}H_{24}O_7$	*G. macrostachyum*	Roots	Sri-in *et al.* (2011)[33]
86	Parvifolol A	$C_{28}H_{22}O_7$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
87	Parvifolol B	$C_{28}H_{22}O_7$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
88	Parvifolol C	$C_{28}H_{22}O_8$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
89	Parvifolol D	$C_{30}H_{22}O_8$	*G. parvifolium*	Lianas	Tanaka *et al.* (2001)[28]
90	Ampelopsin E	$C_{42}H_{32}O_9$	*G. gnemon*	Roots	Iliya *et al.* (2002d)[66]
91	Cuspidan A	$C_{35}H_{28}O_{10}$	*G. cuspidatum*	Barks	Shimokawa *et al.* (2012)[43]
92	Gnemonol G	$C_{28}H_{20}O_7$	*G. gnemon*	Roots	Iliya *et al.* (2002d)[66]
93	Gnemonol H	$C_{42}H_{32}O_{10}$	*G. gnemon*	Roots	Iliya *et al.* (2002d)[66]
94	Gnemonol I	$C_{42}H_{31}O_{10}$	*G. gnemon*	Roots	Iliya *et al.* (2002d)[66]
95	Gnemonol J	$C_{42}H_{31}O_{11}$	*G. gnemon*	Roots	Iliya *et al.* (2002)[66]
96	Gnemonol K	$C_{42}H_{32}O_9$	*G. gnemon*	Roots	Iliya *et al.* (2003a)[27]
97	Gnemonol L	$C_{42}H_{32}O_9$	*G. gnemon*	Roots	Iliya *et al.* (2003a)[27]
98	Gnemonoside F	$C_{60}H_{62}O_{24}$	*G. gnemonoides*	Stems	Iliya *et al.* (2002c)[53]
99	Gnemonoside G	$C_{54}H_{52}O_{19}$	*G. gnemonoides*	Stems	Iliya *et al.* (2002c)[53]
100	Gnemonoside K	$C_{60}H_{62}O_{24}$	*G. gnemon*	Roots	Iliya *et al.* (2003a)[27]

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

101	Gnemonoside M	$C_{48}H_{48}O_{14}$	*G. gnemon*	Fruits	Kato *et al.* (2011)[50]
102	Gnetin E	$C_{42}H_{32}O_{9}$	*G. gnemon*	Fruits	Kato *et al.* (2011)[50]
103	Gnetin J	$C_{42}H_{32}O_{10}$	*G. venosum*	Seeds	Boralle *et al.* (1993)[67]
104	Gnetin K	$C_{43}H_{34}O_{10}$	*G. venosum*	Seeds	Boralle *et al.* (1993)[67]
105	Gnetubrunol A	$C_{45}H_{38}O_{11}$	*G. brunonianum*	Lianas	Yao *et al.* (2012)[70]
106	Gnetuhainin M	$C_{42}H_{32}O_{11}$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
107	Gnetuhainin N	$C_{45}H_{38}O_{12}$	*G. hainanense*	Lianas	Huang *et al.* (2000)[62]
108	Gnetumontanin B	$C_{42}H_{33}O_{11}$	*G. montanum*	Lianas	Li *et al.* (2004)[64]
109	Gneyulin A	$C_{42}H_{32}O_{12}$	*G. gnemonoides*	Barks	Shimokawa *et al.* (2010)[37]
110	Latifoliol A	$C_{42}H_{32}O_{10}$	*G. latifolium* Blume	Leaves	Cho *et al.* (2019)[68]
111	Latifoliol B	$C_{42}H_{32}O_{11}$	*G. latifolium*	Leaves	Cho *et al.* (2019)[68]
112	Latifoliol C	$C_{42}H_{32}O_{11}$	*G. latifolium*	Leaves	Cho *et al.* (2019)[68]
113	Latifolol	$C_{42}H_{32}O_{10}$	*G. latifolium*	Stems	Iliya *et al.* (2002a)[30]
114	Macrostachyol B	$C_{42}H_{33}O_{10}$	*G. macrostachyum*	Roots	Sri-in *et al.* (2011)[33]
115	Gnemonol B	$C_{56}H_{42}O_{12}$	*G. gnemon*	Roots	Iliya *et al.* (2002b)[32]
116	Gnemonol C	$C_{56}H_{42}O_{13}$	*G. gnemonoides*	Stems	Iliya *et al.* (2002b)[32]
117	Gneyulin B	$C_{42}H_{31}O_{12}$	*G. gnemonoides*	Barks	Shimokawa *et al.* (2010)[37]
118	Macrostachyol A	$C_{56}H_{42}O_{13}$	*G. macrostachyum*	Roots	Sri-in *et al.* (2011)[33]
119	Gnetoflavanol A	$C_{30}H_{26}O_{9}$	*G. africanum*	Stems	Iliya *et al.* (2003b)[69]
120	Gnetoflavanol B	$C_{29}H_{24}O_{8}$	*G. africanum*	Stems	Iliya *et al.* (2003b)[69]
121	Gnetoflavanol C	$C_{29}H_{24}O_{9}$	*G. africanum*	Stems	Iliya *et al.* (2003b)[69]
122	Gnetoflavanol D	$C_{29}H_{24}O_{9}$	*G. africanum*	Stems	Iliya *et al.* (2003b)[69]
123	Gnetoflavanol E	$C_{29}H_{24}O_{8}$	*G. gnemon*	Roots	Iliya *et al.* (2003b)[69]
124	Gnetoflavanol F	$C_{29}H_{24}O_{8}$	*G. gnemon*	Roots	Iliya *et al.* (2003b)[69]

Trimeric Stilbenes

Gnetuhainin M (106), a trimeric stilbene, was isolated from the lianas of *G. hainanense*. It is composed of one resveratrol unit and two oxyresveratrol units, with two dihydrobenzofuran moieties.[62] Another trimer, latifolol (113), consists of three resveratrol units and was first isolated from the stem of *G. latifolium.* [30] Gnetubrunol A (105), a resveratrol trimer with two dihydrobenzofuran rings, was isolated from the lianas of *G. brunonianum.* [70]

Tetrameric Stilbenes

[69] isolated two tetrameric stilbenes, gnemonol B (115) and C (116), from the roots of *G. gnemon*. [32] These tetramers are formed through the oxidative coupling of gnetin E (102) with a resveratrol unit. Macrostachyol A (118), another tetramer, results from the oxidative coupling of latifolol (113) with resveratrol units and was isolated from the roots of *G. macrostachyum.* [33] To date, 124 stilbenoids (Figure 1) have been identified from various *Gnetum* species (1–124). *Alkaloids and Flavonoids* In addition to stilbenes, *Gnetum* species have yielded alkaloids (Table 2) and flavonoids (Table 3). The leaves of *G. montanum* provided new benzylisoquinoline alkaloids, including N-methyllaudanosolinium trifluoroacetate (125) and 3′-hydroxy-N,N-dimethylcoclaurinium trifluoroacetate (126), as well as new aporphine alkaloids such as 1,9,10-trihydroxy-2-methoxy-6-methylaporphinium trifluoroacetate (127) and 6a,7-didehydro-1,9,10-trihydroxy-2-methoxy-6-methylaporphinium trifluoroacetate (128). Known alkaloids like (−)-latifolian A (129) and magnocurarine (130) were also identified. [9] isolated three new benzylisoquinoline alkaloids—(±)-N-methylhigenamine (134), (-)-N-methylhigenamine N-oxide (135), and (±)-8-(p-hydroxybenzyl)-2,3,10,11-tetrahydroxyprotoberberine (136)—along with the known compound higenamine (137) from the lianas of *G. parvifolium.* [34]

Pharmacological Activities of Gnetum Extracts And Isolated Compounds

Previous studies have emphasized the importance of thoroughly investigating the pharmacological properties of extracts and isolated compounds from *Gnetum* species. Various biological activities, including antimicrobial, antioxidant, anti-inflammatory, cytotoxic, antidiabetic, pancreatic lipase inhibition, tyrosinase inhibition, and antiplatelet effects, have been reported.

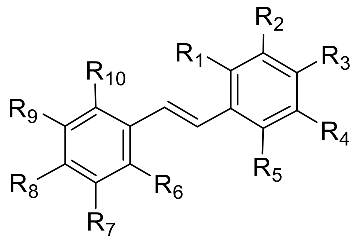
Antimicrobial Activity

Antimicrobial agents are substances that kill or inhibit the growth of microorganisms without harming the host. In a study by,[50] gnetin L, isolated from the seeds of *G. gnemon*, exhibited strong antimicrobial activity with a minimum inhibitory concentration (MIC) of 10 µg/mL against Bacillus subtilis. [14] Gnetin C showed moderate activity with an MIC of 20 µg/mL. Additionally, (-)-latifolian A demonstrated moderate inhibitory activity against Pseudomonas aeruginosa, with an IC_{50} value of 9.8 µM. [9]

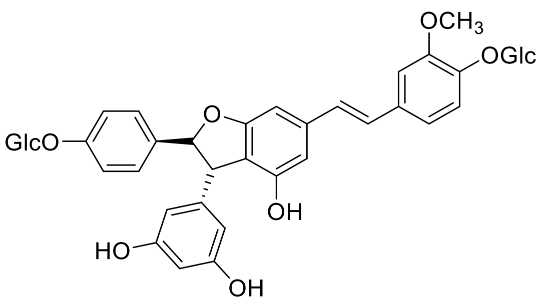
Antioxidant Activity

Compounds isolated from the lianas of *G. macrostachyum* were tested for their DPPH free radical scavenging capacity. Resveratrol and other stilbenoids displayed strong inhibition, with IC_{50} values ranging from 0.21 to 4.23 mM. Gnetulin was identified as the most potent antioxidant. Stilbenes are recognized as effective oxygen radical scavengers, likely due to their ability to form stable oligostilbenes through oxidative coupling reactions. [15] [40] reported the antioxidant activity of *G. gnemon* seed protein hydrolysates at different maturation stages. [40] All stages exhibited antioxidant activity, with EC_{50} values below 12.5 µg/mL, and hydrolyzed proteins showed greater activity than non-hydrolyzed proteins. [41] found that DPPH radical inhibition increased with seed maturity, and the highest reducing power (80.26 ± 0.06%) was observed in mature *G. gnemon* seed extracts macerated with 50% ethanol. [41]

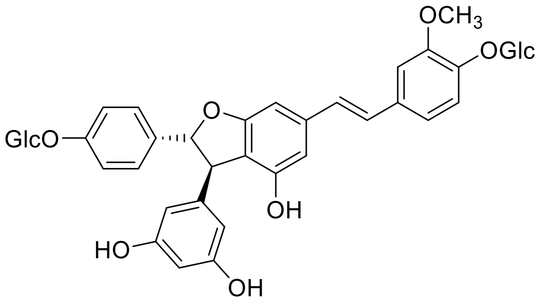
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



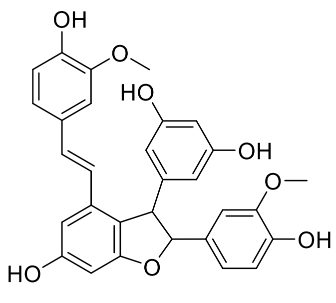
	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}
1	OH	H	H	H	OH	H	OH	H	H	H
2	H	OH	OH	OH	H	OH	H	H	H	H
3	H	OH	H	OH	H	H	H	OH	H	OCH_3
4	H	OH	H	OH	H	H	H	OCH_3	OCH_3	H
5	H	OH	H	OH	H	H	H	OGlc	OCH_3	H
6	H	OGlc	H	OH	H	H	H	OGlc	OCH_3	H
7	H	H	H	OCH_3	H	H	OH	H	H	H
8	OH	H	H	H	OH	H	OCH_3	H	OCH_3	H
9	H	H	H	H	H	H	OH	H	H	H



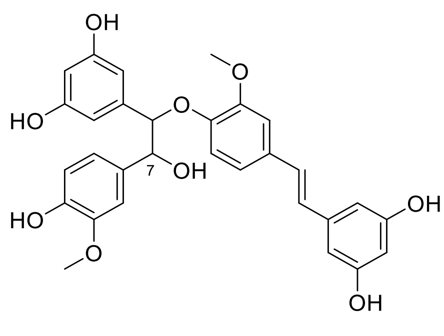
10



11

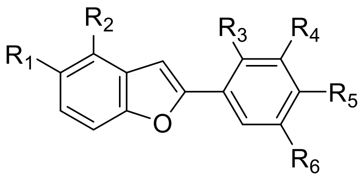


	R_1	R_2	R_3	R_4	R_5	R_6
12	OH	OCH_3	H	OCH_3	OH	H
23	OGlc	H	H	H	OGlc	H
26	OGlc	H	OH	H	OGlc	H
57	OH	H	H	H	OH	OH

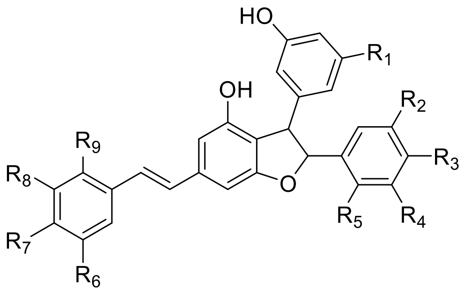


28 7α - OH
29 7β - OH

Trop J Nat Prod Res, July 2025; 9(7): 2941 - 2963 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

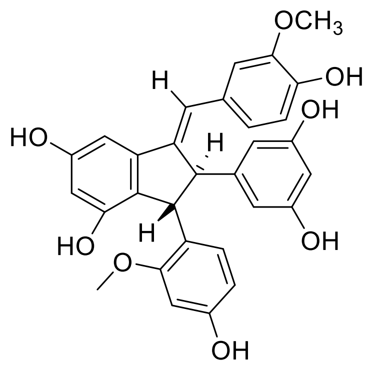


	R_1	R_2	R_3	R_4	R_5	R_6
14	H	OH	H	OH	H	OH
36	OH	OCH_3	H	OH	OCH_3	OH
52	OH	OCH_3	H	OCH_3	H	OH
53	OH	OCH_3	H	OH	H	OH
55	H	OCH_3	H	OH	H	OH
73	OH	OCH_3	OCH_3	OH	OCH_3	OH

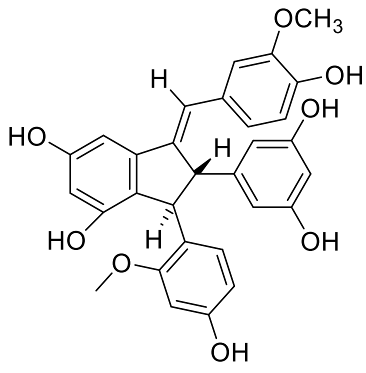


	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9
13	OH	H	OH	OCH_3	H	H	OH	OCH_3	H
15	OH	H	OH	H	OH	H	OH	OCH_3	H
16	OH	H	OH	OH	H	H	OH	OCH_3	H
17	OH	OH	OH	H	H	OH	OH	H	H
19	OH	H	OGlc	H	H	H	OGlc	H	H
20	OH	H	OGlc	H	H	H	OGlc	H	H
21	OH	H	OGlc	H	H	H	OH	H	H
22	OH	H	OH	H	H	H	OGlc	H	H
24	OGlc	H	OGlc	H	H	H	OGlc	H	H
25	OH	H	OGlc	H	OH	H	OGlc	H	H
27	OGlc	H	OH	H	H	H	OH	H	H
48	OH	H	H	OH	H	H	OH	H	H
49	OH	H	OH	H	OH	H	OH	H	H
50	OH	OH	H	OCH_3	H	H	OH	H	H
77	OH	H	OH	H	OH	H	OH	H	OH
82	OH	H	OH	H	OH	H	OH	H	H
85	OH	H	OH	OCH_3	H	H	OH	H	H

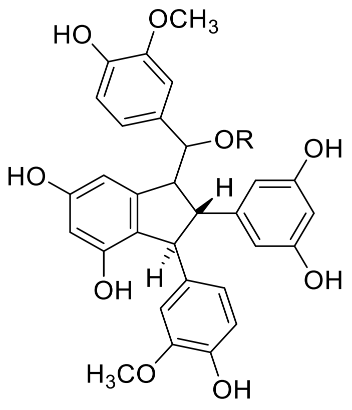
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



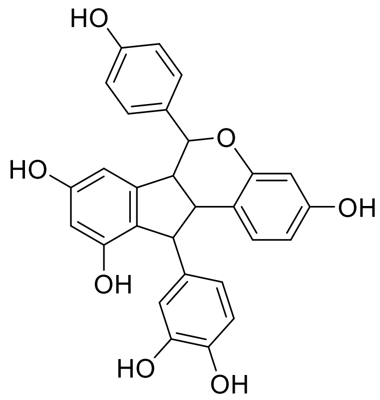
30



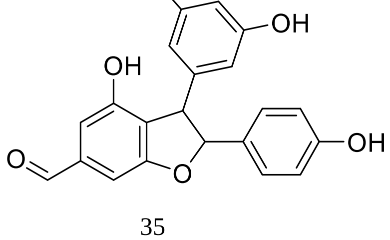
31



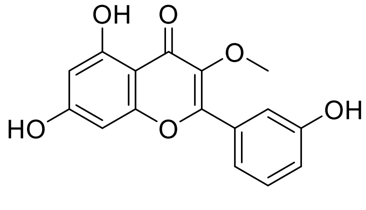
R
32 : H
33 : OH



34

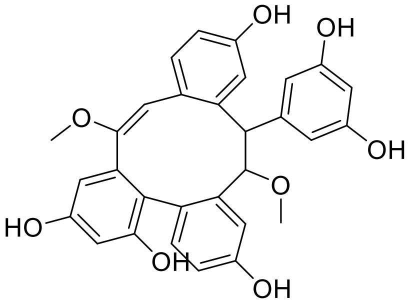


35

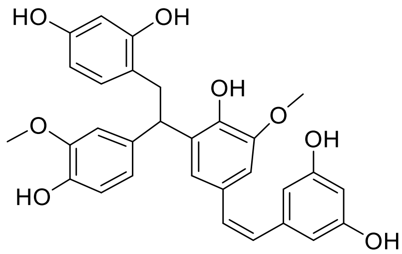


37

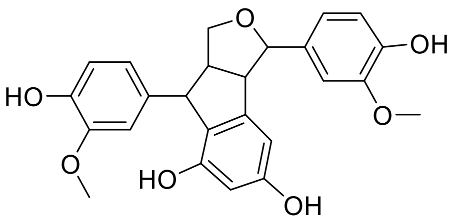
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



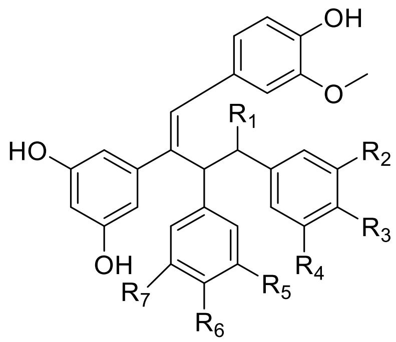
38



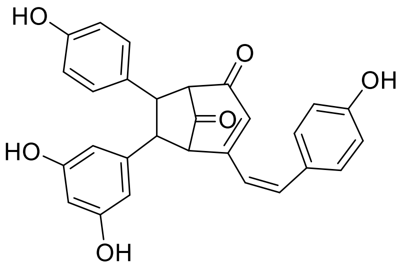
39



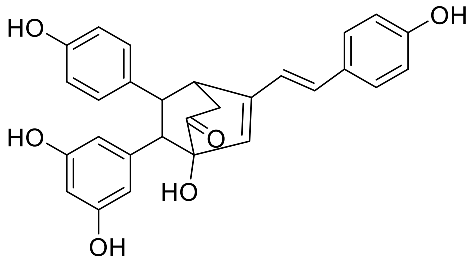
40



	R_1	R_2	R_3	R_4	R_5	R_6	R_7
41	H	OH	H	OH	OCH_3	OH	H
44	OH	OH	H	OH	OCH_3	OH	H
69	OH	OCH_3	OH	H	OH	H	OH

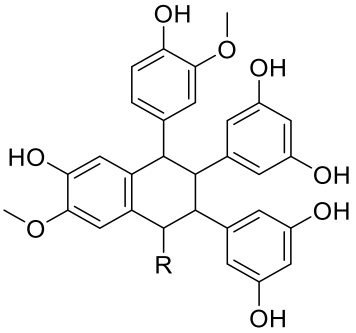


46

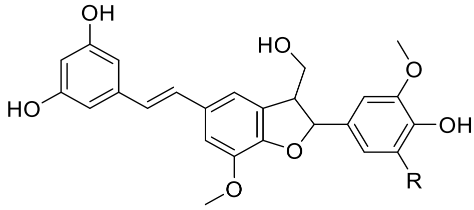


47

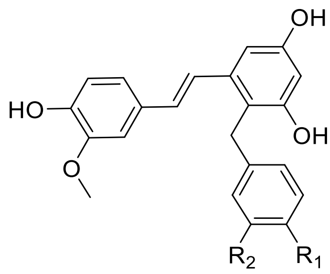
Trop J Nat Prod Res, July 2025; 9(7): 2941 - 2963 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



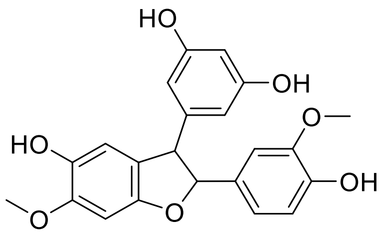
	R
42	OH
43	OH
45	H



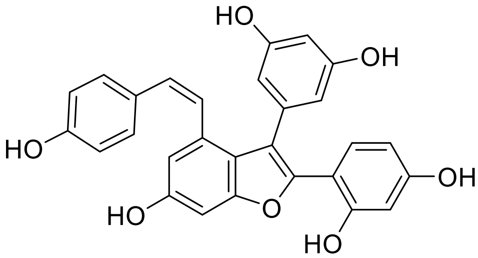
	R
51	H
56	OCH_3



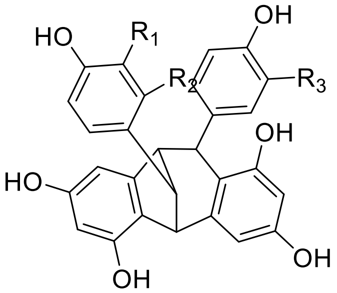
	R_1	R_2
72	H	H
80	H	OH
81	OH	OH



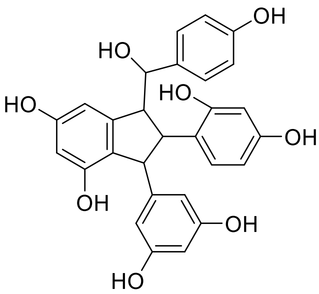
54



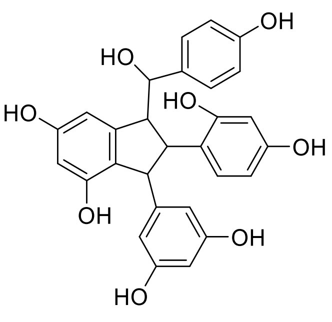
58



	R_1	R_2	R_3
18	OCH_3	H	OCH_3
59	H	OH	H

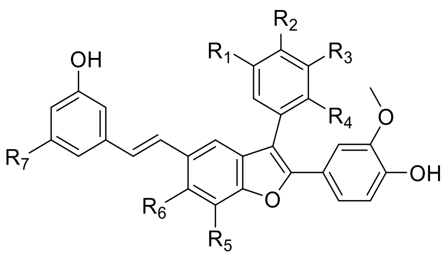


60

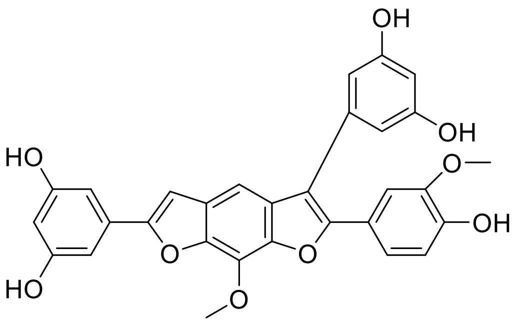


61

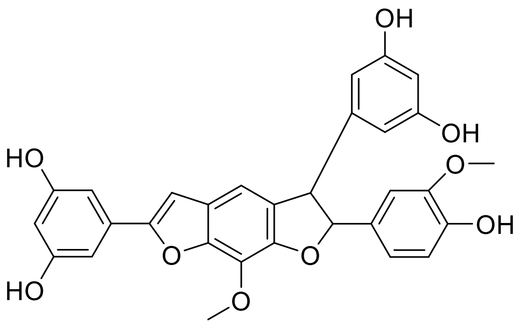
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



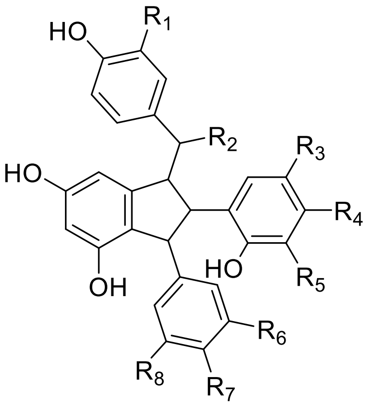
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
62	H	OH	H	OH	OCH_3	H	OH
68	OH	H	OH	H	H	OH	OH
70	OH	H	OH	H	H	H	OH
83	OH	H	OH	H	OCH_3	H	OCH_3
89	OH	H	OH	H	OCH_3	H	OH



63

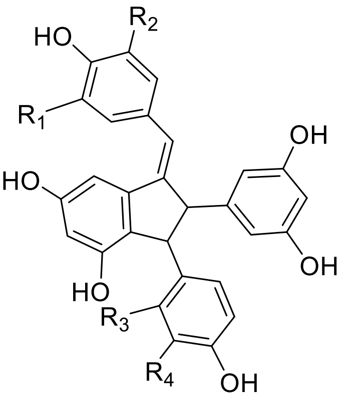


64

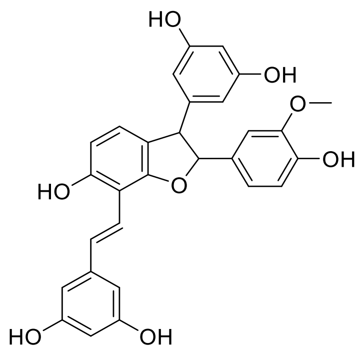


	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
65	OCH_3	OH	OH	H	OH	OCH_3	OH	H
84	H	OCH_3	H	OH	H	OH	H	OH

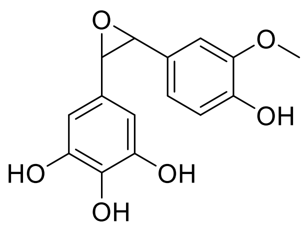
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



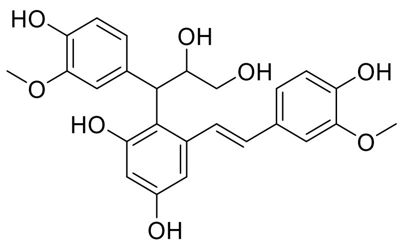
	R_1	R_2	R_3	R_4
66	OCH_3	H	OH	H
71	H	OCH_3	H	OCH_3



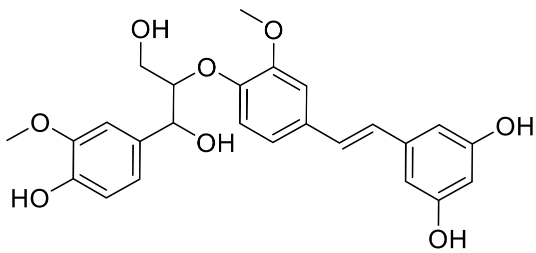
67



74

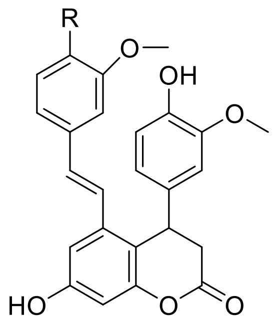


75

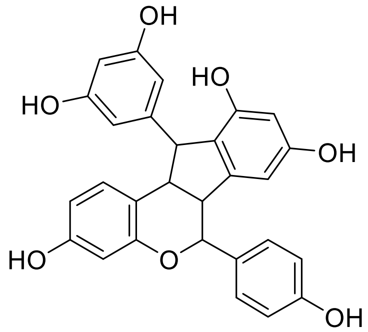


76

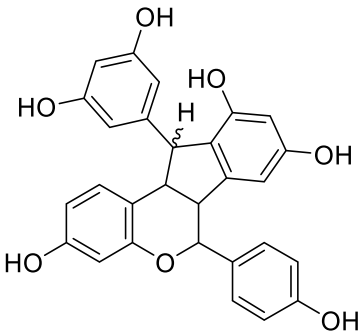
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



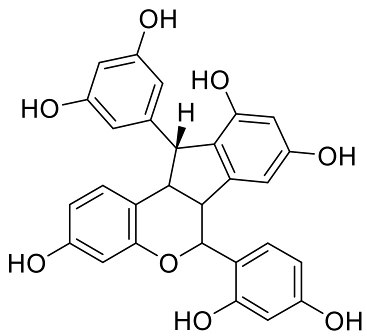
	R
78	OH
79	OGlc



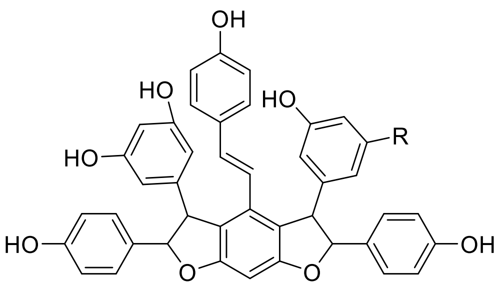
86



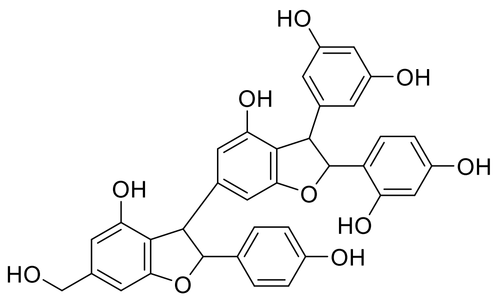
87



88

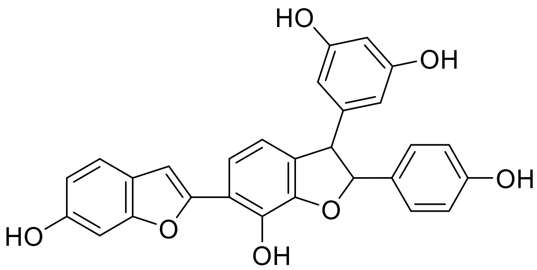


	R
90	OH
105	$OCH(CH_2OH)CH_2OH$

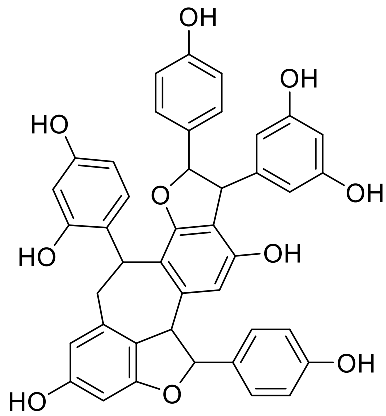


91

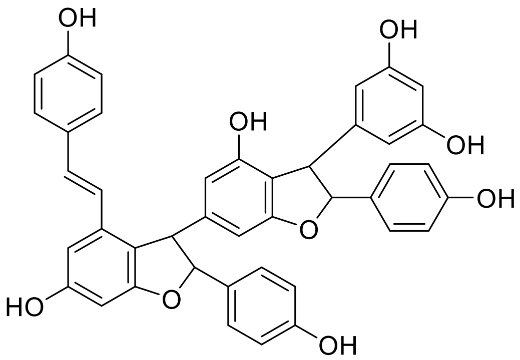
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



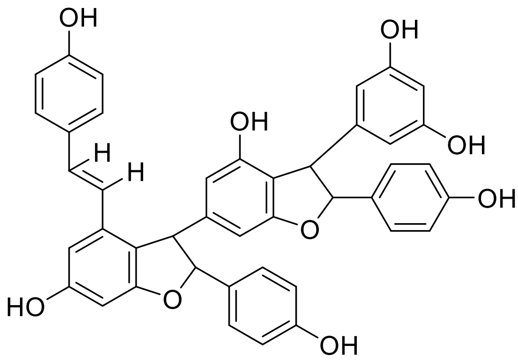
92



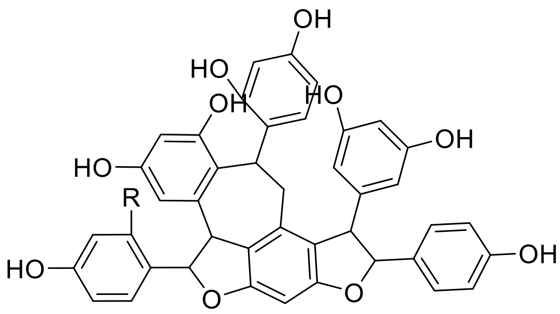
93



96

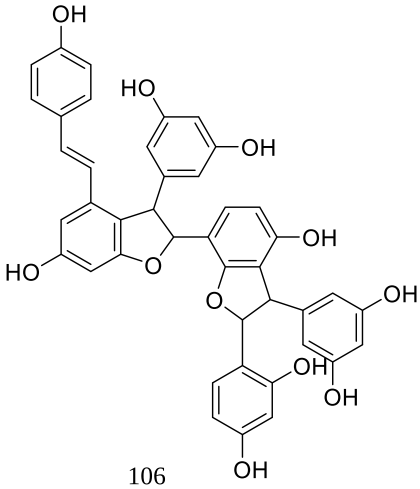


97

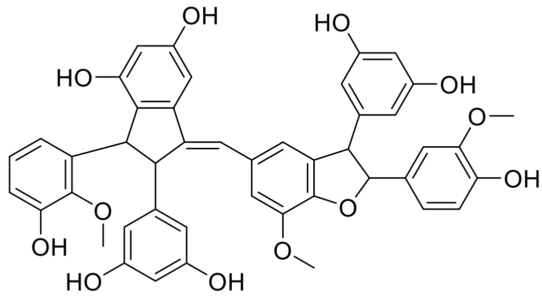


	R
94	H
95	OH

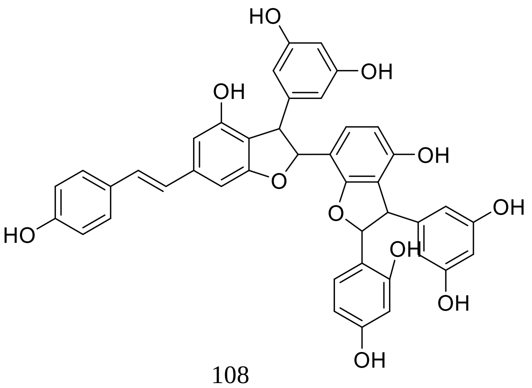
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



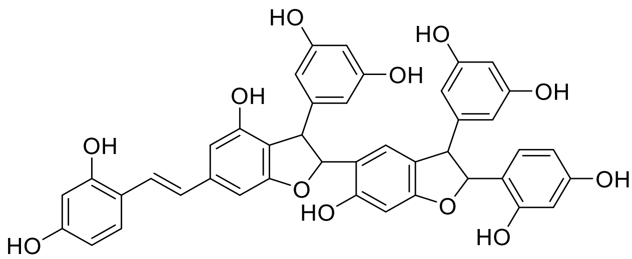
106



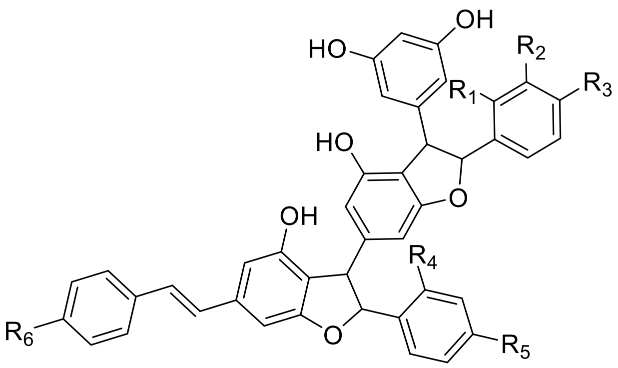
107



108

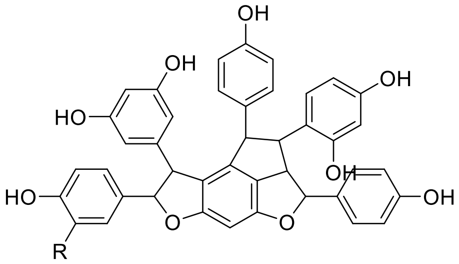


109

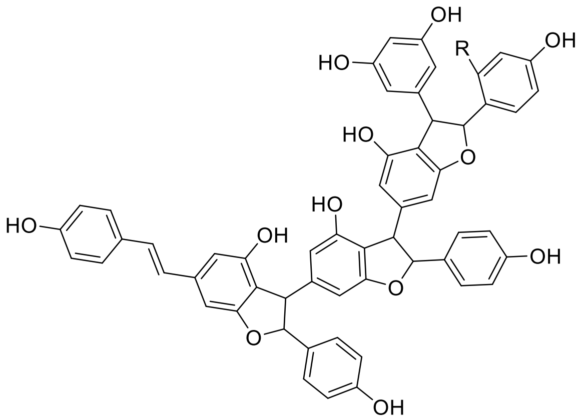


	R_1	R_2	R_3	R_4	R_5	R_6
98	H	H	OGlc	H	OGlc	OGlc
99	H	H	OGlc	H	OH	OGlc
100	H	H	OGlc	H	OGlc	OGlc
101	H	H	OH	H	OGlc	OH
102	H	H	OH	H	OH	OH
103	H	OH	OH	H	OH	OH
104	H	OCH_3	OH	H	OH	OH
113	OH	H	OH	H	OH	OH

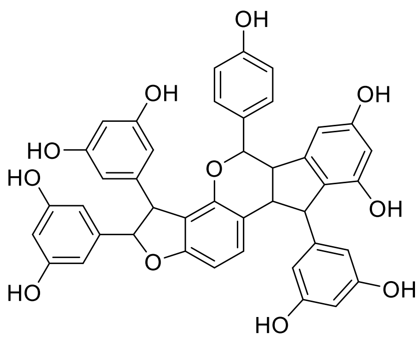
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



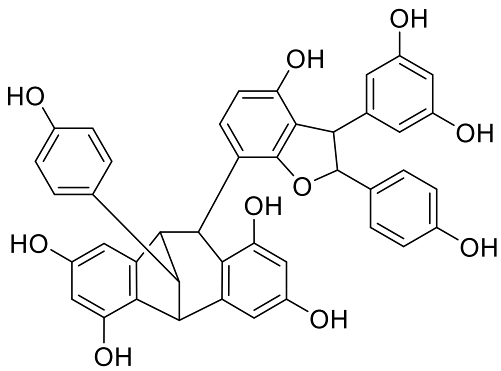
	R
110	H
111	OH



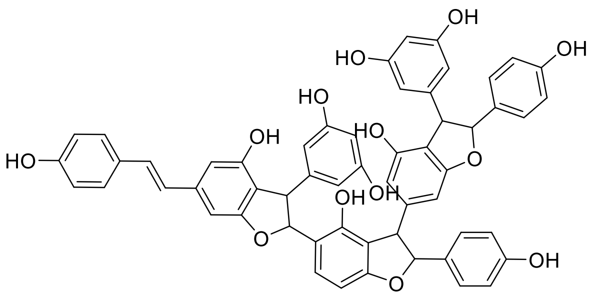
	R
115	H
118	OH



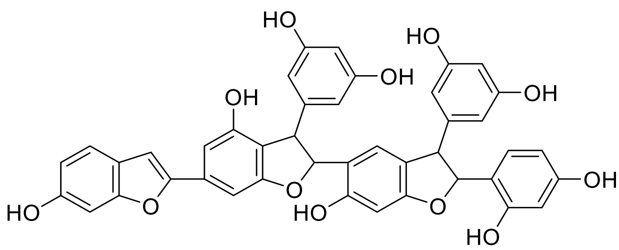
112



114

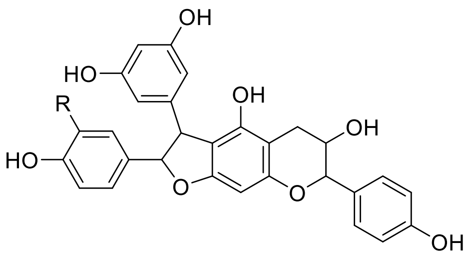


116

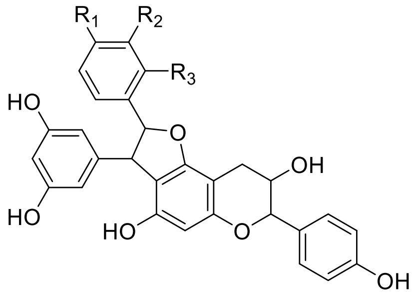


117

 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



	R
119	OCH_3
120	H



	R_1	R_2	R_3
121	OH	OH	H
122	OH	H	OH
123	OH	H	H
124	OH	H	H

Figure 1: Structures of stilbenes isolated from *Gnetum* species

Table 2: Alkaloids from *Gnetum* species.

No	Compounds	Molecular formula	Species	Part	References
125	N-methyllaudanosolinium trifluoroacetate	$C_{18}H_{22}NO_4$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
126	3′-hydroxy-N,N-dimethylcoclaurinium trifluoroacetate	$C_{19}H_{24}NO_4$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
127	1,9,10-trihydroxy-2-methoxy-6-methylaporphinium trifluoroacetate	$C_{19}H_{22}NO_4$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
128	6a,7-didehydro-1,9,10-trihydroxy-2-methoxy-6-methylaporphinium trifluoroacetate	$C_{19}H_{20}NO_4$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
129	(−)-latifolian A	$C_{26}H_{22}NO_8$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
130	Magnocurarine	$C_{19}H_{24}NO_3$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
131	N-Methylboldine trifluoroacetate	$C_9H_{10}NO_2$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
132	N-Methylsecoboldine trifluoroacetate	$C_{18}H_{20}NO_4$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
133	N,N-Dimethylsecoboldine trifluoroacetate	$C_{19}H_{22}NO_4$	*G. montanum*	Leaves	Martin *et al.* (2011)[9]
134	(-)-N-methylhigenamine	$C_{17}H_{19}NO_3$	*G. parvifolium*	Lianas	Xu & Lin (1999)[34]
135	(-)-N-methylhigenamine N-oxide	$C_{17}H_{19}NO_4$	*G. parvifolium*	Lianas	Xu & Lin (1999)[34]
136	(±)-8-(p-hydroxybenzyl)-2,3,10,11-tetrahydroxyprotoberberine	$C_{34}H_{33}NO_{10}$	*G. parvifolium*	Lianas	Xu & Lin (1999)[34]
137	Higenamine	$C_{16}H_{17}NO_3$	*G. parvifolium*	Lianas	Xu & Lin (1999)[34]

Table 3 Flavonoids from *Gnetum* species.

No	Compounds	Molecular formula	Species	Part	References
138	(-)-epicatechin	$C_{15}H_{14}O_6$	*G. africanum*	Leaves	Udeh *et al.* (2020)[36]

 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

139	Noidesols A	$C_{22}H_{24}O_{12}$	*G. gnemonoides*	Barks	Shimokawa *et al.*, (2010)[37]
140	Noidesols B	$C_{22}H_{24}O_{12}$	*G. gnemonoides*	Barks	Shimokawa *et al.*, (2010)[37]
141	(2S)-naringenin 8-C-α-Lrhamnopyranosyl-(1 → 2)-*β*-D-glucopyranoside	$C_{26}H_{30}O_{15}$	*G. macrostachyum*	Stems	Seo *et al.* (2020)[35]
142	Isohemiphloin	$C_{21}H_{22}O_{10}$	*G. macrostachyum*	Stems	Seo *et al.* (2020)[35]

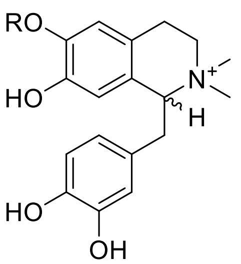
Flavonoids such as (2S)-naringenin 8-C-α-L-rhamnopyranosyl-(1 → 2)-*β*-D-glucopyranoside (141) and isohemiphloin (142) were reported from the stems of *G. macrostachyum.* [35] (-)-Epicatechin (138) was isolated from the leaf extract of *G. africanum.* [36] Two new dihydroflavonol-C-glucosides, noidesols A (139) and B (140), were identified from the bark of *G. gnemonoides.* [37] In total, 13 alkaloids (Figure 2) and 5 flavonoids (Figure 3) have been isolated from *Gnetum* species (125–142).

Other Compounds

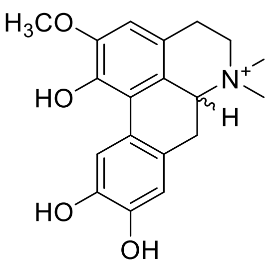
Other compounds (Table 4) isolated from *Gnetum* include 3-O-(13-hydroxy-9Z,11E,15E-octadecatrienoyl) cycloeucalenol (143), 24′-hydroxy-tetracosyl ferulate (144) (a steroid), and tetracosyl ferulate (145) (a coumaric acid derivative). [38] Phenyletanoids like trysol (147) and homovanillyl alcohol (148), as well as the benzene aldehyde vanillin (149), were isolated from the stems of *G. macrostachyum.* [35] Additionally, 3,4-dimethoxychlorogenic acid (146) (Figure 4) was isolated from the stem bark of *G. gnemon.* [39] In summary, *Gnetum* species are a rich source of diverse phytochemicals, including stilbenes, alkaloids, flavonoids, and other bioactive compounds, making them a valuable subject for further pharmacological and chemical research

Table 4 Other compounds from *Gnetum* species.

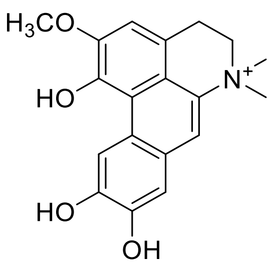
No	Compounds	Molecular formula	Species	Part	References
143	3-O-(13-hydroxy-9Z,11E,15E-octadecatrienoyl) cycloeucalenol	$C_{18}H_{30}O$	*G. pendulum*	Stems	Xiang *et al.* (2008)[38]
144	24'-hydroxy-tetracosyl ferulate	$C_{34}H_{58}O_4$	*G. pendulum*	Stems	Xiang *et al.* (2008)[38]
145	Tetracosyl ferulate	$C_{34}H_{58}O_3$	*G. pendulum*	Stems	Xiang *et al.* (2008)[38]
146	3,4-dimethoxychlorogenic acid	$C_{19}H_{22}O_8$	*G. gnemon*	Stems	Atun *et al.* (2007)[39]
147	Trysol	$C_{10}H_8N_6$	*G. macrostachyum*	Stems	Seo *et al.* (2020)[35]
148	Homovanillyl	$C_9H_{12}O_3$	*G. macrostachyum*	Stems	Seo *et al.* (2020)[35]
149	Vanillin	$C_8H_8O_3$	*G. macrostachyum*	Stems	Seo *et al.* (2020)[35]



125: R = H
126: R = CH_3

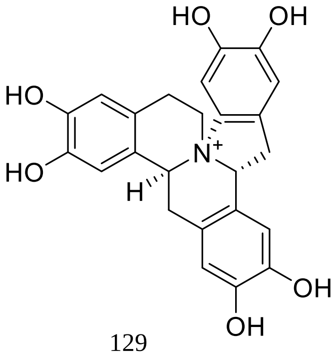


127

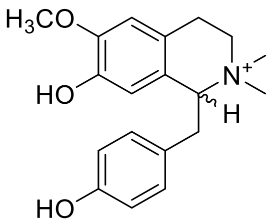


128

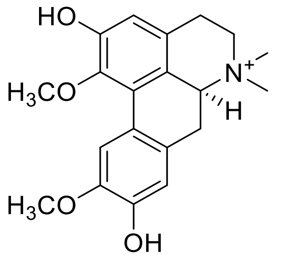
 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)



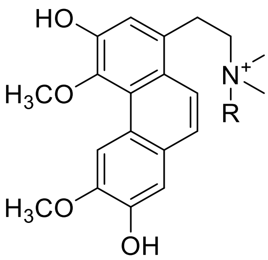
129



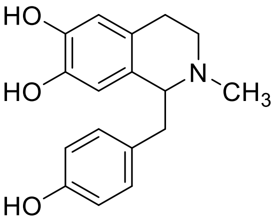
130



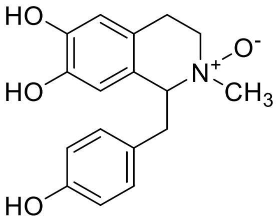
131



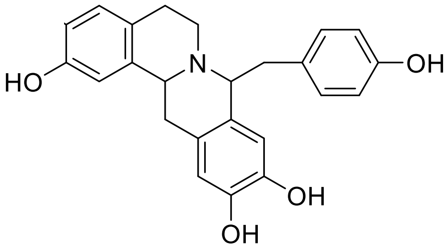
132: R = H
133: R = CH_3



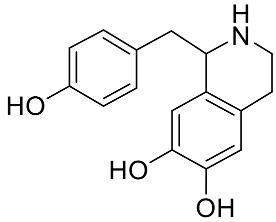
134



135

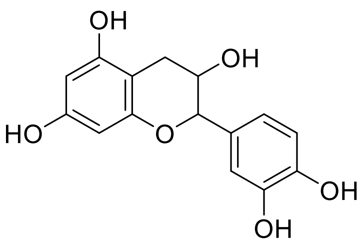


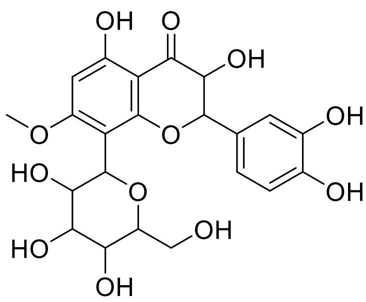
136



137

Figure 2: Structure of alkaloids isolated from *Gnetum* species

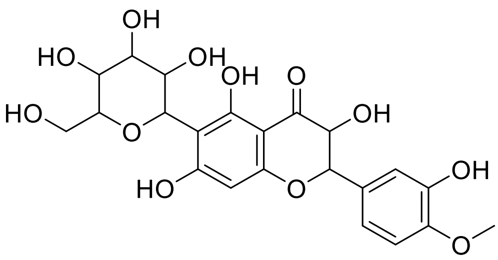




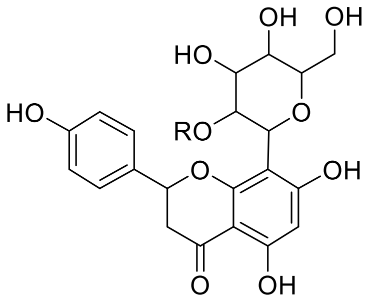
ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

138

139

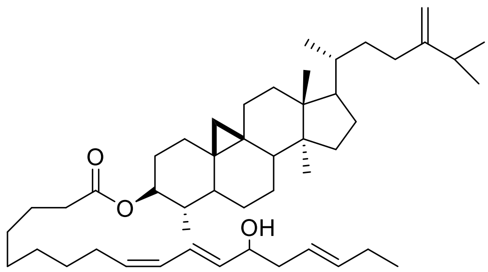


140

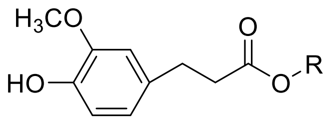


141: R = Glc
142: R = H

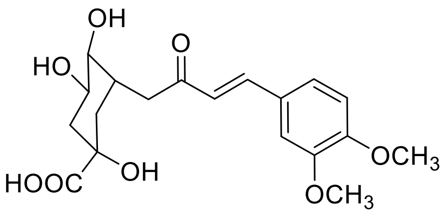
Figure 3: Structure of flavonoids isolated from *Gnetum* species



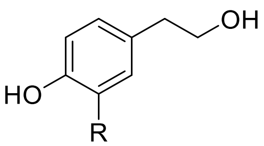
143



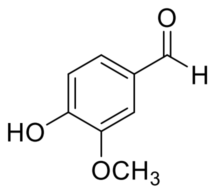
144: R = $(CH_2)_{23}CH_2OH$
145: R = $(CH_2)_{23}CH_3$



146



147: R = H
148: R = OCH_3



149

Figure 4: Structure of other compounds isolated from *Gnetum* species

Anti-Inflammatory Activity
Purified compounds from the leaves of *G. latifolium* were evaluated for their ability to suppress neuroinflammation induced by Aβ1-42 transfection in microglial BV-2 cells. Most compounds, except lehmbachol B, inhibited NO release, with cis-shegansu B, trans-shegansu B, and latifolol showing the strongest effects at concentrations of 5–20 µM. [8] Gnetuhainin M and N, isolated from *G. hainanense*, exhibited histamine receptor antagonism with inhibitory rates of -29% and 26%, respectively, at 10^{-5} mol/L, outperforming the positive control, chlorpheniramine maleate, which had a 50% inhibitory rate at the same concentration. [42]

Cytotoxicity
Compounds isolated from the roots of *G. macrostachyum* were tested for cytotoxicity against KB and HeLa cell lines. Macrostachyol D showed significant cytotoxicity against HeLa cells, with an IC_{50} value of 4.13 µM. [33] Cuspidan A and B, isolated from the bark of *G. cuspidatum*, were tested against HL-60 cells. While cuspidan A showed no cytotoxicity (IC_{50} >100 µM), cuspidan B exhibited moderate growth inhibition (IC_{50} 33.5 µM). [43]

Antidiabetic Activity
The ethanolic extract of *G. gnemon* increased SIRT1 activity and inhibited endothelial senescence in mice, with gnetin C concentrations in blood plasma six-fold higher than those of trans-resveratrol. [44] Ikuta *et al.* (2015) reported that melinjo seed extract (MSE) suppressed plasma insulin levels in high-fat diet (HFD) mice, reducing weight gain and blood insulin. [45] [40] found that hydrolyzed proteins from *G. gnemon* seeds at different maturation stages enhanced α-amylase and α-glucosidase inhibition. [40] For example, green melinjo hydrolysate (GMH) showed IC_{50} values of 6.98 and 5.72 µg/mL for α-amylase and α-glucosidase, respectively. [36] demonstrated that (-)-epicatechin, isolated from *G. africanum*, reduced fasting blood sugar (FBS) by 71.4% in alloxan-induced diabetic rats, outperforming glibenclamide (41.2% reduction). [36]

Pancreatic Lipase Inhibition

Gnetin L, isolated from *G. gnemon* seeds, exhibited the strongest pancreatic lipase inhibition activity, with an IC_{50} of 7.2 µM against the hydrolysis of 4-methylumbelliferyl oleate (MUO). [14]

Tyrosinase Inhibition

Gnetol, isolated from *G. gnemon* roots, was identified as a potent tyrosinase inhibitor, with an IC_{50} value of 4.5 mM in murine B16 melanoma cells. Gnetin C and resveratrol also showed similar inhibitory effects, with IC_{50} values of 7.0 and 7.2 µM, respectively. [7,46]

Antiplatelet Activity

Stilbenoids isolated from *G. macrostachyum* roots were evaluated for antiplatelet activity. Trans-resveratrol, isorhapontigenin, and gnetol inhibited arachidonic acid (AA)-induced platelet aggregation, while isorhapontigenin and bisisorhapontigenin B were most effective against thrombin-induced aggregation. Dimeric stilbenoids were more potent than monomeric and trimeric forms in inhibiting platelet-collagen adhesion. [47] In summary, *Gnetum* species exhibit a wide range of pharmacological activities, making them a promising subject for further research and potential therapeutic applications.

Conclusion

This paper provides a comprehensive overview of the phytochemical and pharmacological data available for the genus *Gnetum*. Given the limited scope of research on this genus, the findings presented in this review offer valuable insights and a foundation for future studies. Further research is essential to establish a clear correlation between the pharmacological activities of *Gnetum* species and their isolated phytochemicals. Such efforts will aid in identifying promising drug candidates with therapeutic potential. Based on the current evidence, it is scientifically valid to conclude that the genus *Gnetum* represents a rich source of bioactive compounds, warranting continued exploration and investigation.

Conflict of interest

The author reports no conflicts of interest in this work.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgements

This work was supported by the Ministry of Higher Education (MOHE), Malaysia, under the Fundamental Research Grant Scheme (FRGS/1/2023/WAB13/UITM/02/4).

References

1. Ali Z, Tanaka T, Iliya I, Iinuma M, Furusawa M, Ito T, Nakaya K. Ich, Murata J, Darnaedi D. Phenolic constituents of *Gnetum klossii*. J. Nat. Prod. 2003; 66: 558–560. https://doi.org/10.1021/np020532o
2. Carlquist S. Wood and bark anatomy of liamoid Indornalesian and Asiatic species of *Gnetum*. Bot. J. Linn Soc. 1996; 121: 1-24. https://doi.org/10.1111/j.1095-8339.1996.tb00742.x
3. Singh VP. Gymnosperm (naked seeds plant): Structure and development. Prabhat Kumar Sharma for Sarup & Sons. 2006. Delhi, India.
4. Won H Renner S. The internal transcribed spacer of nuclear ribosomal DNA in the gymnosperm *Gnetum*. Mol Phylogenet Evol. 2006; 36: 581-597. DOI: 10.1016/j.ympev.2005.03.011
5. Kubitzki K. Gnetaceae. In: Kramer, K. U, Green, P.S. (eds) Pteridophytes and Gymnosperms. The Families and Genera of Vascular Plant. 1990. Vol 1. Springer. Berlin. Heidelberg.
6. Deng N, Hou C, Liu C, Li M, Bartish I, Tian Y, Chen W, Du C, Jiang Z, Shi S. (2019) Significance of Photosynthetic Characters in the Evolution of Asian *Gnetum* (Gnetales). Front. Plant. Sci. 2019; 10: 1-13. https://doi.org/10.3389/fpls.2019.00039
7. Ohguchi K, Tanaka T, Iliya I, Ito T, Iinuma M, Matsumoto K, Akao Y, Nozawa Y. (2003) Gnetol as a potent tyrosinase inhibitor from genus *Gnetum*. Biosci. Biotechnol Biochem. 2003; 67: 663–665. DOI: 10.1271/bbb.67.663
8. Cho HM, Ha TK, Pham HT, An JP, Huh J, Lee BW, Lee HJ, Oh WK. Oligostilbenes from the leaves of *Gnetum latifolium* and their biological potential to inhibit neuroinflammation. Phytochem. 2019; 165: 112044. https://doi.org/10.1016/j.phytochem .2019.05.017
9. Martin F, Grkovic T, Sykes ML, Shelper T, Avery VM, Camp D, Quinn RJ,Davis RA. Alkaloids from the Chinese vine *Gnetum montanum*. J. Nat. Prod. 2011; 74: 2425–2430. https://doi.org/10.1021/np200700f
10. Ekop AS. Determine of chemical composition of *Gnetum africanum* (AFANG) seeds. PJN. 2007; 6: 40-43. DOI: 10.3923/pjn.2007.40.43
11. Ali F, Assanta MA, Robert C. *Gnetum africanum*: A wild food plant from the african forest with many nutritional and medicinal properties. J Med Food. 2011; 14:1289–1297. https://doi.org/10.1089/jmf.2010.0327
12. Lin M, Lr JB, Li SZ, et al (1992) A dimeric stilbene from *Gnetum parvifolium*. Phytochemistry. 31: 633-638. https://doi.org/10.1016/0031-9422(92)90050-Z
13. Li XM, Wang YH, Lin M. Gnetupendin C, a new stilbene dimer from lianas of *Gnetum pendulum*. Chin. Chem. Lett. 2001a; 12: 611-612.
14. Kato E, Tokunaga Y, Sakan F. Stilbenoids isolated from the seeds of melinjo (*Gnetum gnemon* L.) and their biological activity. J. Agri. Food Chem. 2009; 57: 2544–2549. https://doi.org/10.1021/jf803077p
15. Saisin S, Tip-pyang S, Phuwapraisirisan S. A new antioxidant flavonoid from the lianas of *Gnetum macrostachyum*. Nat. Prod Res: Formerly Nat Prod Lett. 2009; 23: 1472-1477. DOI: 10.1080/14786410802280943
16. Barua CC, Haloi P, Barua I. *Gnetum gnemon* Linn.: A Comprehensive review on its biological, pharmacological and pharmacognostical potentials. Int J Pharm Phyto Res. 2015; 7:531-539. https://doi.org/10.1590/fst.100121
17. Britannica, 2008
18. Yao CS, Mao L, Xin L, Wang YH. Stilbenes from *Gnetum cleistostachyum*. Acta Chim Sinica. 2003; 61: 1331 – 1334.
19. Ali MI, Shabir S, Soni LK, Dobhal MP, Moin S. The phytochemical potential of gnetaceae with peculiar reference to *Gnetum ula* and traditional uses of gnetaceae species. Plant Arch. 2020; 20: 2979–2986.
20. Prashanth KG, Shiddamallayya N. Survey of wild medicinal plants of Hassan district, Karnataka. J. Med. Plants. 2016; 4: 91-102.
21. Biye EH, Balkwill K, Cron, GV. Taste versus shelf life: Intended use should guide selection of indigenous strains of *Gnetum gnemon* L. (Gnetaceae) for domestication in Africa. S. Afr. J. Bot. 2017; 113: 170–181. https://doi.org/10.1016/j.sajb.2017.08.013
22. Isong EU, Adewusi SAR, Nkanga EU, Umoh EE, Offiong EE. Nutritional and phytogeriatological studies of three varietes of *Gnetum africanum*. Food Chem. 1999; 64:489–493.
23. Amelia E, Wahyuni I, Marianingsih P. The Diversification Use of Melinjo (*Gnetum gnemon*) in Banten Local Food. ABSR. 2021; 9: 203–206.
24. Lins AP, Ribeiro M, Gottlieb OR, Gottlieb H, (1989) Gnetins: resveratrol oligomers from *Gnetum* species. Journal of Natural Products. 45: 754-761. https://doi.org/10.1021/np50024a022
25. Rivière C, Pawlus AD, Mérillon JM. Natural stilbenoids: Distribution in the plant kingdom and chemotaxonomic interest in Vitaceae. Nat. Prod. Rep. 2012; 29: 1317–1333. DOI: https://doi.org/10.1039/C2NP20049J
26. Rupasinhe H, Nair S, Robinson R. Chemopreventive properties of fruits phenolic compounds and their possible mode of actions. Stud. Nat. Prod. Chem. 2014; 42: 229-266. DOI:10.1016/B978-0-

444-63281-400008-2
27. Iliya I, Ali Z, Tanaka T, Iinuma M, Furusawa M, Nakaya K, Murata J, Darnaedi D, Matsuura N, Ubukata M. Stilbene derivatives from *Gnetum gnemon* Linn. Phytochem. 2003a; 62(4): 601–606. DOI: 10.1016/s0031-9422(02)00670-2
28. Tanaka T, Iliya I, Ito T, Furusawa M, Nakaya K, Iinuma M, Shirataki Y, Matsuura N, Ubukata, M, Murata J, Simozono F, and Hirai K. Stilbenoids in lianas of *Gnetum parvifolium*. Chem. Pharma. Bull. 2001; 49: 858–862. DOI: 10.1248/cpb.49.858
29. Li XM, Wang YH, Lin M. Stilbenoids from the lianas of *Gnetum pendulum*. Phytochem. 2001; 58: 591–594. https://doi.org/10.1016/S0031-9422(01)00269-2
30. Iliya I, Ali Z, Tanaka T, Iinuma M, Furusawa M, Nakaya K, Murata J, and Darnaedi D. Stilbenoids from the stem of *Gnetum latifolium* (Gnetaceae). Phytochem. 2002a; 61: 959–961. https://doi.org/10.1016/S0031-9422(02)00289-3
31. Yao CS, Lin M, Wang L. Isolation and Biomimetic Synthesis of Anti-inflammatory Stilbenolignans from *Gnetum cleistostachyum*. Chem Pharm Bull. 2005; 54: 1053—1057. DOI:10.1248/cpb.54.1053
32. Iliya I, Tanaka T, Iinuma M, Ali Z, Furasawa M, Nakaya K, Shirataki Y, Murata J, and Darnaedi D. Stilbene derivatives from two species of Gnetaceae. Chemical and Pharm. Bull. 2002b; 50: 796–801. DOI: 10.1248/cpb.50.796
33. Sri-in P, Sichaem J, Siripong P, and Tip-pyang S. Macrostachyols A–D, new oligostilbenoids from the roots of *Gnetum macrostachyum.* Fitoterapia. 2011; 82: 460–465. https://doi.org/10.1016/j.fitote.2010.12.008
34. Xu Q, Lin M. Benzylisoquinoline alkaloids from *Gnetum parvifolium.* J Nat Prod. 1999; 62: 1025-1027. https://doi.org/10.1021/np980472f
35. Seo C, Lym SH, Jeong W, Lee JE, Lee JA, Ahn EK, Kang JS, Kim WH, Choi CW, Oh JS, and Hong SS. Flavonoids, stilbenoids, and phenolic derivatives from the stems of *Gnetum macrostachyum* (Gnetaceae). Biochem. Syst. Ecol. 2020; 90: 104033. https://doi.org/10.1016/j.bse.2020.104033
36. Udeh N, Nnadi C, Anaga A, Asuzu I. Bioactivity-guided fractionation of a methanol leaf extract from *Gnetum africanum* with potential anti-diabetic activity: (-)-epicatechin as the active principle. J. Res. Pharm. 2021; 25: 72–79. DOI:10.35333/jrp.2021.293
37. Shimokawa Y, Akao Y, Hirasawa Y, Awang K, Hamid A, Hadi A, Sato S, Aoyama C, Takeo J, Shiro M, Morita H. Gneyulins A and B, Stilbene Trimers, and Noidesols A and B, Dihydroflavonol-C-Glucosides, from the Bark of *Gnetum gnemonoides.* J. Nat. Prod. 2010; 73: 763–767. https://doi.org/10.1021/np9007987
38. Xiang WS, Wang JD, Wang XJ, Zhang J. Two new components from *Gnetum pendulum*. J. Asian Nat. Prod. Res. 2008; 10: 1081–1085. DOI:10.1080/10286020802318958
39. Atun S, Arianingrum R. Masataka N. Some phenolic compounds from stembark of melinjo (*Gnetum gnemon*) and their activity test as antioxidant and UV-B protection. Proceeding JSChem-ITB-UKM. 2007. DOI:10.1021/jf803077p
40. Supriyadi A, Arum LS, Nugraha AS, Ratnadewi AAI, and Siswoyo TA. Revealing antioxidant and antidiabetic potency of melinjo (*Gnetum gnemon*) seed protein hydrolysate at different stages of seed maturation. Curr. Res Nutr. 2019; 7: 479-487. DOI : https://dx.doi.org/10.12944/CRNFSJ.7.2.17
41. Kurnato B, Sutardi S, Supriyanto, Anwar C. Antioxidant activity of Melinjo Ketan (*Gnetum gnemon* L., 'Ketan') seed extraction at various ripening stages and ethanol solvent concentration. Int J Adv Sci Eng Inf Technol.. 2019; 9: 1344-1351. DOI: https://doi.org/10.18517/ijaseit.9.4.9376
42. Huang KS, Li RL, Wang YH, Lin M. Three new stilbene trimer from the lianas of *Gnetum hainanense.* Planta Med. 2001. 67: 95-98. DOI: 10.1055/s-2001-10875
43. Shimokawa Y, Hirasawa Y, Kaneda T, Hamid A, Hadi A, Morita H. (2012) Cuspidans A and B, Two New Stilbenoids from the Bark of *Gnetum cuspidatum*. Chem. Pharma. Bull. 2012; 60: 790–792. DOI: 10.1248/cpb.60.790
44. Eto M, Shirasawa T, Ouchi Y. *trans*-Resveratrol in *Gnetum gnemon* Protects against Oxidative- Stress-Induced Endothelial Senescence. J. Nat Prod. 2012; 76: 1242–1247.
45. Ikuta T, Saito S, Tani H, Tatefuji T, and Hashimoto K. 2015. Resveratrol derivative-rich melinjo (*Gnetum gnemon* L.) seed extract improves obesity and survival of C57BL/6 mice fed a high-fat diet. Biosci Biotechnol Biochem. 2015; 79: 2044 – 2049.
46. Yanagihara M, Yoshimatsu M, Inoue A, Kanno T, Tatefuji T, Hashimoto K. Inhibitory effect of gnetin C, a resveratrol dimer from melinjo (*Gnetum gnemon*), on tyrosinase activity and melanin biosynthesis. Bio. Pharm. Bull. 2012; 35: 993-996. https://doi.org/10.1248/bpb.35.993
47. Kloypan C, Jeenapongsa R, Sri-In P, Chanta S, Dokpuang D, Tip-Pyang S, and Surapinit N. Stilbenoids from *Gnetum macrostachyum* attenuate human platelet aggregation and adhesion. Phytother Res. 2012; 26: 1564–1568. DOI: 10.1002/ptr.4605
48. Azmin NFN, Ahmat N, Syah Y, Khairunissa N, Zawani NA, Yusof MIM. A new stilbenoid compound from the lianas of *Gnetum microcarpum*. Nat. Prod. Commun. 2014; 9(12), 1743–1744. DOI:10.1177/1934578X1400901221
49. Wang LQ, Zhao YX, Hu JM, Jia AQ, and Zhou J. Stilbene Derivatives from *Gnetum montanum* Markgr. *f. megalocarpum* Markgr. Helv Chim Acta. 2008; 91: 159 – 164. https://doi.org/10.1002/hlca.200890007
50. Kato H, Samizo M, Kawabata R, Takano F, Ohta T. Stilbenoids from the Melinjo (*Gnetum gnemon* L.) Fruit Modulate Cytokine Production in Murine Peyer's Patch Cells Ex Vivo. Planta Med. 2011; 77: 1027–1034. DOI: 10.1055/s-0030-1250742
51. Gabaston J, Buffeteau T, Brotin T, Bisson J, Rouger C, Mérillon JM, Waffo-Téguo P. Diastereomeric stilbenoid glucoside dimers from the rhizomes of *Gnetum africanum*. Phytochem. Lett. 2020; 39, 151–156. https://doi.org/10.1016/j.phytol.2020.08.004
52. Yao CS, Lin M. Bioactive stilbene dimers from *Gnetum cleitostachyum.* Nat Prod Res. 2004; 19: 443-448. DOI: 10.1080/14786410412331271041
53. Iliya I, Tanaka T, Iinuma M, Furasawa M, Ali Z, Nakaya K, Murata J. and Darnaedi D. Five Stilbene Glucosides from *Gnetum gnemonoides* and *Gnetum africanum*. Helv. Chim. Acta. 2002c; 85: 2394 – 2402. https://doi.org/10.1002/1522-2675(200208)85:8<2394::AID-HLCA2394>3.0.CO;2-6
54. Azmin NFN, Ahmat N, Zawawi NKNA. Chemical constituents from the lianas of *Gnetum cuspidatum* blume. MJAS. 2016; 20: 388–392. DOI:10.17576/mjas-2016-2002-23
55. Iliya I, Tanaka T, Furusawa M, Ali Z, Nakaya K, Iinumaa M, Shirataki Y, Murata J. and Darnaedi D. Four New Glucosides of Stilbene Oligomers from the Stem of *Gnetum gnemonoides.* Heterocycles. 2001; 55: 2123 – 2130. DOI:10.3987/COM-01-9317
56. Zhai YM, Jiang K, Qu SJ, Luo HF, Tan JJ, and Tan CH. Structurally diverse stilbene dimers from: *Gnetum montanum* Markgr.: Studies on the 1H chemical shift differences between dimeric stilbene epimers correlating to the relative configurations. RSC Advances. 2016; 6: 50083–50090. DOI: https://doi.org/10.1039/C6RA08238F
57. Chen H, Lin M. (1999). Gnetifolin L and O, Two Dimeric Stilbenes from *Gnetum Montanum.* Chin. Chem. Lett. 1999; 10(7): 579 – 582.
58. Tian LW, Lv J, Liu Y, Song L. A new dimeric stilbene from the lianas of *Gnetum parvifolium.* Nat. Prod Res. 2017; 31: 1-6. DOI: 10.1080/14786419.2017.1278591
59. Tani H, Koshino H, Tanaguchi T, Yoshimatsu M, Hikami S, and Takahashi S. Structural studies on stilbene oligomers isolated from seeds of Melinjo (*Gnetum gnemon* L.). ACS Omega. 2020; 5: 12245-12250. https://doi.org/10.1021/acsomega.0c00910
60. Ali Z, Tanaka T, Iliya I, Iinuma M, Furusawa M, Ito T, Nakaya K, Murata J, Darnaedi, D. Phenolic constituents of *Gnetum klossii*. J Nat Prod. 2003; 66: 558–560.
61. Ma YQ, Zhai YM, Deng Y, Guo L, Wan YQ, and Tan CH. (2017) Stilbeno-phenylpropanoids from *Gnetum montanum* Markgr. Phytochem. Lett. 2017; 21: 42–45. https://doi.org/10.1016/j.phytol.2017.05.025

62. Huang KS, Wang YH, Li RL, Lin M. Stilbene dimer from the lianas of *Gnetum hainanense*. Phytochem. 2000; 54: 875-881. https://doi.org/10.1016/S0031-9422(00)00151-5
63. Wang YH, Huang KS, Lin M. Four New Stilbene Dimers from the Lianas of *Gnetum Hainanense*. J Asian Nat Prod Res. 2001; 3: 169-176.
64. imoXM, Lin M, Wang YH, Liu X. Four New Stilbenoid from the lianas of *Gnetum montanum* f. megalocarpum. Planta Med. 2004; 70: 1-6. DOI: 10.1055/s-2004-815494
65. Li XM, Lin M Wang YH. Stilbenoids from the liana of *Gnetum pendulum*. J. Asian Nat. Prod. Res. 2003; 5: 113-119. https://doi.org/10.1016/S0031-9422(01)00269-2
66. Iliya I, Tanaka T, Iinumaa M, Furusawa M, Ali Z, Nakaya K, Murata J. and Darnaedi D. Four New Stilbene Oligomers in the Root of *Gnetum gnemon*. Helv. Chim. Acta. 2002d; 85: 2538–2546. https://doi.org/10.1002/1522-2675(200208)85:8<2538::AID-HLCA2538>3.0.CO;2-J
67. Boralle N, Gottlieb HE, Gottlieb OR, Kubitzki K, Lopes LMX, Yoshida M. and Young MCM. Oligostilbenoids from *Gnetum venosum*. Phytochem. 1993; 34(5): 1403-1407. https://doi.org/10.1016/0031-9422(91)80038-3
68. Cho HM, Ha TK, Pham HT, An JP, Huh J, Lee BW, Lee HJ, Oh WK. Oligostilbenes from the leaves of *Gnetum latifolium* and their biological potential to inhibit neuroinflammation. Phytochem. 2019; 165: 112044. https://doi.org/10.1016/j.phytochem.2019.05.017
69. Iliya I, Tanaka T, Ali Z, Iinumaa M, Furusawa M, Nakaya K, Shirataki Y, Murata J, Darnaedi, D, Matsuura N, and Ubukata M. Six flavonostilbenes from *Gnetum africanum* and *Gnetum gnemon*. Heterocycles. 2003b; 60: 159-166. DOI:10.3987/COM-02-9632
70. Yao CS, Lin M, Yang QY. A new resveratrol trimer derivative from *Gnetum brunonianum*. J Asian Nat Prod Res. 2012; 14(9): 918-922