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Review

Kadsura longipedunculata Finet & Gagnepain (Schisandraceae): An Overview of Botany, Traditional Uses, Phytochemistry and Pharmacological Activities

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Abstract: *Kadsura longipedunculata* Finet & Gagnepain (Chinese *Kadsura* vine) is an evergreen climbing shrub that is widely found in the southwest province of China. The plant can be used as folk medicine to cure canker sores, dysmenorrhea, traumatic injury, insomnia, rheumatoid arthritis, gastrointestinal inflammation, menstrual disorders, and feminine condition. We conducted an open-ended, online database search with the help of Baidu Scholar, CNKI, Elsevier, Scopus, ScienceDirect, Google, Pubmed, and Web of Science for all publications accessible from 1986 to 2022, using the terms related to traditional uses, botany, phytochemistry, and pharmacological properties. A total of ca. 314 phytochemicals were reviewed and identified in *K. longipedunculata*, with lignans and terpenoids as the predominant groups. The isolated compounds of this plant possess cytotoxic, antioxidant, antitumor, anti-inflammatory, anti-insomnia, anti-trypanosomal, anti-platelet aggregation, hepatoprotective, and other pharmacological effects. This review offers primary data for further research needed to determine the chemical components responsible for its pharmacological effect in order to continue its traditional use. More clinical and preclinical evidence is required to determine the rationale and safety of using *K. longipendunculata* for medicinal and food purposes.

Keywords: *Kadsura longipedunculata*; phytochemistry; pharmacology; medicinal plant

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1. Introduction

Traditional Chinese medicine has been widely acknowledged as a complementary and alternative medicine and has made a substantial contribution to treatment and prevention of numerous kinds of human illnesses for thousands of years in eastern Asian countries. As a result of the widespread use of herbal medicines, safety precautions are necessary, and TCM medication safety monitoring and risk management are increasingly essential tasks. However, the usage of other goods and confusing materials worsen the chaotic situation in clinical application. As a result, it is critical to develop a reliable method for identifying them from one another [1,2].

Kadsura longipedunculata Finet & Gagnepain is a rich source of lignans and terpenoids [3–6]. Recently, the presence of structurally diverse and interesting compounds and their biological properties have prompted many researchers to turn their attention towards *Kadsura longipedunculata* Finet & Gagnepain and identified 314 different biochemical compounds. The isolated compounds of this plant have been reported to possess antimicrobial [7,8], antioxidant [8,9], NO inhibitory Product [10], anti-trypanosomal [8], antitumor [11], anti-HIV [12,13], and cytotoxic properties [7,14]. However, their mechanism of

pharmacological action is poorly known and studied. Therefore, it is very important to investigate the relationship between the pharmacological activities and traditional uses of *K. longipedunculata*, understanding of the chemical constituents and pharmacology, and to provide new directions for further research.

The literature on *K. longipedunculata* was systematically reviewed using the numerous available online databases, including Baidu Scholar, CNKI, Elsevier, Scopus, ScienceDirect, Google, Pubmed, and Web of Science for all publications accessible from 1986 to 2022. To summarize, the scientific data on its botany, traditional uses, phytochemical and biological properties were examined, by searching the keyword "*K. longipedunculata*" individually or in combination with search literature sources.

To date, no review has been published to cover these aspects of *K. longipedunculata*, and this review will further help researchers to better understand the species, and its properties, thereby providing valuable information for further research and development of *K. longipedunculata*.

2. Botany

Kadsura longipedunculata Finet & Gagnepain [15]. Type: China, Sichuan oriental, district de Tchen-Kéou-Tin, *P.G. Fargess.n.* (holotype, P00067518!).

Synonyms: *Kadsura discigera* Finet & Gagnepain [15]; *K. omeiensis* S. F. Lan [16]; *K. peltigera* Rehder & E. H. Wilson [17].

Kadsura longipedunculata Finet & Gagnepain [15] (commonly known as Hong-mu-xiang or the Chinese *Kadsura* vine) is an evergreen shrub, scandent and woody vine that belongs to the family Schisandraceae [18]. The genus *Kadsura* Kaempf. ex Juss. [19], comprises about 17 species [20], of which eight species (four endemic) are recorded in China [21,22], and is mainly distributed in southern and south-western parts of China, as well as eastern Asian countries [23–26]. *K. longipedunculata* is one of the most common species in China, and is recorded from Zhejiang, Anhui, Sichuan, Fujian, Guizhou, Jiangsu, Guangxi, Guangdong, Hunan, Hubei, Jiangxi, and Yunnan [21]. The species is found in the hillsides of forests, or rocky slopes, along streams, at an altitude of 100–1300 (−1500) m. Flowering occurs between June and September, and fruiting between September and December [27]. Individuals of certain *Kadsura* species change sex from year to year, and the plant produces unisexual flowers (monoecious) [28,29]. Male flowers (red or yellow androecium) have a wide range of morphologies, with many different androecial forms [30], while the gynoecial (green) structure is more consistent [23,26]. The fruits have high nutritional value and are rich in vitamin C, higher fat, proteins, and dietary fiber. Furthermore, butanoic acid methyl ester is the most common compound in terms of floral odours (96.8%) [31], and chromosome number ($2n = 28$) of this species [32,33]. Previous molecular studies have reported that the genera *Kadsura* and *Schisandra* are not monophyletic [25,34]. However, the Wu et al. [35] study based on the complete plastome of *K. longipenducluata* confirmed that the genus *kadsura* is monophyletic and formed a clade with *E. heteriocilita* [25]. However, both genera share highly similar morphologic and anatomic characteristics [23,36,37]. Due to morphological similarity, *Schisandra* fruits may easily be confused with the dried fruits from *Kadsura* species [38,39]. Furthermore, stomata and other epidermal characters suggest close phylogenetic affinities of *Kadsura* and *Schisandra*, whereas *Kadsura* seems more complex than *Schisandra* on the basis of the characters of the leaf epidermis [40].

According to Flora of China [21], *K. longipedunculata* is an evergreen climbing shrub, glabrous throughout. Leaves ovate-elliptic, obovate-elliptic, blades 5–12 (–15) × 2–4.5 cm, Petiole 0.6–1.7 (–3) cm;lateral veins (4) 5–7 (–8), leaf base acute or cuneate or rarely broadly cuneate, leaf apex shortly to long acuminate, leaf margin denticulate, serrulate, or subentire, 3–8 (–10) teeth per margin. Inflorscence pedunclate, 1.2–4 (–6.4) cm, and pistillate, (1–) 3–5 (–16) cm. Flowers are borne singly in the leaf axils, when young; tepals 10–15 (–20), yellow, reddish, or pale yellow, ovate outermost, elliptic or obovate innermost, 4–7 × 3–6 mm size, male flowers tepals 10–15 (–20). Stamens 26–54. Carpels 20–58,

1–1.6 (–2.1) × 0.8–1.4 mm. Peduncle 2.5–9.5 cm; apocarps 6.5–11 (–15) × 4.5–6.5 (–11) mm, purple, red, or rarely black. Seeds 1–3 per apocarp, 3.5–4.5 × 4.5–6 mm (Figure 1).

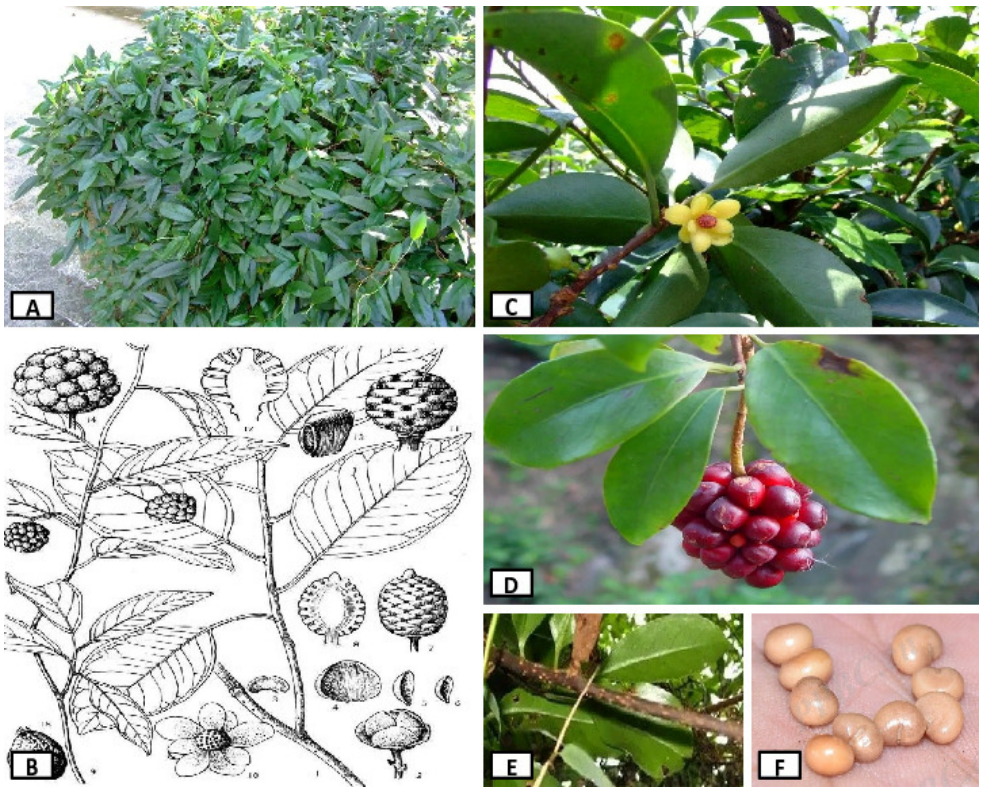


Figure 1. The entire *K. longipenduculate* plant (**A**), all plant characteristic (**B**), flower (**C**), fruit (**D**), stem (**E**), and seed (**F**).

3. Traditional Uses

Kadsura longipedunculata (Chinese *Kadsura* vine) has been used as folk medicine, with a long history, and is recorded in the folk record and official Pharmacopoeia [41–45]. The rootsof the whole plant are used to activate blood and resolve stasis, promote *qi* circulation to relieve pain, dispel wind, and eliminate dampness [46–49]. The roots and stems of *K. longipedunculata* are effective in curing insomnia, rheumatoid arthritis, gastric, duodenal ulcers (gastrointestinal inflammation), dysmenorrhea, traumatic injury, canker sores, menstrual irregularities, and feminine disorders [8,13,50–54], while the fruits are consumed locally [55], or used to produce fragrant oils [19,56] as well also considered to be aphrodisiac, pectoral, and referred to by the Chinese as "Tonic Yin medicine" [57].

In China, the plant extracts of *K. longipedunculata* root and stem are used as analgesics and to treat hepatitis, rheumatism, gastroenteritis, insomnia, and malaria as well as cancer treatment [23,52–54,58–60]. The roots, leaves, and fruit of *K. longipedunculata* are used to make fragrant oils, and the stems have also been used to make rope [23,56]. Lin et al. [27] reported that nigranoic acid and kadsuric acid extracted from *K. longipedunculat* prevented stomach mucosal sores caused by absolute alcohol, indomethacin, and stress. The plant also possesses free radical scavenging activity [61]. The fruits of various species, including *K. coccinea*, *K. longipedunculata*, and *K. oblongifolia* in China, are eaten locally despite their lack of economic value [62]. However, due to similar fruit morphology and taste, the fruits of *Kadsura* species from various geographic regions have been treated as the medicinal "Lengfanteng" [63].

4. Phytochemistry

Phytochemicals are secondary metabolites produced by higher plants and have important roles in plants for preservation under stress conditions, defense against herbivores, attracting pollinators, and their bioactivities for humans are also significant. Isolation and detection of phytoconstituents are critical steps in discovering effective natural drugs. Researchers have discovered over 307 natural products in *K. longipedunculata* so far (including lignans, triterpenoids, sesquiterpenoids, flavonoids, and others). Of which, lignans (**1**–**139**) and terpenoids (**140**–**192**) were the two most prevalent types. These biochemical constituents are summarized herein.

4.1. Lignans

The major chemical components of *K. longipedunculata* are lignans and their derivatives and are classified into four groups based on their skeleton types: dibenzocyclooctadiene, diarylbutanes, spirobenzofuranoiddibenzocyclooctadienes, aryltetralins, and tetrahydrofurans and other novel lignans.

Dibenzocysclooctadienes: The compounds reported in this class are distinguished from otherson the basis of the attached methoxy, angeloyl, acetyl, butyryl, cinnamoyl, tigloyl, propanoyl, and benzoyl group substituents in thedibenzocyclooctadiene lignan basic skeleton. Most compounds included methoxy and hydroxyl groups at C-13 or C-1-3, whereas substituents such as angeloyl, acetyl, butyryl, cinnamoyl, tigloyl, propanoyl, and benzoyl groups were discovered at C-6 or C-9. In this group, 83 different compounds (**1**–**83**) have been reported (Table 1). These included gomisin M1 (**1**) [64], gomisin M2 (**2**) [65], and gomisin H (**3**) [66]. Li et al. [67] identified binankadsurin A (**4**), acetylbinankadsurin A (**5**), isobutyroyalbinankadsurin A (**6**), isovaleroylbinankadsurin A (**7**), and benzoylbinankadsurin A (**8**) from EtOH stem extract of *K. Longpeduncluata*. Schisantherin (**9**) [67], schizandrin (**10**) [66], schisantherin J (**11**) [68], Schizanrin D (**12**) [67], Angeloylgomisin M (**13**) [64], intermedin A (**14**) [69], kadsurarin (**15**) [64,67,70,71], kadsutherin A (**16**) [68], kadsuphilol T (**17**) [72], kadsuphilol B (**18**) [72], kadsuphilol P (**19**) [72], butyrylbinankadsurin A (**20**) [67], kadsuralignan A (**21**) [12], longipedunculatin D (**22**) [4], kadlongilignan G (**23**) [73], kadlongilignan E (**24**) [73], kadsuralignan B (**25**) [12], kadsuralignan C (**26**) [13], schiarisanrin D (**27**) [72], R(+)-schisandrin C (**28**) [74], otobaphenol (**29**) [13], schisanhenol (**30**) [75], schisanhenolA (**31**) [65], schisanhenol B (**32**) [65], schisandrol (**33**) [65], angeloylgomisin H (**34**) [65], schisanhenol (**35**) [65], schisantherin B (**36**) [65], tiglomisin P (**37**) [65], kadsulignan C (**38**) [67], kadsulignan D (**39**) [67], Kadsulignan H (**40**) [67], angeloylbinankadsurin A (**41**) [67], Kadsulignan J (**42**) [67], KadsulignanK (**43**) [67], deoxyschizandrin (**44**) [52], Kadsutherin D (**45**) [75], benzoylgomisin Q (**46**) [51], kadsuphin J (**47**) [73], and (7S,8R,8S)-4,4,9-trihydroxy-3,3,5-trimethoxy-9-O-B-D-xylopryranosyl-2,7-cyclo-lignan (**48**) [76] (Table 1). Liu et al. [72] identified five newdibenzocyclooctadiene lignans, which includes longipedlignan A (**49**), longipedlignan B (**50**), longipedlignan C (**51**), longipedlignan D (**52**), and longipedlignan E (**53**) from 95% ethanol extracts of *K. longipedunculata* dried roots. Similarly, Liu et al. [5] identified longipedlignan K (**54**), longipedlignan L (**55**), longipedlignan M (**56**), longipedlignan N (**57**), longipedlignans O (**58**), longipedlignan P (**59**), longipedlignan Q (**60**), and longipedlignan R (**61**). Similarly, Liu and Huang [77] also reported Kadsulignan E (**62**), Kadsulignan F (**63**), and Kadsulignan G (**64**) from ether extract of the root bark of *K. longipedunculata*,with benzoxyl, acetoxyl, and two methyls substitutes ring. Sun et al. [12] isolated five compounds fromEtOH root and stem extracts of *K. longipedunculata*, which includeslongipedunin A (**65**), longipedunin B (**66**), longipedunin C (**67**), kadsuranin (**68**), benzoylgomisin Q (**69**), longipedunin D (**70**) [12,77], and Renchangianin A-B (**71**–**72**) [12,77]. Qi et al. [10] also reported four secodibenzocyclooctadiene lignans identified as Kadlongilignan A (**73**), Kadlongilignan B (**74**), Kadlongilignan C (**75**), and Kadlongilignan D (**76**) from root extracts of *K. longipedunculata*. Tan et al. [64] reported five new dibenzocyclooctadiene lignans extracted from the ethereal stem and root extracts of *K. longipedunculata*, which included R(+)-wuweizisu C (**77**), R(+)-gomisin M1 (**1**), R(+)-angeloylgomisin M1 (**78**) and angeloylgomisin R (**79**),

angeloylgomisin H (**80**), angeloylbinankadsurin R (**81**) [67], deacetyldeangeloyl-kadsurarin (**82**) [67], and isobutyroylbinankadsurin A (**83**) [67].

Table 1. Lignans isolated from *Kadsura longipenduculata*.

No.	Types	Compounds	References
	Dibenzocyclooctadienes		
1		R(+)-gomisin M	[64]
2		Gomisin M2	[65]
3		Gomisin H	[66]
4		Binankadsurin A	[67]
5		Acetyl-binankadsurin A	[12,67]
6		Isobutyroyalbinankadsurin A	[67]
7		Isovaleroylbinankadsurin A	[67]
8		Benzoylbinankadsurin A	[12,67]
9		Schisantherin	[67]
10		Schizandrin	[66]
11		Schisantherin J	[68]
12		Schizanrin D	[67]
13		Angeloylgomisin M	[64]
14		Intermedin A	[69]
15		Kadsurarin	[64,67,70,71]
16		Kadsutherin A	[68]
17		Kadsuphilol T	[72]
18		Kadsuphilol B	[72]
19		Kadsuphilol P	[72]
20		Butyrylbinankadsurin A	[67]
21		Kadsuralignan A	[12]
22		Longipedunculatin D	[4]
23		Kadlongilignan G	[73]
24		Kadlongilignan E	[73]
25		Kadsuralignan B	[12]
26		Kadsuralignan C	[13]
27		Schiarisanrin D	[72]
28		R(+)-schisandrin C	[74]
29		Otobaphenol	[13]
30		Schisanhenol	[75]
31		Schisanhenol A	[65]
32		Schisanhenol B	[65]
33		Schisandrol	[65]
34		Angeloylgomisin H	[65]
35		Schisantherin A	[65]
36		Schisantherin B	[65]
37		Tiglomisin P	[65]
38		Kadsulignan C	[67]
39		Kadsulignan D	[67]
40		Kadsulignan H	[67]
41		Angeloylbinankadsurin A	[67]
42		Kadsulignan J	[67]
43		Kadsulignan K	[67]
44		Deoxyschizandrin	[52]
45		Kadsutherin D	[75]
46		Benzoylgomisin Q	[51]
47		Kadsuphilin J	[73]
48		(7′S,8R,8′S′)-4,4′,9-trihydroxy-3,3′,5-trimethoxy-9′-O-B-D-xylopryranosyl-2,7′-cyclo-lignan	[76]
49		Longipedlignan A	[12,72]
50		Longipedlignan B	[12,72]
51		Longipedlignan C	[12,72]
52		Longipedlignan D	[72]

Table 1. *Cont.*

No.	Types	Compounds	References
53		Longipedlignan E	[72]
54		Longipedlignan K	[5]
55		Longipedlignan L	[5]
56		Longipedlignan M	[5]
57		Longipedlignan N	[5]
58		Longipedlignan O	[5]
59		Longipedlignan P	[5]
60		Longipedlignan Q	[5]
61		Longipedlignan R	[5]
62		Kadsulignan E	[75]
63		Kadsulignan F	[75]
64		Kadsulignan G	[75]
65		Longipedunin A	[12]
66		Longipedunin B	[12]
67		Longipedunin C	[12,64]
68		Kadsuranin	[12,64]
69		Benzoylgomisin Q	[10,12]
70		Longipedunin D	[12,77]
71		Renchangianin A	[12,77]
72		Renchangianin B	[12,77]
73		Kadlongilignan A	[10]
74		Kadlongilignan B	[10]
75		Kadlongilignan C	[10]
76		Kadlongilignan D	[10]
77		R(+)-wuweizisu C	[64]
78		R(+)-angeloylgomisin M1	[64]
79		Angeloylgomisin R	[3,64]
80		Angeloylgomisin H	[64]
81		Angeloylbinankadsurin R	[67]
82		Deacetyldeangeloyl-kadsurarin	[67]
83		Isobutyroylbinankadsurin A	[67]
	SpirobenzofuranoidDibenzocyclooctadienes		
84		Schiarianrin E	[78]
85		Schiarisanrin A	[78]
86		Isovaleroyloxokadsurane	[67]
87		Kadsulignan C	[67]
88		Kadsulignan G	[75]
89		Heteroclitin D	[72]
90		Heteroclitin H	[72]
91		HeteroclitinIa	[72]
92		Schiarisanrin B	[72,78]
93		Heteroclitin J	[5,13]
94		Benzoyl-oxo-kadsuraol	[73]
95		Propoxyl-oxo kadsuraol	[73]
96		Kadsutherin C	[73]
97		Heteroclitin E	[73]
98		Heteroclitin P	[72,79]
99		HeteroclitinIb	[13,72]
	Aryltetralins		
100		Otobaphenol	[5,13,75]
101		Arisantetralone A	[5,52,75]
102		Arisantetralone B	[5,52,75]
103		Arisantetralone C	[5,52,75]
104		Arisantetralone D	[5,52,75]
105		Kadsulignan I	[72]

Table 1. *Cont.*

No.	Types	Compounds	References
	Diarylbutanes		
106		Meso-dihydroguaiaretic acid	[52,67,77]
107		(+)-anwulignan	[52,75]
108		Dihydroguaiaretic acid	[52]
109		Monomethyl dihydroguaiaretic acid	[52]
110		Saururenin	[52]
111		Isoanwulignan	[52]
112		4-[4-(3,4-dime-thoxyphenol)-2,3-dimethyl-butyl]-2-methoxy-phenol	[13]
113		3-methoxy-3′,4′-(methylenedioxy)-9,9′-epoxylignan-4,7′-diol	[55]
114		Kadsuphilin J	[73]
	Tetrahydrofurans		
115		Grandisin	[13]
116		Kadlongirin A	[13]
117		Kadlongirin B	[13]
118		Fragrasin B_1	[13]
119		Zuihonin A	[13,52]
120		Kadlongilignan F	[73]
121		Kadlongilignan G	[73]
122		Kadsuraol A	[80]
123		Kadsuraol B	[80]
124		Kadsuraol C	[80]
125		Kadlongilignan I	[80]
126		Kadlongilignan J	[80]
127		Kadlongilignan H	[80]
128		Longipedlignan F	[5,72]
129		Longipedlignan G	[5,72]
130		Longipedlignan H	[5,72]
131		Longipedlignan I	[5,72]
132		Longipedlignan J	[5,72]
133		Longipedunculatin A	[5]
134		Longipedunculatin B	[5]
135		Longipedunculatin C	[5]
	Other Novel Lignans		
136	Neolignan glycosides	7S,8R-erthro-4,7,9,9′-tetrahydroxy-3,3′-dimethoxy-8-O-4′-neolignan	[76]
137	SpirodienoneSesquineolignan	Pinobatol	[76]
138	Sesquineolignan	Leptolepisol B	[76]
139	Cyclolignans	Austrobalignans	[76]
140		vladirol F	[13]
141		4-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-phenol	[13]
142		Pregmomisin	[51]
143		Tigloylgomisin P	[65]
144		Schiarisanrin C	[72]
145		Schiarisanrin B	[72]
146		Isolariciresinol-9-O-β-D-xyloside	[77]
147		(-)-gallocatechi	[77]
148		9-O-benzoyloxokadsuranol	[72]

SpirobenzofuranoidDibenzocyclooctadienes: 53 spirobenzofuranoiddibenzocyclooctadienes compounds were extracted from the genus *Kadsura*. The majority of them was found in *K. longipenduculata* and exhibited significant taxonomic importance [79]. The following 16 spirobenzofuranoiddibenzocyclooctadienes were found in *K. longipedunculata*, including: schiarianrin E (**84**) [78], schiarisanrin A (**85**) [78], isovaleroyloxokadsurane (**86**) [67], kadsulignan C (**87**) [67], Kadsulignan G (**88**) [75], heteroclitin D (**89**) [72], heteroclitin H (**90**) [72], heteroclitinIa (**91**) [72], schiarisanrin B (**92**) [72,78], heteroclitin J (**93**) [5,13], benzoyl-oxo-kadsuraol (**94**) [73], propoxyl-oxo kadsuraol (**95**) [73], kadsutherin C (**96**) [73], heteroclitin E (**97**) [73], heteroclitin P (**98**) [72,79], and heteroclitin Ib (**99**) [13,72].

Aryltetralins: Six compounds with the same nuclear structure were included in this category, namely, otobaphenol (**100**) [5,13,75], arisantetralone A (**101**) [5,52,75], arisantetralone B (**102**) [5,52,75], arisantetralone C (**103**) [5,52,75], arisantetralone D (**104**) [5,52,75], andkadsulignan I (**105**) [72].

Diarylbutanes: Nine diarylbutane-type lignans were discovered in *K. longipedunculata*. Extensive phytochemical research was conducted on *K. longipedunculata* roots and stems extracts collected from various locations that led to the isolation of mesodihydroguaiaretic acid (**106**) [52,67,77], (+)-anwulignan (**107**) [52,75], dihydroguaiaretic acid (**108**) [52], monomethyl dihydroguaiaretic acid (**109**) [52], saururenin (**110**) [52], isoanwulignan (**111**) [52], 4-[4(3,4-dime-thoxyphenol)2,3-dimethyl-butyl]2-methoxy-phenol (**112**) [13], 3-methoxy-3,4(methylenedioxy)9,9-epoxylignan-4,7diol (**113**) [55], and kadsuphilin J (**114**) [73].

Tetrahydrofurans: Pu et al. [13] identified grandisin (**115**), kadlongirin A (**116**), kadlongirin B (**117**), fragrasin B_1 (**118**), and zuihonin A (**119**) from 70% aqueous Me2CO leaves and stem extract of *K. longipeduculata*. Shao et al. [73] isolated three tetrahydrofurans lignans from 95% aqueous ethanol root extract of *K. longipedunculata*, which included Kadlongilignan F (**120**) and Kadlongilignan G (**121**). Wang et al. [80] identified three new tetrahydrocyclobutaphenanthrofuranone-type lignans, named: kadsuraol A (**122**), kadsuraol B (**123**), kadsuraol C (**124**), Kadlongilignan I (**125**), Kadlongilignan J (**126**), andKadlongilignan H (**127**). Liu et al. [5] reported five new tetrahydrobenzocyclooctabenzofuranone Lignans, which includedlongipedlignan F (**128**), longipedlignan G (**129**), longipedlignan H (**130**), longipedlignan I (**131**), and longipedlignan J (**132**), longipedunculatin A–C (**133**–**135**) from the roots of *K. longipedunculata*.

Others Lignans: Other compounds such as spirodienonesesquineolignan, sesquineolignan, cyclolignans, and neolignan glycosides were also reported from this plant (Table 1), including 7S,8R-erthro-4,7,9,9-tetrahydroxy-3,3-dimethoxy-8-O-4-neolignan (**136**) [76], pinobatol (spirodienonesesquineolignan) (**137**) [76], leptolepisol B (sesquineolignan) (**138**) [76], austrobalignans (cyclolignans) (**139**) [76], vladirol F (**140**) [13], 4-[4(3,4-dimethoxyphenyl)2,3-dimethylbutyl]2-methoxy-phenol (**141**) [13], Pregmomisin (**142**) [51], tigloylgomisin P (**143**) [65], schiarisanrin C (**144**) [72], schiarisanrin B (**145**) [72], isolariciresinol-9-O-β-D-xyloside (**146**) [77], (-)-gallocatechi (**147**) [77], and 9-O-benzoyloxokadsuranol (**148**) [72].

4.2. Triterpenoid

A triterpenoid is a sort of distinctive component in *Kadsura* and has produced a number of triterpenoids with various structures that are highly oxygenated. There are numerous distinct structural types, and classifications of triterpenoids are as follows.

Lanostane

Intact lanostanetriterpeniods: This class of compounds has the same skeleton as well as the same tetracyclic core structure. Four new triterpenoids including epianwuweizic acid (**149**) [67], (24Z)3-oxo-12α-acyetoxylanosta-8,24-dien-26-oic acid (**150**) [6], (24Z)3-oxo-12α-ahydroxylanosta-8,24-dien-26-oic acid (**151**) [6], and (24Z)3-oxo-lanosta-8,24-dien-26-oic acid (**152**) [75] were extracted from *K. longipeducalata* roots (Table 2).

Table 2. Terpenoids isolated from *Kadsura longipenduculata*.

No.	Group	Category	Compounds	References
	Lanostane	Intact Lanostane		
149			Epianwuweizic acid	[67]
150			(24Z)-3-oxo-12α-acyetoxylanosta-8,24-dien-26-oic acid	[6]
151			(24Z)-3-oxo-12α-ahydroxylanosta-8,24-dien-26-oic acid	[6]
152			(24Z)-3-oxo-lanosta-8,24-dien-26-oic acid	[75]
		14(13–12)-abe-lanostanes		
153			Neokadsuranic acid A	[6]
154			Neokadsuranic acid B	[6]
155			Neokadsuranic acid C	[6]
156			Seco-neokadsuranic acid A	[6]
		3,4-Seco-lenostane		
157			Schisanlactone F	[68]
	Cycloartane-type triterpenoids	Intact cycloartene		
158			Isoschizandrolic acid	[77]
159			Schisandraflorin	[77]
160			24-methylenecycloartenone	[77]
161			Kadsulactone	[81,82]
		3,4-Seco-cycloartene		
162			Kadsudilactone	[81]
163			Kadsudilactone A	[12]
164			Kadsulactone acid	[83]
165			Changnanic acid	[67]
166			Nigranoic acid	[27]
167			Schisanlactone E	[14,84]
168			Schisanlactone A	[14]
		14(13–12)-abeo-cycloartanes		
169			Longipedlactone A	[4,73]
170			Longipedlactone B	[4,73]
171			Longipedlactone C	[4,73]
172			Longipedlactone D	[4]
173			Longipedlactone E	[4]
174			Longipedlactone F	[4]
175			Longipedlactone G	[4]
176			Longipedlactone H	[4]
177			Longipedlactone I	[4]
	Kadlongilactone-type triterpenoids			
178			Kadlongilactone A	[3,14,73,85]
179			Kadlongilactone B	[3,14,73,85]
180			Kadlongilactone C	[14,73]
181			Kadlongilactone D	[14,73,85]
182			Kadlongilactone E	[14,73]
183			Kadlongilactone F	[14,73]
	Schiartane-type triterpenoids			
184			Micrandilactone I	[73,86]
185			Micrandilactone J	[73,86]
186			22,23-Di-epi-micrandilactone J	[86]
187			Schilancitrilactone A	[87]
188			Schilancitrilactone B	[87]
189			Schilancitrilactone C	[87]
190			Wuweizidilactone P	[87]
191			Arisanlactone A	[87]
192			Propindilactone H	[87]

Table 2. *Cont.*

No.	Group	Category	Compounds	References
193			Micandilactone H	[87]
194			Lanocolides A	[87]
195			Lanocolides B	[87]
196			Lanocolides C	[87]
197			Lanocolides D	[87]
198			Preschisanartanin O	[87]
199			Lancifornin A	[87]
200			Schicagenin A	[87]
201			Rubrifloradilactone C	[87]
202			Wilsonianadilacone A	[87]

14(13–12)-abe-lanostanes: Four14(13–12)-abe-lanostanescompounds, such as Neokadsuranic acid A–C (**153**–**155**), andseco-neokadSsuranic acid A (**156**), were extracted from *K. longipedunculata* [6].

3,4-Seco-lenostane: One seco-lenostane, Schisanlactone F (**157**) is reported in this group, that was extracted from roots of *K. longipedunculata* [68].

Cycloartane-type triterpenoids

Intact cycloartene: This type of category contained a ketone or a hydroxyl group present at C-3. Isoschizandrolic acid (**158**) [77] was extracted from an unidentified *Kadsura* species. Three compounds, including schisandraflorin (**159**) [77], 24-methylenecycloartenone (**160**) [77], and kadsulactone (**161**) [81,82] were extracted from *K. longipedunculata* [77,81,82].

3,4-Seco-cycloartene: This genus was rich in 3,4-Seco-cycloartanes, and 38 triterpenoids have been reported so far. Extensive phytochemical research was conducted on *K. longipedunculata* roots and stem extracts collected from various locations resulted in the isolation of six compounds, which includes kadsudilactone(**162**) [81], schisanlactone A (**163**) [12], kadsudilactone A (**164**) [83], kadsulactone acid (**165**) [67], changnanic acid (**166**) [27], andnigranoic acid (**167**) [14,84]. Pu et al. [14] identified schisanlactone E (**168**) from the leaves and stem of *K. longpedunculata*.

14(13–12)-abeo-cycloartanes: Nine new typesofabeo-cycloartanetrioterpendoids from *K. longipeduncluata* leaves and stems have been identified. The following are 14(13–12)-abeo-cycloartanes, such as longipedlactone A (**169**) [4,73], longipedlactone B (**170**) [4,73], longipedlactone C (**171**) [4,73], longipedlactone D (**172**) [4], longipedlactone E (**173**) [4], longipedlactone F (**174**) [4], longipedlactone G (**175**) [4], longipedlactone H (**176**) [4], and longipedlactone I (**177**) [4].

Nortriterpenoids: This class of compound has not been reported in *K. longipedunculata.* However, one norcycloartane triterpenoid, micranoic acid B, was isolated from *K. angustifolia*, which is an octanor-triterpenoid [88].

Kadlongilactone-type triterpenoids: 11 different kadlongilactone-type triterpenoids were extracted from different species of *Kadsura*. However, six kadlongilactone-type triterpenoids, such as kadlongilactone A (**178**) [3,73,85], kadlongilactone B (**179**) [3,73,85], kadlongilactone C (**180**) [73], kadlongilactone D (**181**) [73,85], kadlongilactone E (**182**) [73], and kadlongilactone F (**183**) [73] were isolated from 95% aqueous ethanol root extract of *K. longipedunculata* [3,73,88]. Pu et al. [14] also reported oxygenated triterpenoids with unique skeletons from leaves and stems of *K. longipedunculate* and were identified as kadlongilactone A (**183**) and Kadlongilactone C–F (**179**–**183**).

Schiartane-type triterpenoids: Phytochemical studies reported 19 different compounds from *K. longipendculata* have isolated and identified asmicandilactone I (**184**) [73,86], micandilactone J (**185**) [73,86], 22,23-Di-epi-micrandilactone J (**186**) [86], schilancitrilactone A (**187**) [87], schilancitrilactone B (**188**) [87], schilancitrilactone C (**189**) [87], wuweizidilactone P (**190**) [87], arisanlactone A (**191**) [87], propindilactone H (**192**) [87], Micandilactone H (**193**) [87], lanocolides Ab (**194**) [87], lanocolides B (**195**) [87], lanocolides C (**196**) [87], lanocolides D (**197**) [87], preschisanartanin O (**198**) [87], Lancifornin A (**199**) [87], Schicagenin A (**200**) [87], rubrifloradilactone C (**201**) [87], and wilsonianadilacone A (**202**) [87].

Other novel terpenoids: 100 (**203**–**315**) other chemical constituents were identified from *K. longipendunculata* including mono- and oxygenated terpenoids, sesquiterpenoids and oxygenated sesquiterpene, cadinane-type, and non-terpene compounds (Table 3). Do et al. [88] isolated 33 sesquiterpenoids and cadinane-type compounds from *K. longipeduncluata* and the result showed that α-muurolol (43.5%) (**203**) was the major sesquiterpenoid along with other minor ones such as α-cadinol (5.4%) (**204**), β-caryophyllene (5.4%) (**205**), and δ-cadinene (5.0%) (**221**). Pu et al. [89] identified seven known compounds, including bsitosterol (**238**), daucosterol (**239**), schizandronic acid (**240**), parkeol (**241**), licarin A (**242**), mangiferolic acid (**243**), and schizandriside (**244**) from the AcOEt extract of *K. longipedunculata*. There were three other triterpenoids including Quercetin-3-O-rhamnoside (**245**), protocatechuic acid (**246**), and 2, 7-di-hyrdroxy-11,12-dehydrocalamenene (**247**) isolated from *K. longipendculata* [90]. Thanh et al. [91] isolated 17 compounds from roots of *K. longipeduncluata* such as α-pinen (**248**), Camphen (**249**), P-cymen (**250**), limonen (**251**), borneol (**252**), terpenolin-4-ol (**253**), bornyl axetat (**254**), α-cubeben (**255**), α-Copaen (**256**), β-cubeben (**257**), α-bergamoten (**258**), aromadendren (**259**), α-amorphen (**260**), epi-bicyclophellandren (**261**), β-gurjunen (**262**), caryophyllenoxit (**263**), and acorenol B (**264**). Mulyaningsih et al. [8] reported 50 monoterpenoids, oxygenated, sesquiterpene, and oxygenated sesquiterpene compounds from *K. longipedunculata* stem extract, such as tricycline (**265**), α-Thujene (**266**), α-Pinene (**267**), camphene (**268**), β-Pinene (**269**), β-Myrcene (**270**), α-Terpinene (**271**), p-Cymene (**272**), limonene (**273**), δ-Terpinene (**274**), terpinolene (**275**), 1,8-Cineole (**276**), camphor (**277**), borneol (**278**), terpinen-4-ol (**279**), α-Tepineo (**280**), bornyl acetate (**281**), δ-Elemene (**282**), α-Copaene (**283**), β-Elemene (**284**), α-Gurjunene (**285**), β-Caryophyllene (**286**), β-Copaene (**287**), +)-Aromadendrene (**288**), α-Humulene (**289**), allo-Aromadendrene (**290**), β-Chamigrene (**291**), germacrene D (**292**), δ-Muurolene (**293**), β-Selinene (**294**), epi-Bicyclosesquiphellandrene (**295**), viridiflorene (**296**), calamenene (**297**), δ-Cadinene (**298**), α-Calacorene (**299**), cadina-1,4-diene (**300**), cadala-1(10),3,8-triene (**301**), α-Calacorene (**302**), spathulenol (**303**), viridiflorol (**304**), trans-Nerolidol (**305**), β-Caryophyllene oxide (**306**), cubenol (**307**), α-Bisabolol (**308**), cadalene (**309**), γ-Muurolol (**310**), δ-Cadinol (**301**), γ-Cadinol (**312**), and bicyclol (**313**). Furthermore, 7-ketocholesterol (**314**) and 5ct-cholest-8(14)-en-3f3-01-l5one (**315**) were reported from *K. longipedunculata* [92,93] (Table 3).

Table 3. Other novel terpenoids isolated from *Kadsura longipenduculata*.

No.	Compounds	References
203	α-muurolol	[88]
204	α-cadinol	[88]
205	β-caryophyllene	[88]
206	α-Terpineol	[88]
207	α-Copaene	[88]
208	β-Elemene	[88]
209	cis-α-Bergamotene	[88]
210	β-Caryophylene	[88]
211	trans-α-Bergamotene	[88]
212	cis-Muurola-3,5-diene	[88]
213	α-Humulene	[88]
214	cis-Muurola-4(14),5-diene	[88]
215	δ-Muurolene	[88]
216	Germacrene D	[88]
217	β-Selinene	[88]
218	Viridiflorene	[88]
219	cis-Cadina-1,4-diene	[88]
220	β-Bisabolene	[88]
221	δ-Cadinene	[88]
222	Zonarene	[88]

Table 3. *Cont.*

No.	Compounds	References
223	trans-Cadina-1(6), 4-diene	[88]
224	Caryophyllenyl alcohol	[88]
225	Caryophyllene oxide	[88]
226	Spathulenol	[88]
227	Humulene Epoxide II	[88]
228	Caryophyllene oxide	[88]
229	epi-Cubenol	[88]
230	10-diepi-Cubenol	[88]
231	Caryophylla-3(15), (7(14)-dien-6-ol e	[88]
232	Cadalene	[88]
233	Eudesma-4(15), 7-dien-1-ol	[88]
234	epi-α-Bisabolol	[88]
235	1,2-Benzenedicarboxylic acid	[88]
236	9-(b-d-glucopyranosyloxy)-3′-methoxy-3,4-(methylenedioxy)-7,9′-epoxylignan-4′-ol	[88]
237	3-methoxy-3′,4′-(methylenedioxy)-9,9′-epoxylignan-4,7′-diol	
238	Bsitosterol	[89]
239	Daucosterol	[89]
240	Schizandronic acid	[89]
241	Parkeol	[89]
242	Licarin A	[89]
243	Mangiferolic acid	[89]
244	Schizandriside	[89]
245	Quercetin-3-O-rhamnoside	[90]
246	Protocatechuic acid	[90]
247	2, 7-di-hyrdroxy-11,12-dehydrocalamenene	[90]
248	α-pinen	[90]
249	Camphen	[91]
250	P-cymen	[91]
251	Limonen	[91]
252	Borneol	[91]
253	Terpenolin-4-ol	[91]
254	Bornyl axetat	[91]
255	α-cubeben	[91]
256	α-Copaen	[91]
257	β-cubeben	[91]
258	α-bergamoten	[91]
259	Aromadendren	[91]
260	α-amorphen	[91]
261	Epi-bicyclophellandren	[91]
262	β-gurjunen	[91]
263	Caryophyllenoxit	[91]
264	Acorenol B	[91]
265	Tricycline	[8]
266	α-Thujene	[8]
267	α-Pinene	[8]
268	Camphene	[8]
269	β-Pinene	[8]
270	β-Myrcene	[8]
271	α-Terpinene	[8]
272	P-Cymene	[8]
273	Limonene	[8]
274	δ-Terpinene	[8]
275	Terpinolene	[8]
276	1,8-Cineole	[8]
277	Camphor	[8]
278	Borneol	[8]

Table 3. *Cont.*

No.	Compounds	References
279	Terpinen-4-ol	[8]
280	α-Tepineo	[8]
281	Bornyl acetate	[8]
282	δ-Elemene	[8]
283	α-Copaene	[8]
284	β-Elemene	[8]
285	α-Gurjunene	[8]
286	β-Caryophyllene	[8]
287	β-Copaene	[8]
288	+)-Aromadendrene	[8]
289	α-Humulene	[8]
290	allo-Aromadendrene	[8]
291	β-Chamigrene	[8]
292	Germacrene D	[8]
293	δ-Muurolene	[8]
294	β-Selinene	[8]
295	epi-Bicyclosesquiphellandrene	[8]
296	Viridiflorene	[8]
297	Calamenene	[8]
298	δ-Cadinene	[8]
299	α-Calacorene	[8]
300	Cadina-1,4-diene	[8]
301	Cadala-1(10),3,8-triene	[8]
302	α-Calacorene	[8]
303	Spathulenol	[8]
304	Viridiflorol	[8]
305	trans-Nerolidol	[8]
306	β-Caryophyllene oxide	[8]
307	Cubenol	[8]
308	α-Bisabolol	[8]
309	Cadalene	[8]
310	γ-Muurolol	[8]
311	δ-Cadinol	[8]
312	γ-Cadinol	[8]
313	Bicyclol	[8]
314	7-ketocholesterol	[92,93]
315	5ct-cholest-8(14)-en-3f3-01-l5one	[92,93]

5. Pharmacological Activities

Compounds isolated from *K. longipedunculata* have been investigated by various researchers. Several in vitro experiments have been conducted on *Kadsura* species against various activities. Of which, anti-viral and cytotoxic activity are the main bioactivity evaluations, followed by hepatoprotective activity, anti-inflammatory, antioxidant, and other pharmacological activities that have also been assessed (Table 4). Aerial parts, such as ethanolic extracts of leaves, roots, and fruits of *K. longipedunculata*, were used in the majority of the experiments.

Table 4. Validated pharmacological uses of *K. longipenduculata*.

Properties	Compounds	Observations	Ref.
Hepatoprotective effects	Longipedlignans F and G	N-acetyl-p-aminophenol-induced toxicity in HepG2 cells with cell survival rates at 10 μM of 52.2% and 50.2%	[5]
Hepatoprotective effects	Micrandilactone I	APAP-induced toxicity in HepG2 cells, with cell survival rates of 53.04%	[73]
Hepatoprotective effects	22,23-di-epi-micrandilactone J and micrandilactone I	APAP-induced toxicity in HepG2 cells, with cell survival rates of 53.0% and 50.2%	[86]
Hepatoprotective effects	Kadsurol C	N-acetyl-paminophenol (APAP)-induced toxicity in HepG2 cells, with a cell survival rate of 48.22 %	[80]
NO production	Longipedunculatin B, M and R	In vitroinhibitory effects on nitric oxide production assays, with inhibition rates of 55.1%, 74.9%, and 89.8%	[5]
Hepatoprotective effects	Longipedlignan M	N-acetyl-p-aminophenol induced toxicity in HepG2 cells, with a cell survival rate of 50.8%	[5]
Cytototoxic effects	Kadlongilactone A and E	HT-29, A549, and K562 cell lines, with IC_{50} values of 0.49–3.61 μ Minvitro	[14]
Cytototoxic effects	Kadlongilactone A and B	Human tumor K562 cells, with IC_{50} values of 1.40 and 1.71 μg/mL	[3]
Cytototoxic effects	Camphene and Borneol	HepG-2, MIAPaCa-2, and SW-480 cell lines with IC_{50} values of 133.53, 136.96, and 136.62 μg/mL	[8]
Cytototoxic effects	Essential oils	HepG2 cells lines, with an IC_{50} value of 147 μg/mL	[7]
Anti-microbial effects	Essential oils	Gram-positive bacteria (*S. aureus* and *B. subtilis*) with inhibition zones of 28.91 mm	[7]
Anti-microbial effects	Camphene and Borneol	Antimicrobial effect with inhibition zones in the range of 6.7–11.0 mm	[8]
Anti-viral effects	Longipedunin A and Schisanlactone A	HIV-1 protease, with IC_{50} values of 50 and 20 μM	[12]
Anti-viral effects	Kadlongirin A and 2,7-dihydroxy-11,12-dehydrocalamenene	HIV-1 in C8166 cells, EC_{50} 2.03 μg/mL and CC_{50} 1146.08 μg/mL	[13]
Anti-viral effects	Kadlongirin B	HIV-1 activity, with an EC_{50} value of 16.0 μg/mL, and therapeutic index (TI) value of 6.7	[13]
Anti-tumor effects	Bicyclol	Enhance impaired liver function, prevent HBV replication in chronic hepatitis B patients, and induce differentiation of human hepatocarcinoma cells (HepG2 and Bel-7402 cells) with no side effects	[94]
Anti-tumor effects	Kadsulignan H, I, and J	Leukemia P-388 cells in vitro, with IC_{50} values of 40, 10, and 10 μg/mL	[95]
NO production effects	Kadlongilignan C and D	Nitric oxide (NO) production of lipo-polysaccharide (LPS)-induced murine macrophages, with the inhibition rates of 36.3% and 26.9%, respectively	[10]
Anti-inflammatory effects	Essential oils	5-lipoxygenase activity, with an IC_{50} value of 38.58 ± 3.8 mg/mL and inhibited prostaglandin E2 formation by 28.82%.	[8]
Anti-inflammatory effects	Borneol and Camphene	5-lipoxygenase activity, with an IC_{50} value of 39.72 ± 2.16 and 69.22 ± 3.66 μg/mL and inhibited prostaglandin E2 formation by 33.74% and 45.78%	[8]
Antioxidant effects	Sal	Prevented iron-induced lipid peroxidation of polyunsaturated fatty acids (PUFA) of liver microsomes	[9]
Antioxidant effects	Essential oils	Reduce the purple-colored DPPH radical to the yellow-colored diphenylpicrylhydrazine with an IC_{50} of 3.06 ± 0.79 μg/mL	[8]
Antioxidant effects	Essential oils	Inhibited lipid peroxidation in the rat liver, with the IC_{50} values of 2.4 μg/mL, which were similar to the IC_{50} (1.2 mg/mL) value of ascorbic acid (1.2 μg/mL)	[7]
Cholesterol biosynthesis inhibition effects	3-oxo-LA	82% inhibits cholesterol biosynthesis in rat liver cells	[75]
Cholesterol biosynthesis inhibition effects	7-oxo-24,25-dihydrolanosterol	Lower the total serum cholesterol in rats fed a cholesterol diet	[96]
Antiplatelet aggregation effects	Petroleum ether extract	Increased the GABA-induced chloride current (IGABA) by 122.5 ± 0.3% (n = 2) when measured at 100 μg/mL in *Xenopus laevis* oocytes expressing GABA A receptors	[52]
Anti-insomnia effects	Administration of lignin extracts	Reduced FST and TST immobility time in the PCPA-induced 5HT-depleted insomnia rat model and suggesting that extracts had 5-HT1AR agonist-like effects	[51]
Anti-trypanosomaleffects	Essential oils	Moderate trypandosomal activity, with an IC_{50} value of 50.52 ± 0.029 μg/mL	[8]
Anti-trypanosomaleffects	Camphene and Borneol	Significant trypandosomal activity, with an IC_{50} value of 80.66 ± 0.87 and 70.00 ± 1.28 μg/mL.	[8]
Anti-enzyme effects	Quercetin-3-O-rhamnoside and Protocatechuic acid	Inhibitory activity on α-amylase, with IC_{50} values of 28.8 and 12.5 μmol/L	[90]

5.1. Hepatoprotective Activity

Liu et al. [5] showed that longipedlignans F and G at a concentration of 10 μM demonstrated modest hepatoprotective efficacy in HepG2 cell lines, with cell survival rates of 52.2 and 50.2%. Shao et al. [73] isolated six known schiartane-type triterpenoids and tetrahydrobenzocyclooctabenzofuranone lignans were extracted from *K. longipedunculata* and identified as kadsuphilin J (**114**), benzoyl oxokadsuranol, heteroclitin E (**97**), propoxyloxokadsuranol, micrandilactone I (**184**), and kadsutherin C (**96**). However, compound micrandilactone I (bicyclol (**313**) as positive control), at a concentration of 10 μM showed a minor hepatoprotective effect, with cell survival rates of 53.04%. Similarly, Wang et al. [86] reported that 22–23-diepimicrandilactone J (**186**) and micrandilactone I at 10 M concentrations had mild anti-APAP toxicity in HepG2 cells, with cell survival rates of 53.0 and

50.2% (bicyclol (**313**) as positive control), whereas micrandilactone J (**184**) was inactive. Wang et al. [80] reported that Kadsurol C (**124**) at concentration of 10 μM was found to have a mild anti-APAP toxicity in HepG2 cells, with a cell survival rate of 48.22% (bicyclol 48.77% as positive control). Liu et al. [5] reported that longipedunculatin B (**134**), longipedlignan M (**56**), and longipedlignan R (**61**) at a concentration of 10 μM had significant invitro inhibitory effects on NO production assays, with inhibition rates of 55.1%, 74.9%, and 89.8%, while longipedlignan M (**56**) at a 10 μM concentration had a moderate effect against N-acetyl-p-aminophenol-induced toxicity in HepG2 cells, with a cell survival rate of 50.8%.

5.2. Cytotoxic Activity

Kadlongilactone A (**178**) and Kadlongilactone E (**182**) showed strong cytotoxicity effects on various cell lines (HT-29, A549, and K562), with IC_{50} values ranging from 0.49 to 3.61 μM [14]. The results of a clinical investigation including the oral administration of 0–20 g/kg dosages of *K. longipedunculata* showed that acute exposure did not result in any obvious adverse effect, and the LD_{50} value in rats was calculated to be more than 20 g/kg [51]. Pu et al. [3] also reported that kadlongilactone A (**178**) and kadlongilactone B (**179**) were cytotoxic to human tumor K562 cells, with IC_{50} values of 1.40 and 1.71 μg/mL, respectively (*cis*-platin as positive control). Mulyaningsih et al. [8] showed that the essential oils camphene (**268**) and borneol (**278**) had some cytotoxicity against various cell lines (HepG-2, MIAPaCa-2, and SW-480), with IC_{50} values of 136.96, 133.53, and 136.62 μg/mL, respectively. They also found cytotoxicity (Caspase 3/7) in the MIA PaCa-2 cell line and demonstrated that after 24 h of incubation with essential oil, the caspase 3/7 activity was raised 2.5–4-fold, whereas camphene (1.75–4.5 fold) and borneol (3–5 fold) both increased caspase activity. *K. longipeduculata* dried root and *S. sphenanthera* dried fruit displayed significant cytotoxicities against HepG2 cell lines, with IC_{50} values of 147 and 189 μg/mL, and further concluded that the cytotoxicity of *K. longipeduculata* essential oil was higher than *S. sphenanthera* in HepG2 cells [7].

5.3. Anti-Microbial Activity

Gram-positive bacteria are typically thought to be more vulnerable to EOs than Gram-negative bacteria [97,98]. This may be due to Gram-negative bacteria having a hydrophilic outer membrane that prevents hydrophobic components from passing through the cell membrane [99]. The antimicrobial properties of both EOs have been related to cadinane-type compounds, and their derivatives, such as δ-cadinene (**221**) which are thought to be responsible for several plants' bacteriostatic activity [100–102]. The antimicrobial activity of cadinane-type compounds may be due to their function as a precursor of phytoalexins.The accumulation of δ-cadinene (**221**) in bacteria-inoculated cotton cotyledons has been demonstrated in the production of sesquiterpenoid phytoalexins. The cadinene compounds accumulated in Gossypium root epidermal cells, most likely as a defense against soil borne pathogens [103,104], and elicited by both bacterial and fungal infection [105]. Furthermore, EO root extract of *K. longipedunculata* minor components such as borneol (**278**) can also contribute to antimicrobial activity [7]. Borneol has been shown to have antimicrobial properties and could be involved in synergistic interactions with other active compounds [106,107].

Song et al. [7] reported that the root extract of *K. longipeduncluta* and dried fruit of *S. sphenanthera* had heavy antibacterial activity against *B. subtilis* and *S. aureus*, with 28.91 and 35.13 mm inhibition zones, while mild activity against *S. cerevisiae*, with an inhibition zone of 12.36 mm. While no significant effects were observed on Gram-negative bacteria (*E. coli* and *E. aerogenes*). Mulyaningsih et al. [8] used the agar diffusion method to assess the antimicrobial activity of essential oils and reported that camphene (**268**) and borneol (**278**) had activity against antimicrobial with inhibition zones in the range of 6.7–11.0 mm, while crude oil developed inhibition zones in the range of 8.0–13.0 mm. The oil was susceptible to all Gram-positive bacteria, with MIC values ranging from

0.06 to 2 μg/mL, whereas *Streptococcus agalactiae* and *Streptococcus pyogenes* were the most sensitive (MIC value of 0.06 μg/mL).

Triterpenoids from the Schisandraceae family exhibit antiviral effectson the herpes simplex virus (HSV), human immunodeficiency virus (HIV), adenovirus, and hepatitis B virus (HBV). Cycloartanes, lanostanes, and schinortriterpenoids exhibit anti-HIV efficacy that ranges from weak to moderate, with EC_{50} values ranging from 1.09 to 80.8 mg/mL, while the anti-HIV activity was also shown to be compatible with its suppression of HIV-1 cytopathic effects in C8166 cells [108], which was found to be more powerful than polymerase activities and anti-reverse transcriptase. Sun et al. [12] reported that longipedunin A (**65**) and schisanlactone A were found to have significant activity against HIV-1 protease, with IC_{50} values of 50 and 20 μM, respectively. Pu et al. [3] reported that lancifodilactones A–G, micrandilactones A–G, and henridilactones A–D showed strong anti-HIV effects. Pu et al. [13] also reported that kadlongirin A (**116**), kadlongirin B (**117**), and 2,7-dihydroxy-11,12-dehydrocalamenene were effective in preventing the cytopathic effects of HIV-1 in C8166 cells, CC_{50} 1146.08 mg/mL and EC_{50} 2.03 ng/mL (AZT as a positive control), and kadlongirin B (**117**) had poor anti-HIV-1 activity, with an EC_{50} value of 16.0 μg/mL.

5.4. Anti-Tumor Activity

The key active ingredients in *Kadsura longipedunculata* are dibenzocyclooctadiene lignans, which are used as a "liver tonic" in Asian herbal medicine for treatment of chronic and poor liver function. Interestingly, schisandrin C (wuweizisu C, 28), Kudsuraols A–C (**122**–**124**), extracted from *K. longipedunculata* and *S. chinensis*, has been used in the development of two liver therapies, diphenyl dimethyl bicarboxylate and bicyclol (**313**) are two of them [11,80,108]. In clinical trials, bicyclol has been shown to enhance impaired liver function, prevent HBV replication in chronic hepatitis B patients, and induce differentiation of human hepatocarcinoma (both HepG2 and Bel-7402 cells) with no side effects [94]. These findings suggest that dibenzocyclooctadiene lignans may be useful chemopreventive agents in the regulation of liver carcinogenesis. Kadlongilactones A–B (**178**–**179**) from *K. longipedunculata* showed substantial cytotoxicity with various cell lines of human hepatocellular carcinoma Bel-7402 cells, leukemia K562 cells, HT-29, and adenocarcinoma A549 cells, with IC_{50} values of less than 0.1 and 1.0 M, respectively (**14**). Liu et al. [95] reported that kadsulignan H (**40**), kadsulignan I (**105**), and kadsulignan J (**42**) had weak effects on leukemia P-388 cells in vitro, with IC_{50} values of 40, 10, and 10 μgmL^{-1}.

5.5. Anti-Inflammatory Activity

Qi et al. [10] reported that Kadlongilignan C (**75**) and Kadlongilignan D (**76**) from *K. longipedunculata* roots extract had potent inhibitory effects against NO production of lipo-polysaccharide-induced murine macrophages, with the inhibition rates of 36.3% and 26.9%, respectively. Mulyaningsih et al. [8] found that the essential oils camphene (**268**), and borneol (**278**) inhibit 5-lipoxygenase. The oil had an IC_{50} of 38.58 ± 3.8 μg/mL, while camphene and borneol had IC_{50} values of 39.72 ± 2.16 and 69.22 ± 3.66 μg/mL, respectively. They also measured the amount of PGE2 released by MIA PaCa-2 cells in order to see whether the essential oil and its components had any inhibitory effects on cyclooxygenase activity. In comparison to the untreated control, 25 μg/mL of the oil inhibited 28.82% of prostaglandin E2 formation, while borneol and camphene showed 33.74 and 45.78% inhibitory effects. Mulyaningsih et al. [8] further reported that essential oil had 5-lipoxygenase activity, with an IC_{50} value of 38.58 ± 3.8 mg/mL, while borneol and camphene had IC_{50} values of 39.72 ± 2.16 and 69.22 ± 3.66 μg/mL. Similarly, they also reported that essential oil inhibited 28.82% of prostaglandin E2 formation, whereas borneol (33.74%) and camphene (45.78%) had inhibitory effects.

5.6. Antioxidant Activity

Nine dibenzocyclooctene lignans isolated from *K. longipedunculata* were tested for the antioxidant activity [9]. Seven out of nine lignans prevented iron-induced lipid peroxida-

tion of liver microsomes. The most potent was Sal, while Sol A and B were reported as the weakest. The variations in anti-lipid peroxidation effects on these lignans might be due to differences in the functional group structures. The result also showed that the iron/cysteine-induced lipid peroxidation reduced the lipid fluidity of microsomal membranes. Sal with its strong anti-lipid peroxidation action was able to counteract the reduction of membrane fluidity caused by iron, while Sin A had no effect on the iron-induced membrane fluidity reduction of liver microsomes. Mulyaningsih et al. [8] showed that the essential oil has an IC_{50} of 3.06 ± 0.79 µg/mL for converting purple to the yellow-colored diphenylpicryl-hydrazine. Camphene (**268**) and borneol (**278**), on the other hand, were barely involved showing a 10% inhibition. Song et al. [7] reported that the *K. longipedunculata* essential oils inhibited lipid peroxidation in the rat liver, with the IC_{50} values of 2.4 µg/mL, which were similar to the IC_{50} (1.2 mg/mL) value of ascorbic acid (1.2 µg/mL).

5.7. Cholesterol Biosynthesis Inhibition Activity

The effects of 12novel triterpenoid acids extracted from *K. longipedunculata* and some other similar triterpenoids on cholesterol biosynthesis were studied in rat liver cells and the most active triterpenoid acids were 3-oxo-LA (**152**) and showed an 82% inhibition effect at 25 µg/mL [75]. Similarly, 7-ketocholesterol (**314**) or 5ct-cholest-8(14)en-3f3-01-15one (**315**), inhibit cholesterol biosynthesis effectively [92,93]. Regardingoral administration to rodents [109], baboons [110], and monkeys [111], 5ct-Cholest-8(14)en-3f3-01-15-one (**307**) was found to have hypocholesteromic activity.Some oxygenated lanosterol derivatives are also cholesterol biosynthesis inhibitors. The most active of these compounds was 7-oxo-24, 25-dihydrolanosterol (7-oxoDHL), which inhibits the demethylation of lanosterol [96]. Similarly, ketoconazol is an antifungal agent that has also shown to prevent lanosterol demethylation [112,113]. Furthermore, 7-oxo-DHL was found to lower the total serum cholesterol in rats fed a cholesterol diet [96].

5.8. Anti-Platelet Aggregation Activity

Spirobenzofuranodibenzocyclooctadiene-type lignans are found in this genus and have strong antagonistic effects on the platelet activating factor, which is thought to be the foundation for improving blood circulation and avoiding blood stasis [114]. Zaugg et al. [52] reported that *K. longipedunculata* petroleum ether extract at 100 µg/mL increased the GABA chloride current (IGABA) by 122.5 ± 0.3% (n = 2) in expressing GABA A receptors in *Xenopus laevis* oocytes.

5.9. Anti-Insomnia Activity

Zheng et al. [51] reported that administration of lignan extracts from *K. longipedunculata* reduced FST and TST immobility time in the PCPA-induced 5HT-depleted insomnia rat model. Extracts of *K. longipedunculata* controlled the expression of proteins linked to the 5-HT1AR pathway, suggesting that extracts had 5-HT1AR agonist-like properties. They also discovered that lignan extracts from *K. longipedunculata* can target 5-HT1AR in insomniac rats, indicating that it might be utilized as a 5-HT1AR agonist medication.

5.10. Anti-Trypanosomal Activity

Kadsura longipedunculata essential oil had moderate trypandosomal effects, with an IC_{50} value of 50.52 ± 0.029 µg/mL, while camphene (**268**) and borneol (**278**) had IC_{50} values of 80.66 ± 0.87 and 70.00 ± 1.28 µg/mL that were statistically significant [8].

5.11. Anti-Enzyme Activity

Cen et al. [90] report that quercetin-3-O-rhamnoside (**245**) and protocatechuic acid (**246**) ethanol extract of *K. longipenduculata* showed inhibitory activity, with IC_{50} values of 28.8 and 12.5 µmol/L.

6. Conclusions

Kadsura longipenculata is a valuable medicinally and economically important plant with a wide range of uses. Most *Kadsura* plants have a long history of traditional effectiveness and medical usage in south and southwest regions of China. Bioactivities cited in official pharmacopeias as well as scientific publications, in addition to traditional medicinal use, support the well-established medicinal use of the *Kadsura* plant. Approximately 148 lignans, 54 triterpenoids, and 113 other terpenoids with various skeleton structures have been isolated and described from *K. longipenculata*, with some of them showing potential developmental prospects. These structurally complex compounds have piqued the attention of phytochemists and pharmacologists and raised new challenges. Extensive pharmacology research on isolated compounds from *K. longipenculata* has shown that they have antimicrobial, antioxidant, NO inhibitory product, anti-trypanosomal, antitumor, cytotoxic, antienzyme and antiplatelet aggregation, and anti-viral activity.

In China, there are over 5000 different types of Chinese herbal medicines. Currently, over 3700 different types of active substances have been recognized with many of them being investigated in pharmacology. However, more extensive research is needed to determine the chemical components responsible for its pharmacological effect in order to continue its traditional use. More clinical and preclinical evidence is required to determine the rationale and safety of using *K. longipendunculata* for medicinal and food purposes.

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