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Murraya koenigii L. Spreng.: An updated review of chemical composition, pharmacological effects, and toxicity studies

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ABSTRACT

Murraya koenigii (L.) Spreng, commonly known as curry leaves or "*Salam India*," belongs to the genus *Murraya* and the Rutaceae family. This is a potential medicinal plant highly valued for its distinctive aroma and bioactive compounds. A comprehensive review was conducted through an online study on websites such as PubMed, Science Direct, Scopus, and Google Scholar. Subsequently, previous studies reported that the chemical content of *M. koenigii* includes alkaloids, phenylpropanoids, alkanes, and sesquiterpenes. This plant exhibits a wide range of pharmacological activities such as antiinflammatory and analgesic effects, antidiabetic properties, anticancer activity, antioxidant activity, wound healing, antipyretic effects, immunomodulation, hepatoprotective effects, antihelminthic properties, antimicrobial activity, antiulcer effects, antidiarrheal effects, antiobesity effects, neuroprotection, and antitrichomonal activity. In addition, the toxicological tests on the extract of *M. koenigii* did not show signs of mortality or morbidity. Therefore, this study aims to examine the phytochemical content, pharmacological activities, and toxicity of *M. koenigii*, serving as the basis for future studies in the field of phytomedicine.

INTRODUCTION

Murraya koenigii is a tropical to subtropical plant belonging to the Rutaceae family. This plant is known as "Salam India" in Indonesia and has various regional names such as temurui (Aceh), koro keling (Semarang), sicerek (Minangkabau), and ki becetah (Sunda). In other countries, this plant is referred to as curry (English), garupillai (Malaysia), kerriebladeren (Dutch), feuilles de cari (French), curryblatter (German), fogli de cari (Italian), and hoja (Spanish) [1].

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Taxonomy of plant

Kingdom	: Plantae
Sub-kingdom	: Tracheobionta
Superdivision	: Spermatophyta
Division	: Magnoliophyta
Class	: Magnoliospida
Subclass	: Rosidae
Order	: Sapindales
Family	: Rutaceae
Genus	: Murraya
Species	: *Murraya koenigii* L. Spreng

Murraya koenigii is a shrub or small tree, typically growing between 2.5 and 6 m in height [2]. This plant has a short stem with a diameter of 15–40 cm, which is grayish or brown, and lush foliage [3]. Its compound leaves are bipinnately, showcasing 11–21 leaflets, each measuring 2–4 cm in length, and 1–2 cm in width, emitting a distinctive aroma. The bisexual

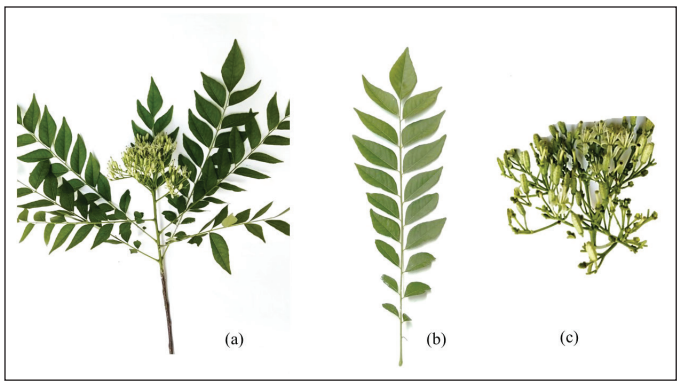

Figure 1. *Murraya koenigii* (L.) Spreng. (a) Plant. (b) Leaves. (c) Flower.

flowers are small, fragrant, and white, while the small egg-shaped fruits have a length of 1.4–1.6 cm and a diameter of 1–1.2 cm, turning purplish–black when ripe [4]. The seeds are approximately 11 mm in length, and 8 mm in diameter, with a weight of about 445 mg [5]. A visual representation of *M. koenigii* plant is presented in Figure 1.

Murraya koenigii is known for its aromatic leaves used in culinary spice. The most important chemical compounds responsible for its strong distinctive aroma are p-gurjunene, p-caryophyllene, p-elemene, and O-phellandrene. This plant is also high in carbazole alkaloids such as mahanimbine, murrayanine, murrayacine, girinimbine, isomurrayazoline, mahanine, koenine, koenigine, koenidine, koenimbine [6,7], O-methylmahanine, O-methylmurrayamine, isomahanine, bismahanine, and bispyrayafoline [8]. Traditionally, this plant has been used for its stimulant, stomachic, antipyretic, analgesic, and medicinal properties in the treatment of diarrhea, dysentery, and insect bites, as well as its anti-inflammatory and antidepressant effects [9]. Topically applying a paste made from fresh leaves is known to neutralize toxins from animal bites [10].

METHODS

A comprehensive literature search for scientific studies published in electronic databases was conducted. This study reviewed more than 200 scientific papers from various international sources, including PubMed [www.ncbi.nlm.nih.gov/pubmed/], Google Scholar [https://scholar.google.com.pk/], and Scopus [www.scopus.com]. Subsequently, the studies were electronically searched from 1965 to 2023, and only 120 papers were found suitable for this review. The following keywords were used to search the databases: "*Murraya koenigii*," "Chemical Composition," "pharmacological effects," and "toxicity." All chemical structures were visualized using ChemDraw Ultra 18.0 software.

RESULTS AND DISCUSSION

Chemical composition

Murraya koenigii is a plant rich in various chemical compounds obtained from extracts using solvents such as petroleum ether, ethyl acetate, chloroform, and ethanol-water. To date, various compounds found including alkaloids, phenylpropanoids, alkanes, sesquiterpenes, flavonoids, and other compound groups.

Alkaloid

Murraya koenigii is rich in alkaloid content, which are the primary components contained in its compounds (summarized in Table 1 and Fig. 2). In recent years, studies have discovered that alkaloids found in this plant play an important role in anti-inflammatory and analgesic effects [11,12], antidiabetic properties [13], anticancer [14], hepatoprotective effects [15], and antimicrobial properties [9].

Fenilpropanoid

Phenylpropanoid compounds isolated are summarized in Table 2 and Figure 3, respectively. Subsequently, Ma *et al.* [43] successfully isolated five phenylpropanoid compounds, while Srivastava and Srivastava [44] isolated two phenylpropanoid compounds.

Alkanes

Ma *et al.* [45], successfully isolated four alkane compounds, which include (3S,4E,6E,10R)-2,10-dihydroxy-2-hydroxy-2-methylethyl-6,10-di-methyl-4,6,11-sencolaninic-3-b-D-glucopyranoside, (3R,5S,6E,8S,10E)-3,7,11-trimethyl-1,6,10-dodecatriene-3,5,8-triol, 5S,6R,7S,8R)-5-amino-(2Z,4Z)-1,2,3-trihydroxybuta2,4-dienyloxy-pentane-6,7,8,9-tetraol, (3E,6S,7E,9R,10S,11S,17R)-octadeca-3,7-diene-6,9,10,11,17-pentaol (presented in Table 3 and Fig. 4).

Terpenoid

Terpenoids are the most diverse and largest class of chemical compounds found in various plant sources. In addition, they are also known as terpenes or isoprenoids, and most plant-derived terpenoids are used by humans in the pharmaceutical, food, and chemical industries. The terpenoids successfully isolated are summarized in Table 4 and Figure 5.

Flavonoid

Flavonoids are important compounds in natural products. Flavonoids are also found in *M. koenigii*, such as quercetin, apigenin, and kaempferol, which can be seen in Table 5 and Figure 6.

Other compounds

Furthermore, *M. koenigii* also contains other compounds such as coumarins (heraclenin, imperatorin), ketones (iso menthone, Z-jasmone), xanthophyll (Lutein), acetate esters (linalyl acetate, lavandulyl acetate, myrtenyl acetate, neryl acetate, and geranyl acetate), alcohols (menthol, tocopherol), and carboxylic acid (nicotinic acid), which are summarized in Table 6 and Figure 7.

Pharmacological effects of *M. koenigii*

Currently, a study of the pharmacological activities of *M. koenigii* indicates that its extracts and chemical components exhibit a wide range of biological activities. These activities include anti-inflammatory and analgesic effects, hemostatic coagulation, antibacterial activity, antioxidant effects, anti-tumor effects, and more. Based on this study, pharmacological effects primarily focused on alcohol, water, and methanol extracts, among others. The active compounds isolated from these extracts

Table 1. Alkaloids reported from *M. koenigii.*

No.	Compound name	Molecular formula	Molecular weight	References
1	Mahanimbine	$C_{23}H_{25}NO$	331.4	[16–21]
2	Murrayazoline or mahanimbidine or curryangin	$C_{23}H_{25}NO$	331.4	[22]
3	Murrayacine	$C_{18}H_{15}NO_2$	277.3	[17–18]
4	Koenimbidine or koenidine or koenigicine	$C_{20}H_{21}NO_3$	323.4	[17–18]
5	Murrayacinine	$C_{23}H_{23}NO_2$	345.4	[23–24]
6	Glycozoline	$C_{14}H_{13}NO$	211.26	[8,25]
7	Mukonicine	$C_{20}H_{21}NO_3$	323.4	[26]
8	Mukonidine	$C_{14}H_{11}NO_3$	241.24	[26]
9	Murrayazolinol	$C_{23}H_{22}NO_2$	347.4	[27]
10	Isomurrayazoline	$C_{23}H_{25}NO$	331.4	[27]
11	Murrayazolinine	$C_{23}H_{27}NO_2$	349.5	[27]
12	3-Methyl carbazole	$C_{13}H_{11}N$	181.23	[25]
13	Mahanine	$C_{23}H_{25}NO_2$	347	[7,19–21,28]
14	Isomahanine/pyrafoline D	$C_{23}H_{25}NO_2$	347.4	[19,28] [29–30]
15	Bismahanine	$C_{46}H_{48}N_2O_4$	692	[6] [29]
16	Mukoenine-A/girinimbilol	$C_{18}H_{19}NO$	265.3	[6]
17	Mukoenine-B	$C_{23}H_{25}NO_2$	224	[6]
18	Mukoenine-C/murrayamin A	$C_{18}H_{17}NO_2$	279,3	[6]
19	Murrastifoline-F	$C_{28}H_{24}N_2O_2$	420.5	[6]
20	Bis-2-hydroxy-3-methylcarbazole	$C_{26}H_{20}N_2O_2$	392.4	[6]
21	Bikoeniquinone-A	$C_{27}H_{20}N_2O_3$	211	[6]
22	Murrayafoline-A	$C_{14}H_{13}NO$	211.26	[6,31]
23	Murrayaquinone-A	$C_{13}H_9NO_2$	211.22	[6]
24	Bis-7-hydroxygirinimbine	$C_{36}H_{32}N_2O_4$	556.2362	[6]
25	Bismurrayaquinone-A	$C_{26}H_{16}N_2O_4$	420.4	[6]
26	Mahanimbilol	$C_{23}H_{27}NO$	333.5	[24,32]
27	Koenine	$C_{18}H_{17}NO_2$	279.3	[33]
28	Koenigine	$C_{19}H_{19}NO_3$	309.4	[33]
29	Mahanimbinine	$C_{23}H_{27}NO_2$	349.5	[34]
30	Murrayanol	$C_{24}H_{29}NO_2$	363.5	[20]
31	Euchrestine B	$C_{24}H_{29}NO_2$	363	[21]
32	Bismurrayafoline E	$C_{48}H_{56}N_2O_4$	724.4237	[21]
33	Cyclomahanimbine or curryanine or Murrayazolidine or currayanine	$C_{22}H_{25}NO$	331.4	[21]
34	Mahanimbicine/isomahanimbine	$C_{23}H_{25}NO$	331	[7,21]
35	8,8”-Biskoenigine	$C_{38}H_{36}N_2O_6$	616.2573	[35]
36	Koenimbine	$C_{19}H_{19}NO_2$	293	[29]
37	O-Methylmurrayamine	$C_{19}H_{19}NO_2$	293	[29]
38	O-Methylmahanine	$C_{24}H_{27}NO_2$	361	[29–30]
39	Bispyrayafoline	$C_{48}H_{56}N_2O_4$	692.3611	[29]
40	8,10’-(3,3’,11,11’-Tetrahydro-9,9’-dihydroxy-3,3’,5,8’-tetramethyl- 3,3’-bis(4-methyl-3-pentenyl))bipyrano(3,2-a)carbazole	$C_{48}H_{56}N_2O_4$	692.362	[29]
41	Girinimbine	$C_{18}H_{17}NO$	263	[30–31]
42	Murrayanine	$C_{14}H_{11}NO_2$	225	[31]

Continued

No.	Compound name	Molecular formula	Molecular weight	References
43	Mukonine	$C_{15}H_{13}NO_3$	255.27	[36]
44	Mukoline	$C_{14}H_{13}NO_2$	227.26	[36]
45	Mukolidine	$C_{14}H_{11}NO_2$	225.24	[36]
46	Kurryam	$C_{20}H_{21}NO_4$	339	[37]
47	Karapinchamine A	$C_{23}H_{27}NO$	333.209	[30]
48	Karapinchamine B	$C_{23}H_{25}NO_2$	347.187	[30]
49	Bicyclomahanimbicine	$C_{23}H_{25}NO$	331.4	[30]
50	Bicyclomahanimbine	$C_{23}H_{25}NO$	331.4	[30]
51	Murrayamine-B	$C_{24}H_{27}NO_2$	361.5	[30]
52	Eustifoline-C	$C_{23}H_{27}NO$	333.5	[30]
53	Murrayamine-E	$C_{23}H_{25}NO_2$	347.4	[30]
54	N-Benzyl carbazole-A	$C_{27}H_{28}NO_5$	446.1962	[38]
55	N-Benzyl carbazole-B	$C_{26}H_{25}NO_4$	416.1856	[38]
56	Iso-koenidine	$C_{20}H_{22}NO_3$	324.1594	[38]
57	Iso-koenigine	$C_{19}H_{20}NO_3$	310.1438	[38]
58	Murrayazolinol	$C_{23}H_{25}NO_2$	348.1964	[32,39]
59	Murrayakoeninol	$C_{23}H_{25}NO_2$	348.1964	[32,39]
60	Bicyclomahanimbine	$C_{23}H_{25}NO$	332.2014	[32,39]
61	Murrayamine-J	$C_{23}H_{23}NO_2$	345.4	[32]
62	Koenoline	$C_{14}H_{13}NO_2$	227.26	[40]
63	Mukonal	$C_{13}H_9NO_2$	211.22	[41]
64	Murrayamine-M	$C_{23}H_{23}NO_2$	345.4	[42]
65	Murrayamine-G	$C_{23}H_{25}NO$	331.4	[42]
66	3,3′,5,5′,8-Pentamethyl-3,3′-bis (4-methylpent-3-en-1-yl)−3,3′,11,11’-tetrahydro-10,10′-bipyrano(3,2-a)carbazole	$C_{47}H_{50}N_2O_2$	674.3872	[13]

and their associated pharmacological effects are summarized in Figure 8. The following activities will be detailed.

Anti-inflammatory and analgesic effects

Ethanol extract of *M. koenigii* leaf has shown significant anti-inflammatory and analgesic activities when tested using the carrageenan-induced paw edema method in rats [62,63], as well as methanol extracts [64], and others. Furthermore, ethanol extracts (300 and 400 mg/kg) also act as antihistamines and can stabilize mast cells [65]. Mani *et al.* [66] further showed that *M. koenigii* leaf extracts effectively relieve pain induced by intraperitoneal acetic acid and subplantar formalin injection in rats.

Methanol extracts from *M. koenigii* have demonstrated the ability to inhibit glutamate-induced pain, with their antinociceptive mechanisms including adenosina trifosfat-sensitive K+ channels [67]. In another study by Nalli *et al.* [12], compounds such as murrayakonine A, O-methylmurrayamine A, and mukolidine isolated from *M. koenigii* leaf and stems were found to inhibit the release of inflammatory mediators tumor necrosis factor alpha (TNF-α) and interleukin (IL)-6. Furthermore, girinimbine exhibited anti-inflammatory activity tested on RAW 264.7 cells induced by lipopolysaccharides by reducing nitric oxide (NO) levels and proinflammatory cytokines IL-1β and TNF-α [11]. Husna *et al.* [68] also proved that ethanol extracts from the leaves pose anti-inflammatory and hepatoprotective activities and play a role in regenerating damaged pancreatic islets.

Antidiabetic

Regarding its antidiabetic properties, studies have shown that feeding rats *M. koenigii* leaf diets leads to hypoglycemic and antihyperglycemic effects [69]. Ethanol extracts of *M. koenigii* have also been shown to significantly reduce blood glucose levels [70], with the hypoglycemic effect attributed to their antioxidant properties and insulin-mimetic effects. In addition, *M. koenigii* exhibits profound antioxidant effects by reducing levels of malondialdehyde, increasing high levels of glutathione, and significantly lowering the homeostatic model assessment-insulin resistance index [71,72].

Oral administration of *M. koenigii* leaf water extracts has been shown to reduce blood glucose levels in diabetic rats and alloxan-induced diabetic rabbits [73–78]. Chloroform leaf extracts also exhibit antidiabetic activity at doses of 250 and 500 mg/kg body weight in alloxan-induced diabetic rats [79]. In addition, the juice of *M. koenigii* fruit also lowers blood glucose levels in diabetic rats [80].

Mahanimbine was isolated from *M. koenigii* using dry petroleum ether extract column chromatography. The

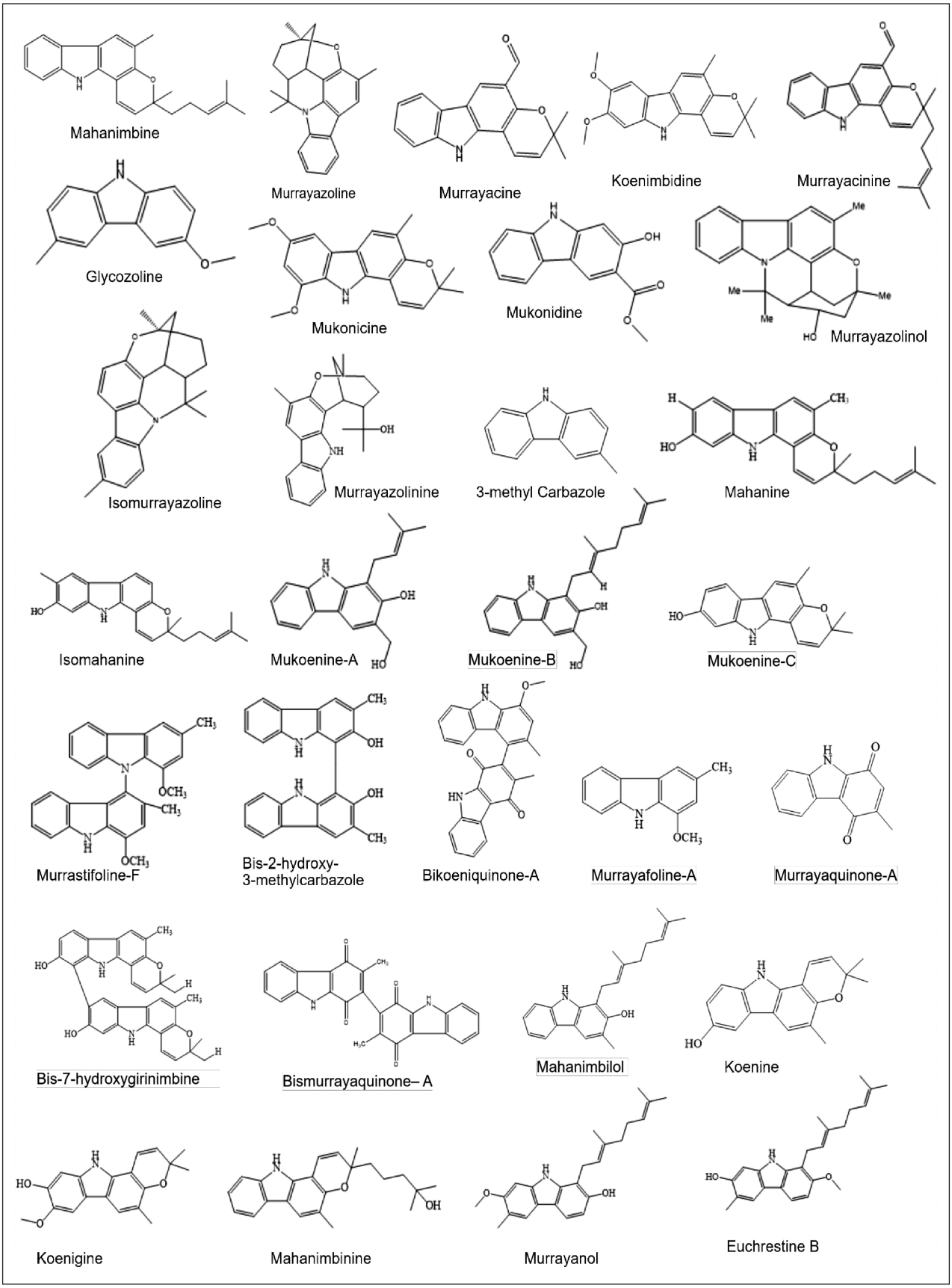

Figure 2. Structures of alkaloids from *M. koenigii* (L.) Spreng.

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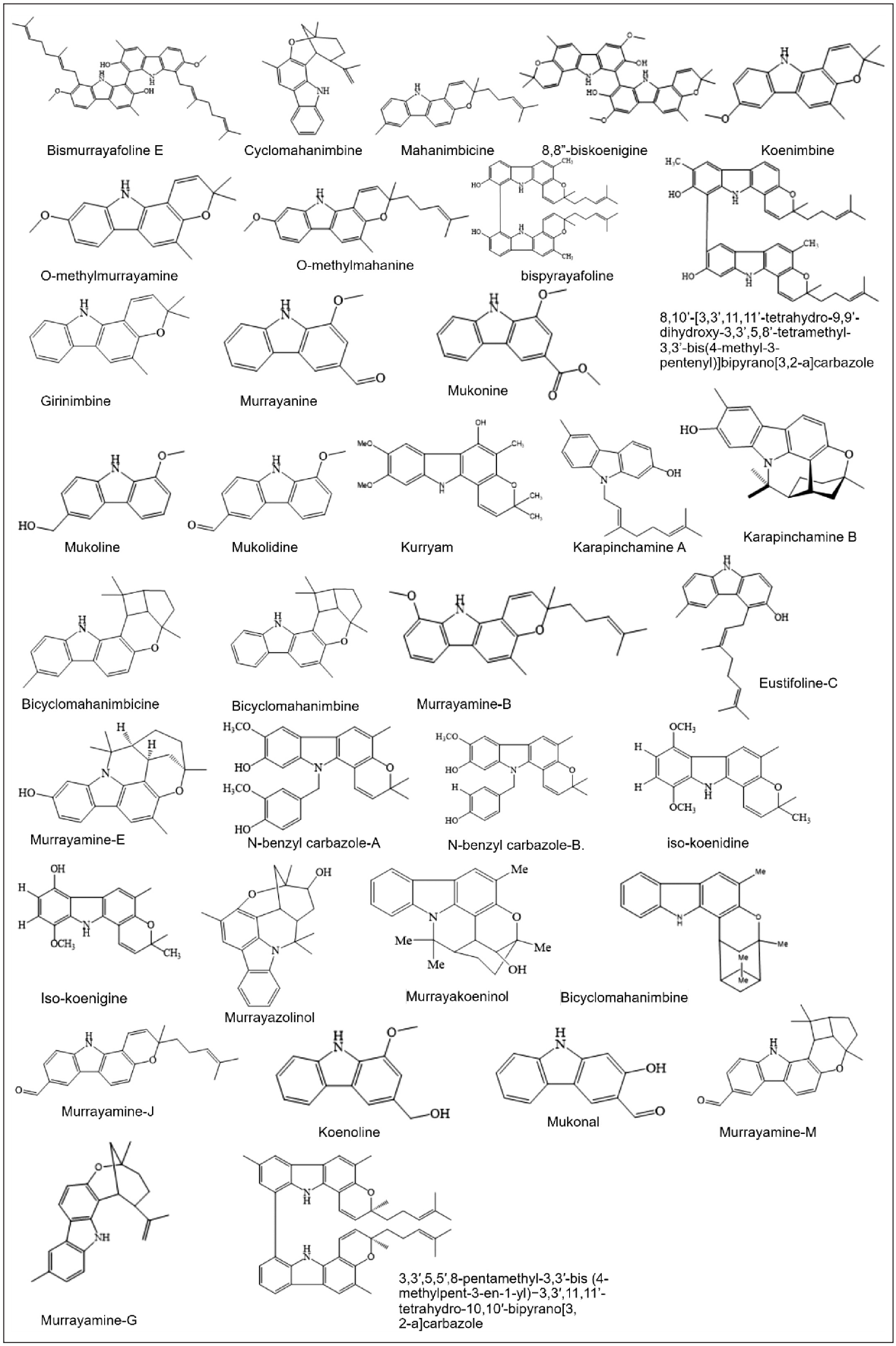

Figure 2. Structures of alkaloids from *M. koenigii* (L.) Spreng.

Table 2. Fenilpropanoid reported from *M. koenigii.*

No.	Compound name	Molecular formula	Molecular weight	References
1	Murrayenol	$C_{30}H_{46}O_4$	470.4	[44]
2	Murrayagetin	$C_{19}H_{20}O_4$	312	[44]
3	[7′E,8S]-9′-Hydroxy-7′-propen-3′,5′-dimethoxyphenyl-3-methoxyphenyl-7,9-propanediol-4-O-β-D-glu-copyranoside.	$C_{27}H_{36}NaO_{12}$	575.2099	[43]
4	[7R]-2,6-Dimethoxyphenyl-7,9-propanediol1-O-β-D-glucopyranoside.	$C_{17}H_{26}NaO_{10}$	413.1418	[43]
5	[2′R,4′R,7S]-2′,4-Dihydroxy-3-methoxyphenyl-4′-hydroxymethyl-tetra-hydro-1H-pyran-1-one.	$C_{13}H_{16}NaO_6$	291.0839	[43]
6	[1R,10S]-1-Hydroxy-7-[10-hydroxybutyl]-2,3-dihydrobenzofuran-8[6H]-one.	$C_{12}H_{16}NaO_4$	247.0941	[43]
7	Citrusin B	$C_{27}H_{36}O_{13}$	568.6	[43]

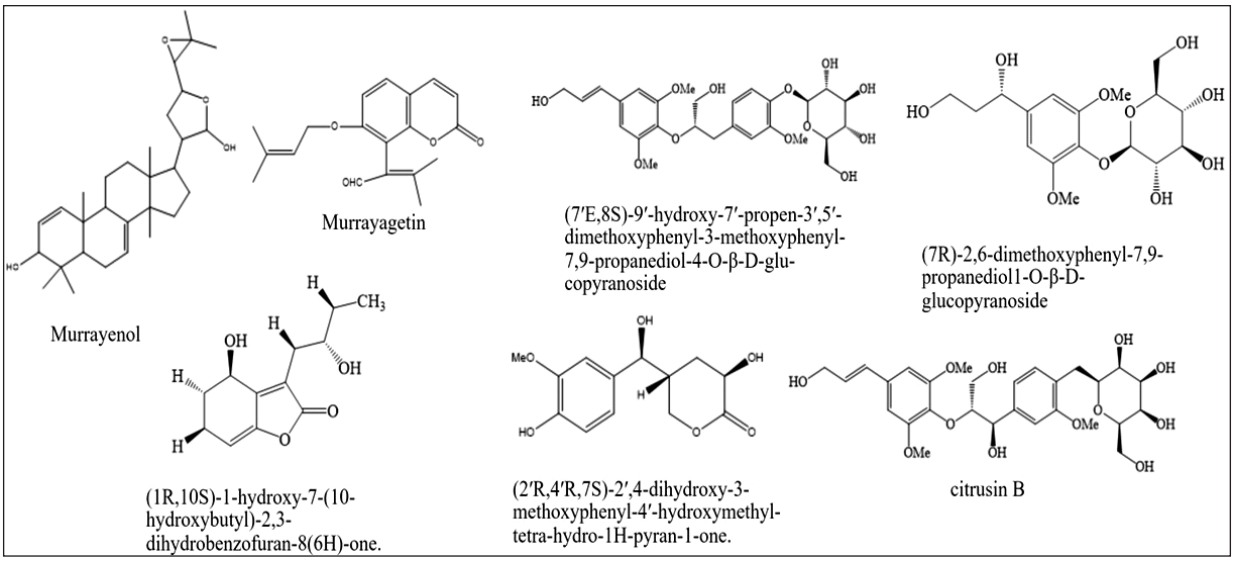

Figure 3. Structures of fenilpropanoid from *M. koenigii* (L.) Spreng.

Table 3. Alkanes reported from *M. koenigii* (L.) Spreng.

No.	Compound name	Molecular formula	Molecular weight	References
1	[3S,4E,6E,10R]-2,10-Dihydroxy-2- hydroxy-2-methylethyl-6,10-di-methyl-4,6,11-sencolaninic-3-b- D-glucopyranoside.	$C_{21}H_{36}O_8$	439.2302	[45]
2	[3R,5S,6E,8S,10E]-3,7,11-Trimethyl-1,6,10-dodecatriene-3,5,8-triol	$C_{15}H_{26}O_3$	277.1774	[45]
3	[5S,6R,7S,8R]-5-Amino-[2Z,4Z]-1,2,3-trihydroxybuta2,4-dienyloxy-pentane-6,7,8,9-tetraol	$C_9H_{17}NO_8$	290.0846	[45]
4	[3E,6S,7E,9R,10S,11S,17R]-Octadeca-3,7-diene-6,9,10,11,17-pentaol.	$C_{18}H_{34}O_5$	353.2298	[45]
5	[2E,6R]-2,6-Dimethyl-2,7-octadiene-1,6-diol	$C_{10}H_{18}0_2$	170.25	[45]
6	[6R,7E,9S,10R]-6,9,10-Trihydroxy-7-octadecenoic acid	$C_{18}H_{34}O_5$	330.5	[45]
7	Capsianoside V	$C_{26}H_{42}O_{10}$	514.6	[45]
8	Oxylipin	$C_{18}H_{32}O_3$	296.4	[45]
9	[9S,10R,11E,13S]-9,10,13-Trihydroxyoctadec-11-enoic acid	$C_{18}H_{34}O_5$	330.5	[45]

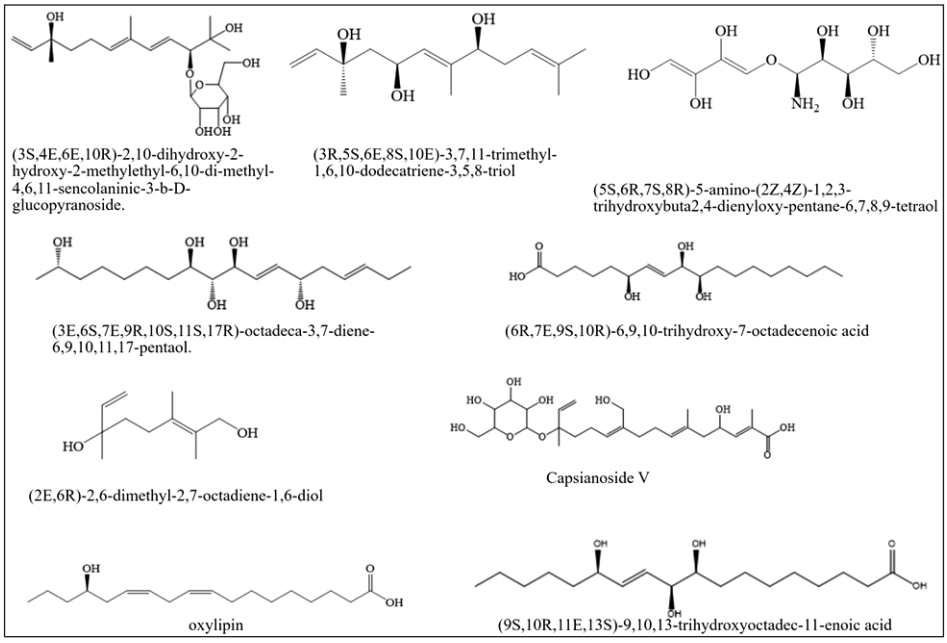

Figure 4. Structures of alkana from *M. koenigii* (L.) Spreng.

antidiabetic activity was conducted on Wistar rats induced with streptozotocin using pure compound at doses of 50 and 100 mg/kg. The results showed the presence of antidiabetic and antilipidemic activities of mahanimbine [47]. In addition, koenidine showed a significant decrease in postprandial blood glucose levels with increased insulin sensitivity in type 2 diabetic rats [81].

In clinical trials, the administration of *M. koenigii* leaf powder showed a significant difference in the average fasting and postprandial blood glucose levels in diabetic patients [82]. Sampath *et al.* [13] demonstrated that a compound derived from *M. koenigii*, known as 3,3′,5,5′,8-pentamethyl-3,3′-bis(4-methylpent-3-en-1-yl)-3,3′,11,11’-tetrahydro-10,10′-bipyrano (3,2-a) carbazole exhibited *in vitro* inhibition activity against α-amylase and α-glucosidase, showcasing its potential as an antidiabetic agent. Furthermore, the findings showed that this compound has antidiabetic activity. Its extract exhibited an antihyperglycemic effect by improving key enzymes on carbohydrate metabolism and increased glucose transporter-4 expression against hyperglycemic rats [83]. A 1-month trial of supplementing with 12 g of *M. koenigii* leaf powder (providing 2.5 g of fiber) was conducted in 30 patients with noninsulin-dependent diabetes mellitus. The findings revealed a temporary decrease in fasting and postprandial blood sugar levels after 15 days, with no significant alterations observed in glycosylated protein levels, glycosylated low-density lipoprotein cholesterol fraction, serum lipids, lipoprotein cholesterol levels, uronic acid, and total amino acids throughout the supplementation period, either at 15 or 30 days [84].

Anticancer effect

Regarding its anticancer properties, *M. koenigii* leaf has shown potential as an anticancer agent against HeLa cells [85], and colorectal cancer [86]. In addition, the methanol extract of *M. koenigii* has been reported to have the ability to reduce proliferation in breast cancer cells [87,88]. Alkaloids extracted from the leaves have also been proven to have cytotoxic activity against breast cancer cells with an inhibition concentration (IC_{50}) of 14.4 µg/ml [89].

Ito *et al.* [90] demonstrated that mahanine, pyrafoline-D, and murrafoline-I exhibited significant cytotoxic activity against HL-60 cells. In addition, girinimbine, a carbazole alkaloid isolated from *M. koenigii*, showed anticancer activity against human hepatocellular carcinoma and lung cancer [48]. Microtetrazolium assays revealed that girinimbine induced cell death with IC_{50} 19.01 µM [91]. Koenimbin, another compound isolated from *M. koenigii* exhibited activity in inhibiting MCF7 breast cancer cells [92,93]. Moreover, murrayazoline and O-methylmurrayamine A, obtained from the isolation of these plant leaves showed activity against colorectal cancer through down-regulation of the Akt/mTOR survival pathway and activation of the intrinsic pathway of apoptosis [94]. Mahanimbine, also isolated from *M. koenigii* leaf, has been shown to inhibit P-glycoprotein involved in lung cancer chemoresistance [14].

Chemoprotective activity

The methanol extract of *M. koenigii* leaf, administered as a single dose of 100 mg/kg before intraperitoneal injection of 50 mg/kg cyclophosphamide in albino rats, exhibited a protective effect by reducing cyclophosphamide-induced chromosomal damage and enhanced bone protection [95].

Antioxidant effect

In terms of its antioxidant properties, a study by Tachibana *et al.* [21] indicated that compounds such as mahanimbine and koenigine, derived from leaves, possess antioxidant activity. Antioxidant activity was assessed using

Table 4. Terpenoid reported from *M. koenigii.*

No.	Compound name	Molecular formula	Molecular weight	References
1	β-*Elemene*	$C_{15}H_{24}$	204.35	[8]
2	β-*Bisabolene*	$C_{15}H_{24}$	204.35	[46]
3	β-*Caryophyllene*	$C_{15}H_{24}$	204.35	[46]
4	α-*Copaene*	$C_{15}H_{24}$	204.35	[47]
5	α-*Humulene*	$C_{15}H_{24}$	204.35	[47]
6	*Dehydro aromadendrene*	$C_{15}H_{22}$	202.33	[48]
7	*Aromadendrene*	$C_{15}H_{24}$	204.35	[49]
8	*Junipene*	$C_{15}H_{24}$	204.35	[50]
9	β-*Selinene*	$C_{15}H_{24}$	204.35	[51]
10	*Cadinene*	$C_{15}H_{26}$	206.37	[50]
11	Myrcene	$C_{10}H_{16}$	136.23	[52]
12	β-Pinene	$C_{10}H_{16}$	136.23	[52]
13	p-Cymene	$C_{10}H_{14}$	134.22	[52]
14	Limonene	$C_{10}H_{16}$	136.23	[52]
15	1,8-Cineole	$C_{10}H_{18}O$	154.25	[52]
16	[Z]-β-Ocimene	$C_{10}H_{16}$	136.23	[52]
17	[E]-β-Ocimene	$C_{10}H_{16}$	136.23	[52]
18	γ-Terpinene	$C_{10}H_{16}$	136.23	[52]
19	α-Terpinolene	$C_{10}H_{16}$	136.23	[52]
20	Linalool	$C_{10}H_{18}O$	154.25	[52]
21	1-Octen-3 yl acetate	$C_{10}H_{18}O_2$	170.25	[52]
22	3-Octanyl acetate	$C_{10}H_{20}O_2$	172.26	[52]
23	Allo-ocimene	$C_{10}H_{16}$	136.23	[52]
24	α-Terpineol	$C_{10}H_{18}O$	154.25	[52]
25	Nerol	$C_{10}H_{18}O$	154.25	[52]
26	Carvone	$C_{10}H_{14}O$	150.22	[52]
27	α-Gurjunene	$C_{15}H_{24}$	204.35	[52]
28	Germacrene D	$C_{15}H_{24}$	204.35	[52]
29	α-Amorphene	$C_{15}H_{24}$	204.35	[52]
30	Elemol	$C_{15}H_{26}O$	222.37	[52]
31	Viridiflorol	$C_{15}H_{26}O$	222.37	[52]
32	γ-Eudesmol	$C_{15}H_{26}O$	222.37	[52]
33	B- Eudesmol	$C_{15}H_{26}O$	222.37	[52]
34	A- Eudesmol	$C_{15}H_{26}O$	222.37	[52]
35	(3R,5S,6R)-3,5,6-Trihydroxy-1,1,5-trimethylcyclohexyl-8-butyn-9-one	$C_{13}H_{20}O_4Na$	263.1254	[53]
36	(8E,9R)-Ethyl-7-(3S,5R,6S)-3,6-dihydroxy-1,1,5-trimethylcyclohexyl-9-hydroxybut-8-enoate	$C_{15}H_{26}O_5Na$	309.1672	[53]
37	(3R)-3-O-β-D-Glucoside-6′-D-apiose-β-ionone	$C_{24}H_{38}O_{11}Na$	525.2306	[53]
38	4-O-β-D-Rutinosyl-3-methoxyphenyl-1-propanone	$C_{22}H_{32}O_{12}Na$	511.1786	[53]
39	1-O-β-D-Rutinosyl-2(R)-ethyl-1-pentanol	$C_{19}H_{36}O_{10}Na$	447.2201	[53]
40	(R)-(−)-Dehydrovomifoliol	$C_{13}H_{18}O_3$	222.28	[53]
41	Blumenol C	$C_{13}H_{22}O_2$	210.31	[53]
42	Blumenol A	$C_{13}H_{20}O_3$	224.30	[53]
43	Icariside B1	$C_{19}H_{30}O_8$	386.4	[53]
44	Loliolide	$C_{11}H_{16}O_3$	196.24	[53]
45	(−)-Epiloliolide	$C_{11}H_{16}O_3$	196.24	[53]
46	Cubenol	$C_{15}H_{26}O$	222.37	[54]

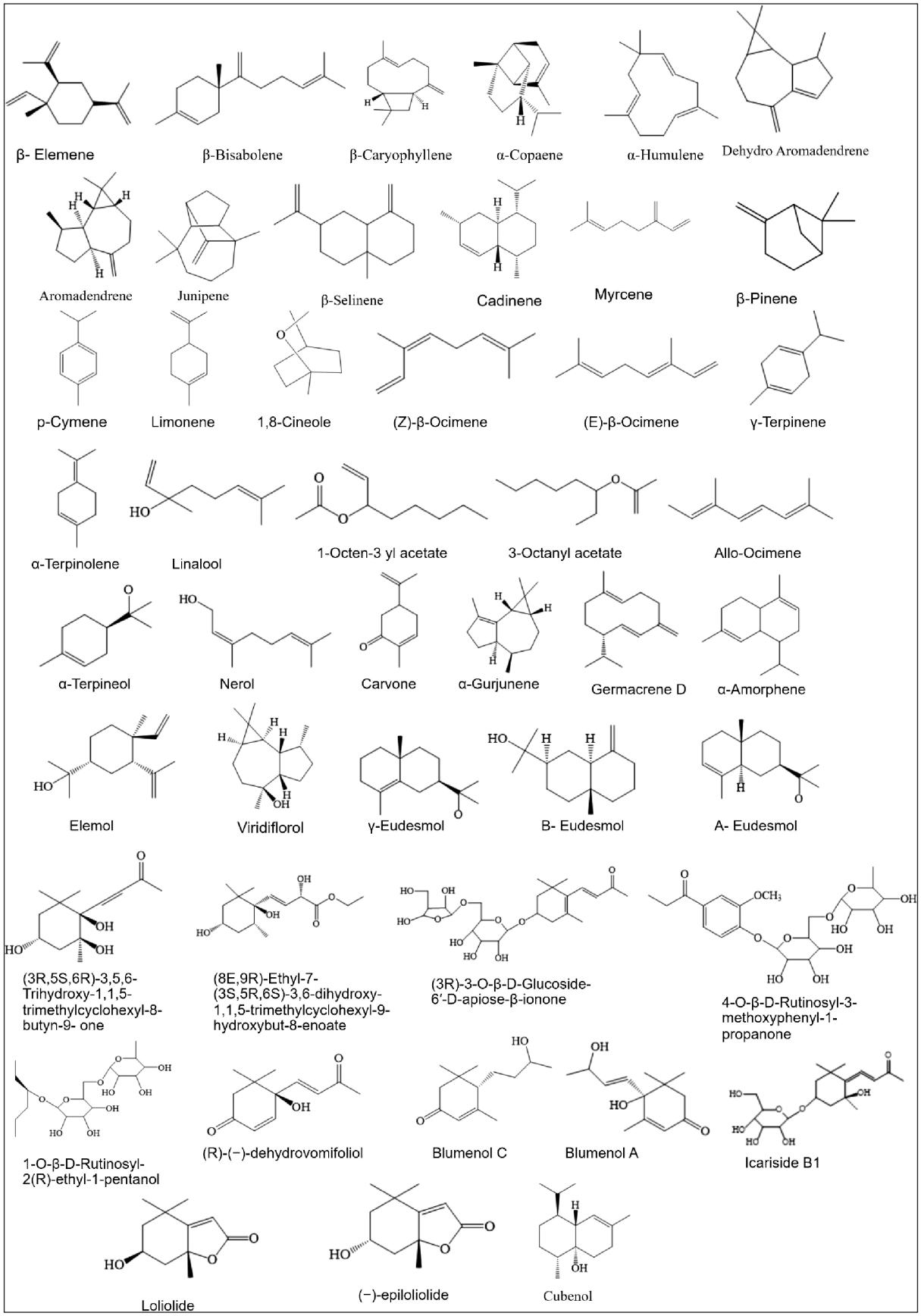

Figure 5. Structures of terpenoids from *M. koenigii* (L.) Spreng.

the β-carotene-linoleic acid method. Among the various extracts, *M. koenigii* oleoresin exhibited a maximum activity of 83.2% at 100 ppm, while methanol and water extracts showed activities of 16.7% and 11.3%, respectively. Subsequently, butylhydroxyanisole (a synthetic antioxidant) exhibited 90.2% activity at the same concentration [96]. The ethanol extract obtained from the leaves demonstrated activity against free radical scavenging as tested using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) and NO methods [97]. The ethanol extract also showed high antioxidant activity with an inhibition value of 63.54% in the DPPH assay [98].

Wound healing effect

Murraya koenigii leaf has been found to possess wound-healing activity by reducing epithelialization and supporting collagen synthesis [7]. In addition, the ethanol extract of its leaves exhibited wound-healing activity in excision and incision wound models in male rats [99].

Antipyretic activity

Regarding its antipyretic effects, this study has shown that the ethanol extract derived from *M. koenigii* leaves has antipyretic activity. This was demonstrated in fever-induced rats using intraperitoneal administration of brewer's yeast [100] and pyrexia induction methods comparable to paracetamol [101]. Furthermore, the ethanol extract from the leaves also exhibited significant antipyretic activity with the PG1-induced hyperpyrexia method in rabbits [102].

Table 5. Flavonoid reported from *M. koenigii* (L.) Spreng.

No.	Compound name	Molecular formula	Molecular weight	References
1	Quercetin	$C_{15}H_{10}O_7$	302.23	[55]
2	Apigenin	$C_{15}H_{10}O_5$	270.24	[55]
3	Kaempferol	$C_{15}H_{10}O_6$	286.24	[55]
4	Rutin	$C_{27}H_{30}O_{16}$	610.5	[55]
5	Catechin	$C_{15}H_{14}O_6$	290.27	[55]
6	Myricetin	$C_{15}H_{10}O_8$	318.23	[55]

Immunomodulatory activity

The water extract of *M. koenigii* leaf possesses both specific and nonspecific immunomodulatory activities [103]. The immunomodulatory and anti-inflammatory activities are characterized by the expression of ILs-2, 4, 10, and TNF-α [104].

Hepatoprotective activity

In terms of hepat`oprotective activity, experimental studies have demonstrated that *M. koenigii* extract offers protection against chronic liver disorders [104]. The hepatoprotective compounds identified in this context include carbazole alkaloids such as mahanimbine, girinimbine, isomahanimbine, murrayazoline, and mahanine [15].

Long-term alcohol consumption is a prevalent and significant factor leading to liver failure and death. Due to the lack of reliable hepatoprotective drugs, the situation becomes more complex. This encourages patients to choose and turn to complementary and alternative medicines to address and handle hepatic complications. The tannins and carbazole alkaloids found in the aqueous extracts showed impressive hepatoprotective effects against ethanol-induced liver toxicity, comparable to the standard drug L-ornithine L-aspartate [105].

Anthelmintic activity

The leaf of *M. koenigii* has shown anthelmintic effects on the eggs and larvae of *Haemonchus contortus* [106,107]. In addition, ethanol and water extracts of the leaves exhibit anthelmintic effects comparable to the standard drug piperazine against *Pheretima posthuma* [108]. Ethanol and water extracts from *M. koenigii* roots also exhibit anthelmintic activity against *Eudrilllus eugeniae* [109].

Antimicrobial activity

Regarding its antimicrobial activity, various extracts from *M. koenigii* have been reported to exhibit antimicrobial activity against Gram-positive bacteria, Gram-negative bacteria, and fungi, assessed through *in vitro* methods such as agar well diffusion and disk diffusion. Hexane, methanol, and chloroform extracts from *M. koenigii* roots exhibit antimicrobial activity

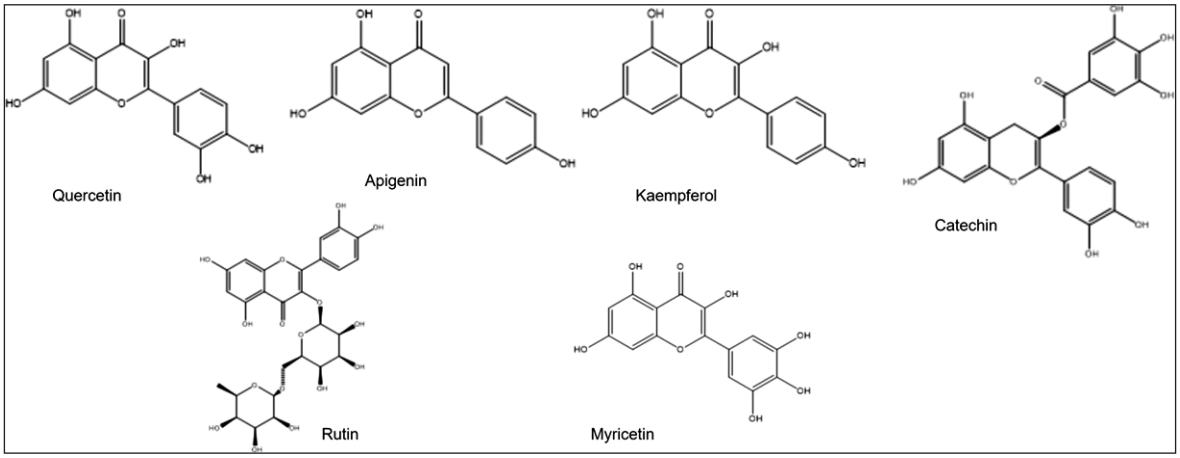

Figure 6. Structures of flavonoid from *M. koenigii* (L.) Spreng.

against *Bacillus subtilis, Escherichia coli, Staphylococcus aureus,* and *Salmonella typhi,* as well as fungi such as *Aspergillus niger, Candida albicans,* and *Trichophyton rubrum* [110]. The ethanol leaf extract of *M. koenigii* shows antibacterial activity against *Staphylococcus*, *E. coli*, *Streptococcus*, *Proteus*, *Klebsiella pneumoniae,* and *Pseudomonas aeruginosa* with clear inhibition zones comparable to antibiotics such as *amikacin* and *gentamicin*, although not effective against *K. pneumoniae* and *P. aeruginosa* [111].

Derivatives of benzoisofuranone and carbazole alkaloids obtained from the stem bark of *M. koenigii* also possess antibacterial and antifungal activities [9]. In addition, the ethanol leaf extract exhibits antifungal activity against *Trichophyton mentagrophytes* and *Microsporum gypseum* [112].

Antiulcer activity

The water extract of the leaves at doses of 250 and 400 mg/kg inhibits gastric lesions induced by nonsteroidal anti-inflammatory drugs and pylorus ligation models [113].

Table 6. Other compounds reported from *M. koenigii.*

No.	Compound name	Molecular formula	Molecular weight	References
1	Heraclenin	$C_{16}H_{14}O_5$	286.28	[56]
2	Imperatorin	$C_{16}H_{14}O_4$	270.28	[57]
3	Iso menthone	$C_{10}H_{18}O$	154.25	[58]
4	Z-Jasmone	$C_{11}H_{16}O$	164.24	[52]
5	Lutein	$C_{40}H_{56}O_2$	568.9	[59]
6	Linalyl acetate	$C_{12}H_{20}O_2$	196.29	[60]
7	Lavandulyl acetate	$C_{12}H_{20}O_2$	196.29	[60]
8	Myrtenyl acetate	$C_{12}H_{18}0_2$	194.27	[52]
9	Neryl acetate	$C_{12}H_{20}O_2$	196.29	[52]
10	Geranyl acetate	$C_{12}H_{20}O_2$	196.29	[52]
11	Menthol	$C_{10}H_{20}O$	156.26	[60]
12	Tocopherol	$C_{29}H_{50}O_2$	430.7	[48]
13	Nicotinic acid	$C_6H_5NO_2$	123.11	[61]

Antidiarrheal activity

The water extract of the leaves exhibits antidiarrheal activity in models of castor oil-induced diarrhea, charcoal meal test, and prostaglandinE2-induced diarrhea [114,115]. Subsequently, koenimbine obtained from *M. koenigii* seeds exhibits antidiarrheal activity in castor oil-induced diarrhea in rats [37].

Antiobese activity

The ethanol leaf extract of *M. koenigii*, administered orally to male Wistar rats for 30 days, effectively reduces body weight, cholesterol, triglycerides, and controls glycemic levels [116].

Neuroprotektif activity

The ethanol leaf extract of *M. koenigii* inhibits brain aging in diabetic rats [117]. The extract also improves memory in rats with chronic partial global cerebral ischemia [118]. In addition, mahanimbine exhibited potential neuroprotective properties against lipopolysaccharide-induced nerve inflammation [119].

Antitrichomonal activity

Carbazole alkaloids and their derivatives from the leaves have activity against *Trichomonas gallinae*. Girinimbin and girinimbilol are the most active compounds with IC_{50} values of 1.08 and 1.20 mg/ml [120].

Toxicity test

The methanol extract of *M. koenigii* leaf exhibited moderate toxicity in rats, with an lethal dose (LD_{50}) value of 316.23 mg/kg body weight, causing liver inflammation at higher doses [121]. However, no signs of death or morbidity were observed in male or female rats given ethanol leaf extract (300 and 500 mg/kg) for 28 days. At a dose of 900 mg/kg, there were no deaths, but congestion, hemorrhage, and lymphocyte infiltration were noted [122]. Other studies have shown that leaf powder and methanolic leaf extract are safe up to 9,000 mg/kg doses in rats [123]. Another study found no signs of death or

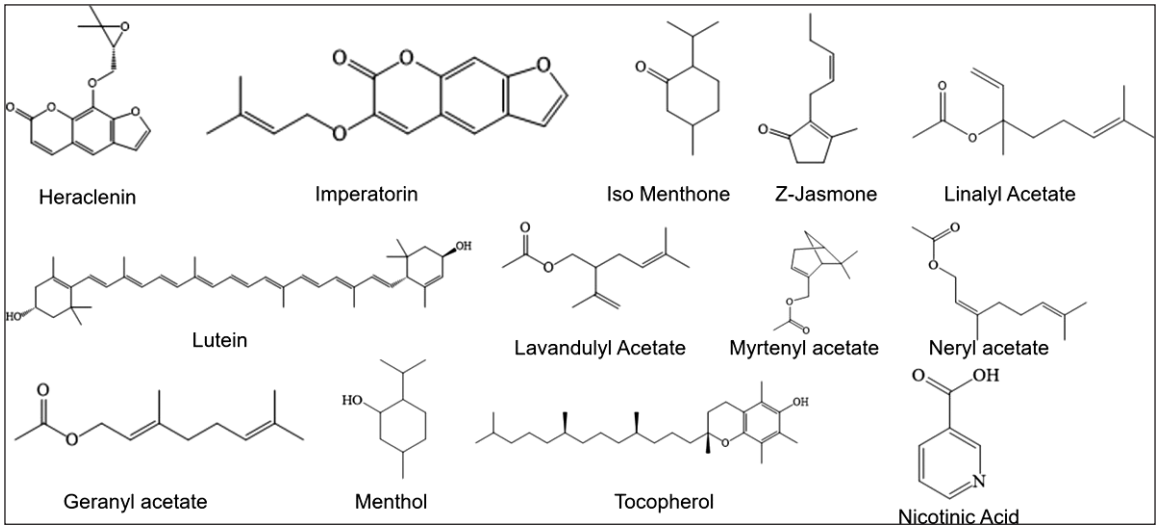

Figure 7. Structures of another compound from *M. koenigii* (L.) Spreng.

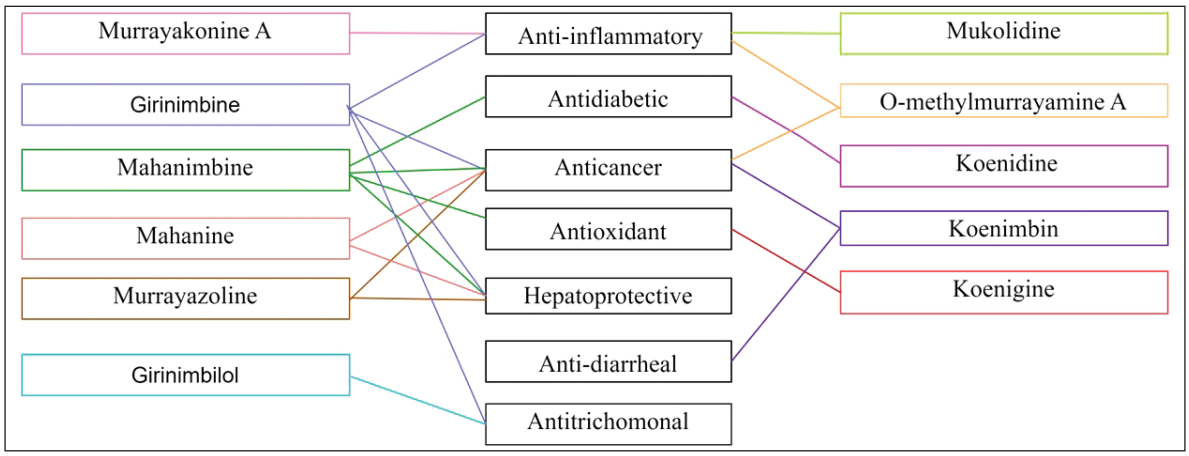

Figure 8. Relationship between chemical compounds from *M. koenigii* (L.) Spreng and their pharmacological effects.

toxicity at an LD_{50} value of 200 mg/kg/day for methanol extract of *M. koenigii* [124].

Ethanol leaf extract at doses of 300 and 500 mg/kg for 28 days did not result in death or morbidity in male or female rats. At a dose of 900 mg/kg, it did not cause death but led to bleeding and lymphocyte infiltration. At a dose of 900 mg/kg, it did not cause death but led to bleeding and lymphocyte infiltration. This study concluded that consumption at a dose of 500 mg/kg is safe and does not cause structural organ damage [120]. Subsequently, rats given a magazine-enriched fraction at a single dose of 5,000 mg/kg body weight, 300–1,500 mg/kg body weight per day for 14 days, and 300 mg/kg body weight for 180 days showed no toxicity, mortality, or significant behavioral changes [124]. Azzubaidi *et al.* [123] stated that the LD_{50} of *M. koenigii* leaf extract is 200 mg/kg/day, and the safest extract dose should not exceed 50 mg/kg/day.

CONCLUSION

In conclusion, *M. koenigii* has been extensively studied, thereby contributing to the understanding of secondary metabolites and their biological activities in nature. Furthermore, alkaloids were observed to have been the dominant compounds from *M. koenigii,* followed by terpenoid and fenil propanoid. The literature reports showed that the plant exhibited various biological activities, such as anti-inflammatory, cytotoxic, antidiabetic, and antimicrobial activity. This study showed that most pharmacological activity studies are still limited to *in-vitro* and *in-vivo* screenings, with mechanisms of action, bioavailability, and pharmacokinetics not yet explored. Subsequently, further studies should focus on the isolation of phytochemical compounds guided by bioassays, formulation, and drug delivery methods, serving as the basis for drug discovery. This review focuses on scientific studies of the pharmacological effects of *M. koenigii*.

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AUTHOR CONTRIBUTIONS

YDF has equally contributed to conceptualization and writing. NF, and AN reviewed and edited. All authors have read and agreed to the published version of the manuscript.

CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

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