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Review article

Chemical constituents, usage and pharmacological activity of *Cassia alata*

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ABSTRACT

Cassia alata or locally known as Ketepeng Cina (Indonesia) and Gelenggang (Malaysia) has been used as a traditional medicine to treat various diseases, especially skin diseases. In addition, *C. alata* has been reported to have potential anti allergic, anti inflammatory, antioxidant, anticancer, antidiabetic, and antifungal. Metabolite compounds that have been isolated from *C. alata* include flavones, flavonols, flavonoids glycosides, alatinon, alanonal and β-sitosterol-β-D-glucoside. The compounds have been isolated mainly from the leaves. Further identification is needed to discover the secondary metabolites from other parts of the plant such as seed, flower and bark which are reported to have potent antibacterial and antifungal activity. Therefore, this article highlights the secondary metabolites and biological activity of this plant which has been shown to have pharmacological properties against selected diseases.

1. Introduction

Cassia alata is a plant originating from Argentina [1]. Commonly referred to as Candle brush, Candlestick, *Senna alata* and others [2]. In Indonesia *C. alata* is called as "ketepeng china". In other part of South Asia, *C. alata* has become a herbs plant to treat various diseases in many countries including France [3]. *C. alata* root can be used to treat rheumatism and laxative [4]. Seeds and leaves have high potency as fungicides and medicine for eczema in India [5]. *C. alata* can be used to reduce stomach pain during pregnancy, headaches and paralysis. *C. alata* extracts are used in the practice of traditional herbs medicine to cure skin diseases in some countries [6]. In Thailand, *C. alata* leaves are used to treat constipation. This can be done with fresh leaves pounded with water, garlic, red chalk and balm and then applied to skin infected with ringworm. Besides, the boiled shoots and leaves of *C. alata* can be used to clean the wound and act as anti-inflammatory agent [7]. In Indonesia (especially in South Sulawesi), leaves *C. alata* has been used traditionally to get rid of fungus on the skin which can cause hives and others by grinding or rubbing directly on the affected skin.

Several studies have been reported the biological activity of *C. alata*. Crude extract of *C. alata* leaf has very strong antioxidant activity with IC_{50} value of 2.27 μg/mL [8]. *n*-hexane leaf extract of *C. alata* showed strong anti-inflammatory potential by significantly reducing rat knee swelling (CFA) [9]. *C. alata* leaf extract was reported that possessed good antifungal activity against *Trichophyton verrucosum* and *Epidermophyton floccosum* as well as other microbes [10]. Secondary metabolite compounds in *C. alata* include alkaloids, saponins, steroids, flavonoids and terpenoids [11].

2. Botany

C. alata is a plant that can grow freely in the tropics. *C. alata* comes from the family of Fabaceae [2]. This plant has characteristic of unpleasant odor, stems erect (about 10–15 feet tall), skin of thin stems not spiked, leaves yellowish green and slightly wide. The flowers are bright yellow and form a race. The fruit is hard to resemble a brown pod when ripe and has brown seeds [1] (see Figure. 1).

3. Isolation of compounds

3.1. Leaf

C. alata has been reported to have diverse bioactive compounds in the leaves [12, 13, 14]. Chemical constituents of *C. alata* leaves have been reported from Pattalung Province, Thailand [15]. The leaves were dried and macerated for three days with methanol solvent to obtain methanol extract. The methanol extract was further fractionated using a liquid vacuum gel chromatography method and eluted using chloroform:methanol to obtain 6 fractions. The fractions were separated

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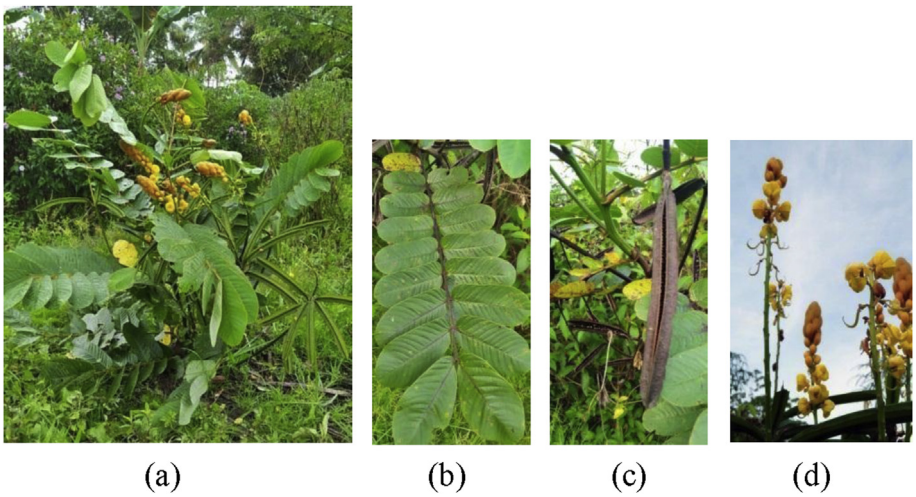


Figure 1. (a) All part of *Cassia alata*, (b) leaves, (c) fruit, (d) flower.

using column chromatography of LH-20 sephadex and eluted with methanol solvent to obtain 8 fractions. Fraction VII (yellow in colour) showed strong antioxidant activity. The structure identification was performed using IR, ^{1}H NMR dan ^{13}C NMR. The identification results indicated as a type of flavonol, namely **1** (kaempferol) [15]. In addition, **2** (kaempferol-3-*O*-β-D-glucopyranoside) has also been identified using HPLC [8].

In addition to flavonols, flavone compounds have been isolated from *C. alata* leaf ethanol extracts in the BCSIR area at Rajshahi Campus [16, 17]. Compound **3** was a flavone compound with the name of 3,5,7, 4′-tetrahydroxy flavone and **4** was 2,5,7,4′-tetrahydroxy isoflavones. The compound was obtained from an ethyl acetate fraction eluted with *n*-hexane and ethyl acetate that enhanced by its polarity. The resulting fraction was still have impurities, and therefore proceeded by purification with PTLC of 60G254 silica gel and eluted with the same eluent. The results showed two bright yellow bands with different Rf values [16, 17]. Other researchers also reported other types of flavonoid compounds, namely **5** (anthraquinone) and **6** (kaempferol 3-*O*-gentiobioside) [18]. GC/MS characterization results on *C. alata* leaves showed that there were 7 compounds including **7** ((6Z)-7,11-dimethyl-3-methylidenedodeca-1, 6,10-triene), **8** (4a,8-dimethyl-2-(prop-1-en-2-yl)-1,2,3,4,4a,5,6,8a-octahydronaphthalene), **9** (4,4,7a-trimethyl-5,6,7,7a-tetrahydro-1-benzofuran-2(4H)-one), **10** (3,7-dimethylocta-1,6-diene), **11** (hexadecanoic acid methyl ester), **12** (hexadecanoic acid), and **13** (octadecanoic acid methyl ester) [19]. Alkaloid compounds from *C. alata* leaves have also been identified, namely **14** (adenine) [20], **15** (Chrysoeriol), **16** (quercetin), **17** (5,7,4′-trihydroflavanone), **18** (kaempferol-3-O-beta-D-glucopyranosyl-(1→6)-beta-D-glucopyranoside), **19** (*n*-dotriacontanol), **20** (*n*-triacontanol), **21** (stearic acid), **22** palmitic acid [21], **23** diomestin [22], **24** (luteolin) [23], and **25** (1,3,5-trihydroxy-7-methylanthracene-9, 10-dione) [24].

3.2. Seed

C. alata seeds were reported to have many bioactive compounds [25]. The grain of *C. alata* was mashed and extracted by maceration method using ethanol solvent. The obtained extract was analyzed using TLC. Fractionation was performed by using Flash Column Chromatography eluted with a solvent enhanced by its polarity resulting in two types of flavonoid glycoside compounds ie **26** chrysoeriol-7-O-(2″-*O*-β-D-manno pyranosyl)-β-D-allopyranoside and **27** rhamnetin-3-*O*-(2″-*O*-β-D-mannopyranosyl)-β-D-allopyranoside [26]. Chemical compounds of *C. alata* seeds that analyzed by GC-MS were **28** (*n*-hexadecanoic acid), **29** (15-tetracosenoic acid), **30** (oleic acid), **31** (octadecanoic acid), **32** (2-methyl-1-octanol, pentanoic acid), and **33** (2-ethyl-1-decanol) [27]. In addition, **34** α-D-galactopyranosyl has also been identified [28].

3.3. Stem

The chopped *C. alata* stem were extracted with benzene and hot ethanol. The two extracts were combined and then mixed with silica gel. The fractionation was performed using column chromatography (60–120 mesh) to obtain the compound **35** (1,5,7-trihydroxy-3-methyl-anthraquinone) with orange crystalline [29].

3.4. Twig

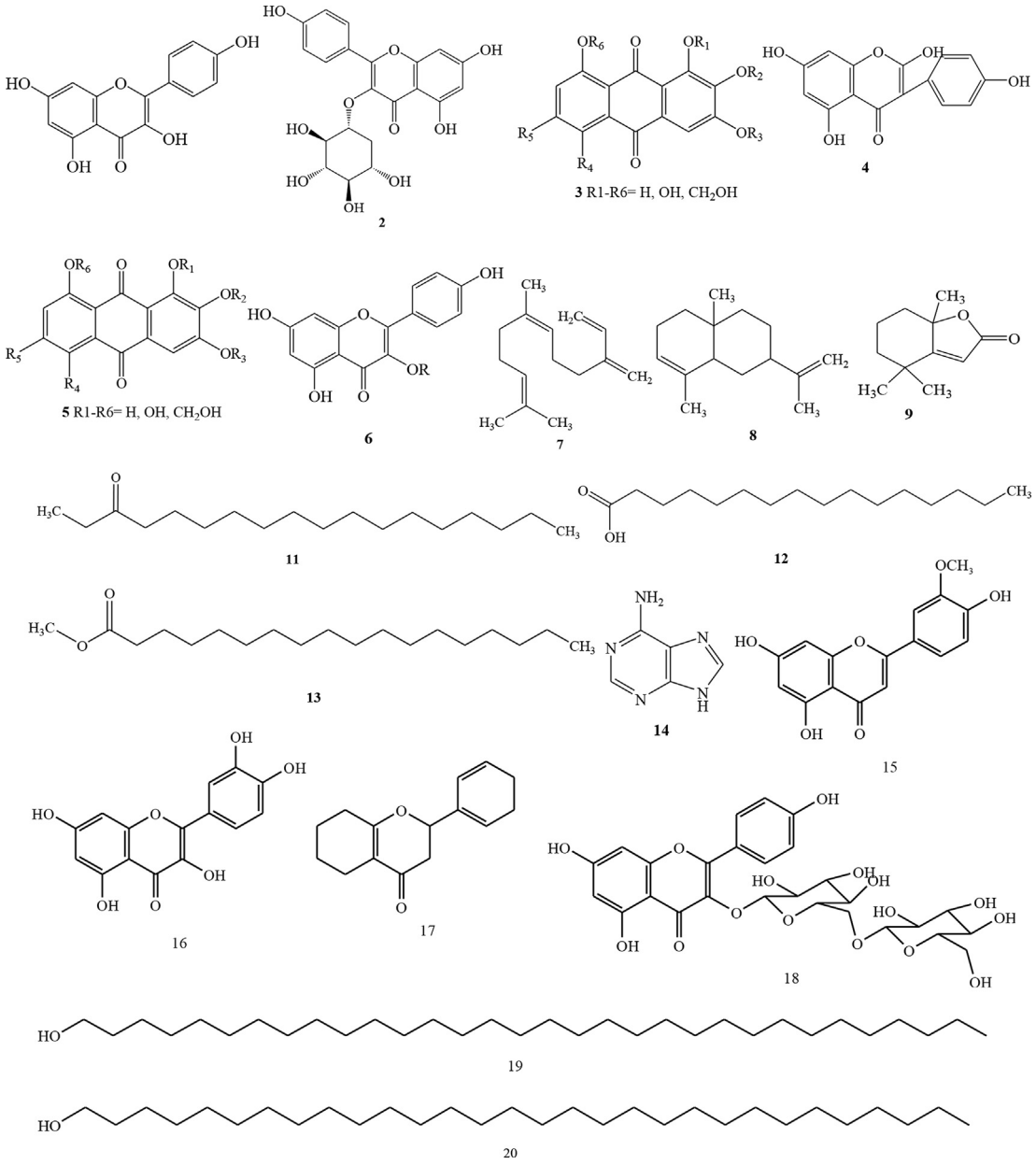
The chemical constituent of *C. alata* twigs has been reported. The characterization used 1D and 2D NMR spectra were performed on a Bruker AVANCE 300 or a Bruker FTNMR Ultra Shield 400 MHz. The isolated compounds were **36** (lunatin), **37** (7,4′-dihydroxy-5-methoxyflavone), **38** (luteolin), and **39** (trans-dihydrokaempferol) [22].

3.5. Root

Some anthraquinone compounds have been identified using high-performance liquid chromatographic method with photodiode arrays. The types of anthraquinone compounds were **40** (aloe-emodin), **41** (rhein), **42** (emodin) and **43** (chrysophanol) [30]. Others anthraquinone that have also been isolated were **44** (1,3,8-trihydroxy-2-methyl-anthraquinone), **45** (1,5-dihydroxy-8-metoxy-2-methyl-anthraquinone -3-O-β-D-(+)-glucopyranoside) [31] and **46** emodin (1,6,8-trihydroxy-3-methyl-anthraquinone) [31]. Alkaloid compounds from *C. alata* leaves have also been identified using ^{1}H-NMR, ^{13}C-NMR and MS [32]. In addition, **47** (physcion) has been identified from *C. alata* root [33]. Five compounds, **48** (ω-hydroxyemodin), **49** (ziganein), **50** (apigenin), and **51** (trans-resveratrol) were isolated from the *C. alata* roots [22].

3.6. Flower

Isolation of the compound on *C. alata* flower has been reported [34]. *C. alata* flowers were extracted with hot methanol solvent. The obtained extract was mixed with a number of silica and further dried. The extract was then fractionated with several types of eluent comparisons using chromatographic columns to obtain three types of compounds i.e stearic acid compounds **52** (alanonal) and **53** (β-sitosterol-β-D-glucoside) [34]. Furthermore, chemical compounds of flower of *C. alata* that analyzed by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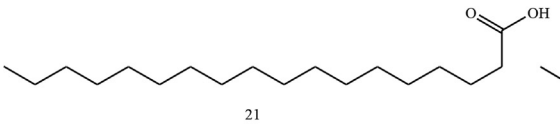

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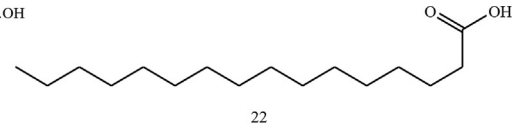

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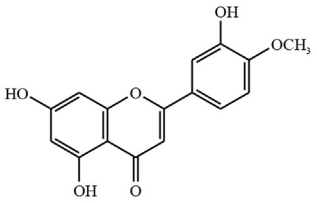

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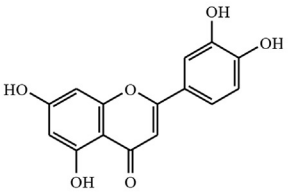

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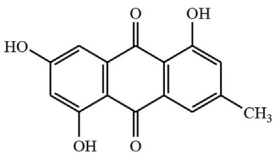

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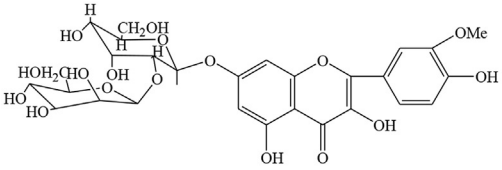

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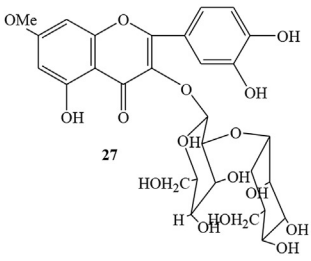

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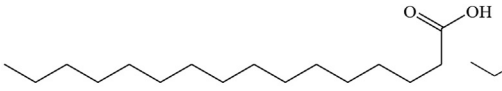

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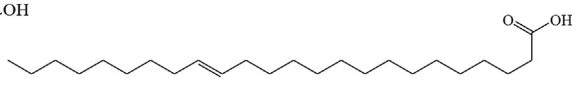

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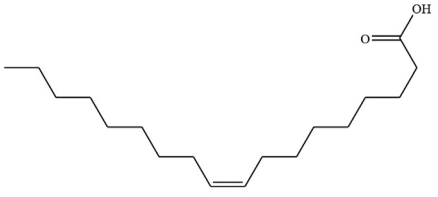

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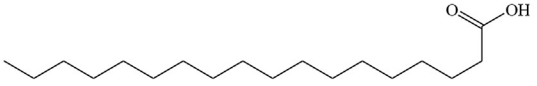

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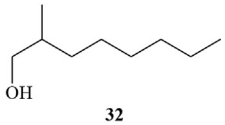

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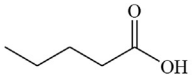

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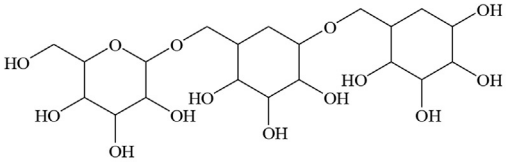

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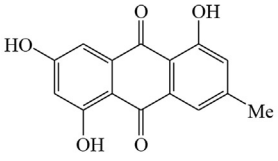

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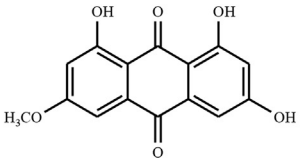

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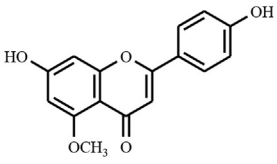

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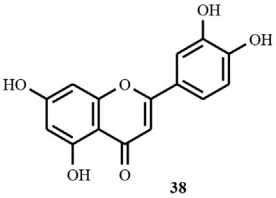

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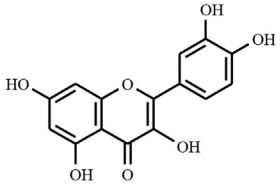

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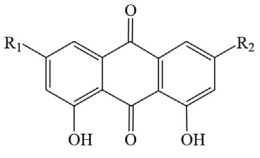

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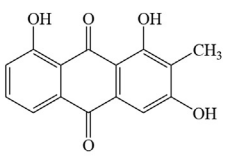
41 $R_1 = COOH$; $R_2 = H$
42 $R_1 = CH_3$; $R_2 = OH$
43 $R_2 = CH_3$; $R_2 = H$



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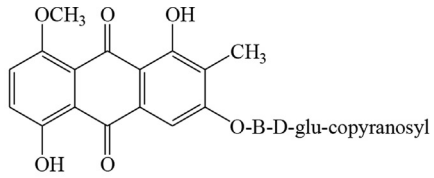

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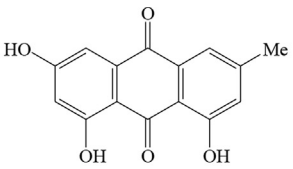

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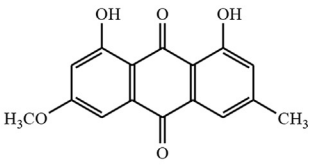

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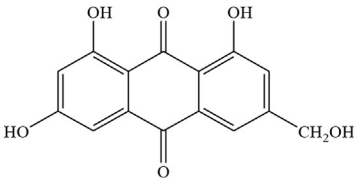

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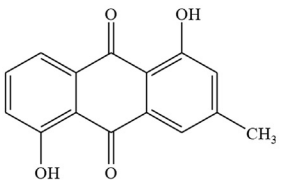

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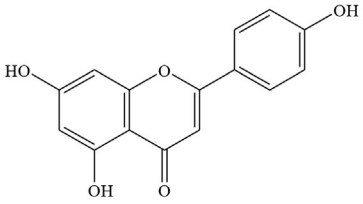

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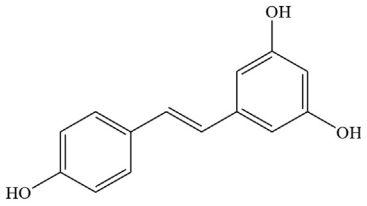

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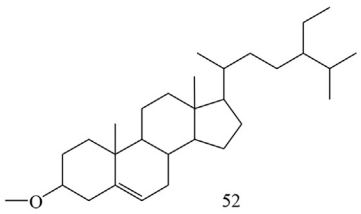

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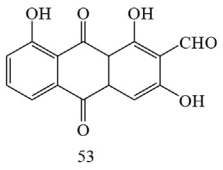

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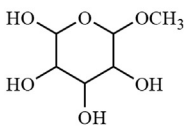

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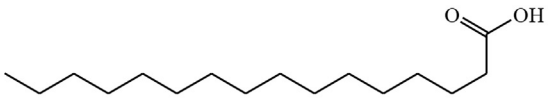

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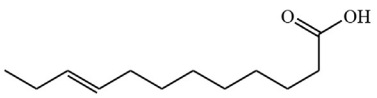

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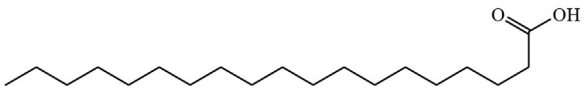

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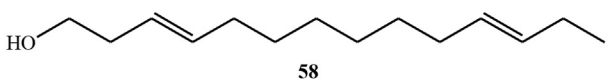

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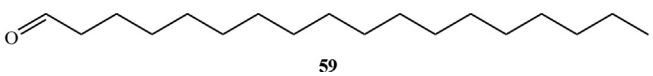

59

Table 1. Biological activity of *C. alata*.

Part of Plant	Biological activity	Method	Result	Reference
Leaf	Anti allergic	*In vivo* (mast cell stabilization)	At 200 mg/kg (75% inhibition) while rhein and kaemferol at 76% at 5 mg/kg.	[40]
		In vitro (lipoxygenase)	Extract hydrocalohol and rhein showed IC_{50} values of 90.2 and 3.9 μg/mL, respectively.	
	Anti inflammatory	Carrageenan-induced rat paw oedema model	The butanol fraction was the highest mean percent inhibition as 78.36% followed by ethyl acetate (58.21%) and methanol (20.89%) at 100 mg/kg as compared to Indomethacin (79.59%) at a dose of 10 mg/kg after 4 h of carrageenan injection.	[41]
		Concanavalin A-induced histamine, 5-lipoxygenase inhibition, cyclooxygenases (COX-1 and COX-2),	Strong inhibitory effects on Concanavalin A-induced histamine release from rat peritoneal exudate cells. The heat treated leaf extract had stronger inhibitory effects than the sun-dried leaf extract at low concentrations in the studies of Concanavalin A-induced histamine release, 5-lipoxygenase inhibition, and also inhibition of cyclooxygenases (COX-1 and COX-2), whereas K3G showed weak inhibitory effects on Concanavalin A-induced histamine release, 5-lipoxygenase, and COX-1.	[20]
		Oral gavage to CFA arthritic rats (500 mg/kg, n = 6)	Extract significantly (P = 0.0032) reduced knee circumference (swelling) in the CFA arthritic rats Extract significantly (P = 0.0032) reduced knee circumference in the CFA arthritic rats.	[9]
	Antioxidant	DPPH radical scavenging	Methanol extract gave inhibition ED_{50} of 28.50 μg/ml, while BHT has ED_{50} 14.17 ± 1.38 μg/ml.	[15]
		DPPH radical scavenging	Methanol extract gave IC_{50} concentration lower (54 ± 2.20) than BHT standard (72 ± 2.20).	[42]
		DPPH, Nitric Oxide (NO), Deoxiribose (DOR)	Methanol extract: DPPH (% scavenging activity 58.80 ± 2.02), Nitric Oxide (NO) (% scavenging activity 35.01 ± 1.91) and Deoxiribose (DOR) (% scavenging activity 50.52 ± 0.77).	[11]
Leaf	Antioxidant	DPPH radical scavenging Lipid peroxidation Hydroxyl radical	DPPH (IC_{50} 71.35 ± 0.32 μg/ml). Lipid peroxidation (IC_{50} 38.17 ± 1.2 μg/ml). Hydroxyl radical (IC_{50} 95.46 ± 0.79 μg/ml).	[43]
		Ammonium thiocyanate	Acetone extract gave % inhibition 37.02 ± 0.45 and total phenolic 23.29 + 0.89 mg/g.	[44]
		DPPH radical scavenging	Essential oil 95.2% linalool (23.0%), borneol (8.6%) and pentadecanal (9.3%) were major constituents. The antioxidant activity of the oil was lower than butylated hydroxytoluene (BHT).	[46]
	Anticancer and antitumor	Brine Shrimp Lethality by using shrimp larvae (*Artemia salina* Leach)	The cytotoxicity of ethanol extract of *C. alata* seed and gallic acid had LC_{50} value 5.29 and 4.53 ppm, respectively.	[49]
		In vitro MMT	The extract was fractionated and then tested against five types of human cancer cells. The results showed that isolate f6I had selectivity in MCF-7, T24, and Col 2 cells with IC_{50} values of 16, 17, and 17 μg/ml, respectively.	[50]
		In vitro MMT	The cytotoxicity of *n*-hexane *C. alata* leaves extract showed selectivity to OV2008 cancer cells with IC_{50} 160 μg/ml. The cytotoxicity shown by *C. alata* is caused by flavonoid compounds, kaempferol which was the compound of *n*-hexane *C. alata* extract.	[51]
		WST-1 cytotoxicity	Hydromethanolic leaf extract of *C. alata* was reported cytotoxic to the K562 leukaemia cell line.	[52]
		Bearing carcinomatous cells on Nude mice	At 100 and 200 mg/kg body weight, the levels of MDA decreased significantly (3.44 ± 0.76 to 1.97 ± 0.48) while the glutathione and the activities of CAT and SOD increased significantly.	[53]
	Antidiabetic	*In vitro* by inhibitory assay against α-Glucosidase	Ethanol extract of *C. alata* (63.75 ± 12.81 μg/mL) was better to inhibit α-glucosidase than the standard acarbose drug (107.31 ± 12.31 μg/mL), the active fraction inhibiting α-glucosidase ie chloroform, ethyl acetate and *n*-butanol with IC_{50} of 44.25 ± 10.23, 2.95 ± 0.47 and 25.80 ± 2.4301 μg/ml respectively, and pure isolates of the *n*-butanol fraction (kaemferol 3-*O*-gentiobioside) inhibited α-glucosidase with IC_{50} 82.5 ± 13.7 μg/ml.	[54]
		Streptozotocin-induced hyperglycemia in rats	The mean decreased blood sugar levels were 277.1 ± 0.8, 267.7 ± 0.9 and 259.1 ± 2.7 % at each dose of 100, 200 and 400 mg/kg.	[55]
Leaf	Antidiabetic	Blood glucose levels used albino Swiss Webster mice	Ethyl acetate extract of *C. alata* showed an effective result as a antidiabetic agent with percent decrease of blood glucose level (56.7%) while CMC control (38.0%).	[56]

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Table 1 (*continued*)

Part of Plant	Biological activity	Method	Result	Reference
	Choleretics	Bile secretion of rats	The activity of choleretic extract of *C. alata* at 15 mg/kg had good activity than Hebucol ND. But at high doses, plants dispose to inhibit bile secretion.	[57]
	Analgesic	*In vivo* using an albino rat by the method of tail clamping, tail wagging, tail immersion and the reflexes of writhing with induction of acetic acid	The analgesic effect of *C. alata* was ignificantly better at doses of 400 mg/kg than at doses of 200 and 100 mg/kg. The analgesic effect produced by kaempferol 3-*O*-sophoroside was greatest in ±120 min. Assay writhing of acetic acid at 400 mg/kg *C. alata* showed a considerable increase in analgesic effect (56.4%) rather than dosage of 200 and 100 mg/kg (46% and 35.9%) while the percentage of inhibitory stretching produced by kaempferol 3-*O*-sophoroside was close to 100 mg/kg *C. alata* extract (36.9%).	[58]
	Antimicrobial	Disk diffusion	Methanol extract inhibited *Salmonella thypi*, *Proteus mirabilis, Bacillus coagulans*, *Micrococcus luteus.* Petroleum ether extract inhibited the growth of *B. coagulans.* Dichloromethane extract inhibited the growth of *Lactobacillus casei*, *Staphylococcus epidermidis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis.* Ethyl acetate extracts inhibited the growth of *B. coagulans* and *T. vaginalis.*	[59]
		Disk diffusion	The methanol extract of *C. alata* leaf inhibited *Actinomyces bovis and Mucor* sp.	[60]
			The ethanol extract inhibited the growth of *Escherichia coli* bacterium and *Rhizopus* sp., *Aspergillus niger*, *Saccharomyces* fungi.	[61]
		Agar well diffusion	The acetone extract inhibited *Proteus vulgaris* and *Bacillus subtilis.*	[62]
		Disk diffusion	Water extract inhibited *Stahylococcus aureus* bacterium.	[63]
Leaf	Antimicrobial	Disk diffusion	The *n*-hexane extract had been reported to inhibit the growth of *Trichopyton simii*, *E. floccosum*, *Candida albicans.* Methanol extract inhibited *T. metagrophytos*, *T. simii*, *Curvularia hunata*, *C. albicans.* Ethanol extract inhibited *Trichophyton rubrum, Trichophyton metagrophytos, T. simii, Trichophyton tonsuran*, *E. floccosum*, *C. hunata*, *C. albicans, Cryptococcus neoformans, Microsporum canis*, *Microsporum gypseum*, *Penicillium notatum.*	[68, 68, 69, 70, 71, 72]
Leaf	Antiviral	*In vivo* with male white rats with various doses (100 mg/kg body weight, 300 mg/kg BW and 900 mg/kg BW	At 21st day dose of 300 mg/kg body weight and 900 mg/kg body weight can have an effect on shortening time bleeding, blood clots and increase the number of mice platelets white male.	[75]
		The toxicity was measured by MTT assay	*C. alata* leaves extract and butanol subfraction were reported to have strong antiviral activity against DENV-2 with the IC_{50} 0.0256 and 6.47 μg/ml and CC_{50} 323.45 and 645.8 μg/ml, respectively.	[76]
		In vitro MMT	Several extracts (methanol, chloroform, ethyl acetate, *n*-butanol, and aqueous) from *C. alata* leaves had activity against rotavirus (RV) infection	[77]
	Antiucler	Pylorus ligation and ethanol induced ulcer models in experimental rats	Ethanolic extract of *C. alata* leaves at a dose of 150 and 300 mg/kg produced significant inhibition of the gastric lesions induced by pylorus ligation induced ulcer and ethanol induced gastric ulcer. The extract (150 mg/kg and 300 mg/kg) showed sgnificant ($p < 0.05$) reduction in gastric volume, free acidity and ulcer index as compared to control.	[78]
	Hepatoprotective	Hepatic injury in albino rats	The alcoholic extract of *C. alata* leaves had been reported to have hepatoprotective activity. The experiment showed that the methanol extract had activity against Paracetamol induced hepatic injury in albino rats. Additionally, pretreatment of the extract reduced the biochemical markers of hepatic injury like serum glutamate pyruvate transaminase (SGPT), serum oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), total bilirubin and gamma glutamate transpeptidas from paracetamol induced liver damage.	[79]
Leaf	Antidepressant	Forced Swim Test (FST) and Tail Suspension Test (TST)	*C. alata* showed significant decrease in the time of immobility in both the standard drug (22.0 ± 0.26 s) and the test extract (21.25 ± 0.12 s) compared to the control group (62.5 ± 0.54 s). The leaf extracts of *C. alata* (200 mg/kg) showed an increased effect compared to the standard drug fluoxetine (10 mg/kg). Therefore, a significant decrease in the immobility of mice in test extract (59.6 ± 2.23 s) and a standard drug (57 ± 3.5 s) in comparison to the control group (153.4 ± 1.97 s) after administration of the standard and	[80]

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Table 1 (*continued*)

Part of Plant	Biological activity	Method	Result	Reference
			test extract. These results clearly indicated that aqueous leaf extracts of *S. alata* exhibited a strong antidepressant activity similar to that of the control drug of administration of the standard (Imipramine).	
Leaf	Antimalarial	WHO microtest assay (Mark III)	The result showed that *C. alata* leaves had activity against the 3D7 strain of the *Plasmodium falciparum* parasite with IC_{50} 17.270 μg/ml. While the IC_{50} of artesunate-amodiaquine was 0.313 μg/ml.	[81]
	Antihelmintic	Scanning electron microscope studies (SEM)	The ethanol extract at 40 mg/ml, paralysis occurred at 1.68 ± 0.06 h which is comparable with praziquantel (1.18 ± 0.04 h) at 0.001 mg/ml. The post-paralytic time was comparatively shorter in all concentrations of *C. alata*, while it took more time in all concentrations of praziquantel. However, the control parasite survived up to 69.22 ± 0.23 h.	[82]
	Cardiovascular	DPPH and lipid peroxidation	In hyperglycemic rats, the aorta and heart shown significant increased in lipid peroxidation, decreased in total antioxidant activity (DPPH) and decrease in antioxidant catalase activity. Furthermore, administration of *C. alata* leaf aqueous extract to hyperglycemic rats reduced lipid peroxidation (MDA levels), increased in total antioxidant activity and antioxidant catalase activity as well as reduced in the blood glucose level.	[83]
	Ansthetic	ALT (Alanine Transaminase), AST (Aspartate Transaminase) and ALP (Alkaline Phosphatase)	The result showed that AST, ALT and ALP were reduced in groups 3 to 7 compared to group 2, while ALP and ALT were significantly reduced ($P < 0.05$) when treated with 4000 mg/kg body weight.	[84]
Seed	Antioxidant	DPPH radical scavenging and ferric reducing	The antioxidant IC_{50} values of seed in DPPH and ferric reducing were 4.01 ± 0.11 and 0.40 ± 0.21 μmol/mg, respectively.	[23]
	Thrombolitic	*In vitro* thrombolytic activity	The extract showed potent thrombolytic activity against negative control (water).	[21]
	Anticancer	Brine Shrimp Lethality by using shrimp larvae (*Artemia salina* Leach)	The cytotoxicity of ethanol extract of *C. alata* seed and gallic acid had LC_{50} value 4.31 and 4.53 ppm, respectively.	[49]
	Antimicrobial	Disk diffusion	The methanol extract of *C. alata* seeds inhibited the growth of *Sarcina lutea* and *Klebsiella pneumonia.*	[57]
Stem Bark	Antimicrobial	Disk diffusion	Methanol extract inhibited *S. typhi* bacterium growth. Petroleum ether extract inhibited bacterial growth of *B. megaterium*, *Spectrococcus faecalis*, *S. typhi.* Dichloromethane extract inhibited bacterial growth of *B. coagulans.* Ethyl acetate extract inhibited bacterial growth *B. cereus, B. megaterium, St. pneumoniae, K. pneumoniae, N. gonorrhoeae* and *S. typhi.*	[59]
		Disk diffusion	Ethanol and water extracts inhibited *C. albicans.*	[52]
Root	Antioxidant	DPPH and ABTS	Ethanol extract had IC_{50} value for DPPH and ABTS assays 45.18 and 39.14 μg/ml, respectively.	[48]
	Antimicrobial	Disk diffusion	Methanol root extract inhibited *B. cereus, B. subtilis, S. albus, S. aureus, S. epidermidis, St. faecalis, E. coli, S. typhi,* and *S. typhymurium.* Petroleum, chloroform, and ethyl acetate fractions of *C. alata* root had activity against *B. cereus, B. coagulans, B. megaterium, B. subtilis, L. casei, M. luteus, M. roseus, S. albus, S. aureus, S. epidermidis, St. faecalis, St. pneumoniae, S. mutans, Agrobacterium tumefaciens, Citrobacter freundii, Enterobacter aerogenes, E. coli, K. pneumoniae, N. gonorrhoeae, P. mirabilis, P. vulgaris, P. aeruginosa, S. typhi, S. typhymurium, Serratia marcescens.*	[59]
		Broth dilution	The water, methanol, and chloroform extracts of *C. alata* had activity against *S. aureus, E. coli, S. pyogenes, P. aeruginosa,* and *P. mirabillis.*	[66]
		Broth dilution	The ether and methanol extracts had activity against clinically resistant *N. gonorrhoeae.*	[67]
Pod	Antioxidant	DPPH radical scavenging	Methanol extract gave ED_{50} 100.18 μg/ml, while BHT had 14.17 ± 1.38 μg/ml.	[15]
Flower	Antioxidant	Protective gainst carbon tetrachloride (CCl_4)	After administration with CCl_4, the extract more active than CCl_4. In the extract, serum aspartate aminotransferase and alanine aminotransferase decreased significantly ($P \leq 0.05$) in rats.	[45]
				[23]

(*continued on next page*)

Table 1 (*continued*)

Part of Plant	Biological activity	Method	Result	Reference
		DPPH radical scavenging and ferric reducing	The antioxidant IC_{50} values of flower in DPPH and ferric reducing were 4.16 ± 0.21 and 0.33 ± 0.51 μmol/mg, respectively.	
		DPPH radical scavenging	Methanol extract gave ED_{50}175.36 μg/ml, while BHT had 14.17 ± 1.38 μg/ml.	[15]
		DPPH radical scavenging	Aqueous extract had EC_{50} 823 μg/ml.	[47]
	Antimicrobial	Disk diffusion	Methanol extract inhibited *E. coli* and *C. albicans*.	[73]
		Disk diffusion	The extracts of water, methanol, chloroform and petroleum ether of *C. alata* flowers at 500 mg/mL were active against *S. aureus, E. coli, P. vulgaris, P. aeruginosa, B. subtilis* and *C. albicans*.	[70]
		Broth dilution technique	The crude extract *C. alata* flower at 500 μg/mL had activity against *S. aureus, St. faecalis, M. luteus, B. subtilis* and *P. putida*. But at concentration above 1000 mg/mL, the extract inactive against *E. coli, P. vulgaris, P. aeruginosa, S. marcescens*, and *P. fluorescens*.	[65]
		Disk diffusion	Methanol extract inhibited *S. typhi* growth. Petroleum ether extract inhibited the growth of *B. megaterium*. Dichloromethane extract inhibited the growth of *B. cereus* and *S. epidermidis*. Ether extract inhibited *N. gonorrhoeae*.	[72]
Flower	Antimicrobial	Disk diffusion	The water, methanol and chloroform of *C. alata* root extracts had activity against *S. aureus, E. coli, S. pyogenes, P. aeruginosa and P. mirabilis*.	[71]
		Broth dilution method	Methanol extract and fraction inhibited the growth of fungi *A. brevipes, Penicillium* sp., *Geotricum candidum, C. utlis*.	[74]
		Disk diffusion	Methanol extract inhibited *S. epidermidis*. Chloroform extract inhibited *B. subtilis*. Petroleum ether extract inhibited the growth of *B. coagulans*. Dichloromethane extract inhibited the growth of *L. casei, S. epidermidis, N. gonorrhoeae* and *T. vaginalis*. Ethyl acetate extracts inhibited the growth of *B. coagulans* and *T. vaginalis*.	[64]

GC-MS were **54** (β-d-mannofuranoside), **55** (*n*-hexadecanoic acid), **56** (9-dodecenoic acid), **30** (oleic acid), **57** (nonadecanoic acid), **58** (3, 11-tetradecadien-1-ol), and **59** (octadecanal) [27].

4. Pharmacological effect

Biological activity has been known contained in plants [35, 36], such as antidiabetic, antioxidant, antimicrobial, etc. [37, 38, 39]. *C. alata* has biological activity which is summarized in Table 1. This present review provided the biological activities of *C. alata* as antiallergic, anti-inflammatory, antioxidant, thrombolytic, anticancer and antitumor, antidiabetic, choleretic, analgesic, antimicrobial, antiviral, antiucler, hepatoprotective, antidepressant, antimalarial, anthelmintic, cardiovascular and anasthetic. The plant has been reported not to have side effect in clinical medicine.

5. Clinical effect

The therapeutic efficacy of *C. alata* leaf extract against *Pityriusis versicolor* has been reported for the first time involving humans. For the collection of clinically effective antifungal compounds from the leaves of *C. alata,* a simple procedure has been devised. Ten years human study indicates that the leaf extract can be reliably used as a herbal medicine to treat *P. versicolor*. The leaf extract has no side-effects [85]. *C. alata* has been reported as new treatment tools in bronchorespiratory and chemopreventive activity against various DNA damaging agents [86]. Folkloric on *C. alata* claims as an antimicrobial agent for treating skin infection [87]. The *C. alata* was found to have potential as herbal soap [88]. Furthermore, *C. alata* leaves gave significant effect in healing burns [89] and has been reported to against clinical isolates of Gram-positive and Gram-negative bacteria viz., *Vibrio cholerae, B. subtilis, S. aureus, Stretococcus* sp. and *E. coli* as well as against a few fungi which are mostly dermatophytes causing skin infection in human beings like, *A. niger, A. flavus. A. candidus, P. patulum, C. albicans and R. stolonifer, T. mentagrophytes, T. tubrum, M. gypseum* and *M. canis* [90, 91].

6. Toxicity studies

C. alata has been reported not to have obvious toxicity based on the experiment used Swiss albino male mice weighed 24–28 g. At 3,000 mg/kg body weight of alcoholic *C. alata* leaves extract did not change in the general behavior of the test animals [92]. Aqueous dried leaf extract of *C. alata* was reported not to have toxic at 250, 500 and 1000 mg/kg based on the experiment used male albino rats (80–100 g). The histopathology of the liver and kidney did not reveal any pathological changes [93]. Furthermore, the aqueous extract of *C. alata* flower has been reported safe with administered orally in rat based on the experiment used albino wistar rats of either sex (150–180 g). The histological sections of the liver, lung, kidney, spleen and heart did not show any remarkable changes [94]. But, the alkaloids that isolated from *C. alata* at 250–1000 mg/kg reported changes plasma membrane of the liver and kidney [95]. Additionally, emodin, kaempferol, aloe-emodin, and rhein were reported caused subtle hepatorenal toxicity [96].

7. Conclusions

C. alata plant is a herbal medicine that has been used in Asian countries. Several secondary metabolite compounds from the plant have been isolated from parts of leaves, seeds, stems and flowers. The results of research on the biological activity of *C. alata* which has been reported by some researchers gives scientific fact that this plant has pharmacological aspects. However, research on isolation of secondary metabolite compounds is still needed to be continued to investigate potentially pharmacological compounds.

Declarations

Author contribution statement

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The authors declare no conflict of interest.

Additional information

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