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

Sri Fatmawati a,*, Yuliana a, Adi Setyo Purnomo a, Mohd Fadzelly Abu Bakar b

a Department of Chemistry, Faculty of Science and Data Analytics, Institut Teknologi Sepuluh Nopember, Kampus ITS Sukolilo, Jalan Arif Rahman Hakim, Sukolilo, 60111, Surabaya, Indonesia
b Centre of Research for Sustainable Uses of Natural Resources, Faculty of Applied Sciences & Technology, Universiti Tun Hussein Onn Malaysia (UTHM), Hub Pendidikan Tinggi Pagoh, KMI, Jalan Punchor, 84600, Muar, Johor, Malaysia

ARTICLE INFO

Keywords:
- Cassia alata
- Phytochemical
- Pharmacological activity
- Disease
- Natural product chemistry
- Bioorganic chemistry
- Pharmaceutical chemistry
- Alternative medicine
- Evidence-based medicine

ABSTRACT

*Cassia alata* or locally known as Ketepeeng 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, anti diabetic, and antifungal. Metabolite compounds that have been isolated from *C. alata* include flavones, flavonoids, flavonoid glycosides, alatinon, alanos 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 of *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 anti oxidant activity with IC50 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...
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 BCSR 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-methylidenededeca-1,6,10-triene), 8 (4a,8-dimethyl-2-(prop-1-en-2-yl)-1,2,3,4,4a,5,6,8a-octahydro-1-benzofuran-2(4H)-one), 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 (adine) [20], 15 (Chrysoeriol), 16 (quercetin), 17 (5,7,4′-trihydroxyflavanone), 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 diosmetin [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. Fractionisation 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-D-mannopyranosyl)-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-tetraicosenoic 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-anthaquinone) 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-anthaquinone), 45 (1,5-dihydroxy-8-methoxy-2-methyl-anthaquinone -3-O-β-D-(+)-glucopyranoside) [31] and 46 emodin (1,6,8-trihydroxy-3-methyl-anthaquinone) [31]. Alkaloid compounds from C. alata root 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 (β-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 (alanolan) and 53 (β-sitosterol-3-O-D-glucoside) [34]. Furthermore, chemical compounds of flower of C. alata that analyzed by
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* (lipoxigenase) | 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] |
| | | | 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. | [9] |
| | Antioxidant | DPPH radical scavenging | Methanol extract gave inhibition EC\(_{50}\) of 28.50 μg/ml, while BHT has EC\(_{50}\) 14.17 ± 1.38 μg/ml. | [15] |
| | | | Methanol extract gave IC\(_{50}\) concentration lower (54 ± 2.20) than BHT standard (72 ± 2.20). | [42] |
| | | | 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, kaemferol 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 ± 12.91 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 i.e 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] |
| | | Blood glucose levels used albino Swiss Webster mice | Ethyl acetate extract of *C. alata* showed an effective result as an antidiabetic agent with percent decrease of blood glucose level (56.7%) while CMC control (38.0%). | [56] |

(continued on next page)
### 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 Hebacol 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 significantly 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 with 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 thyphi*, *Proteus mirabilis*, *Bacillus coagulans*, *Micrococcus luteus*. Petroleum ether extract inhibited the growth of *B. coagulans*. Dichloroacetate extract inhibited the growth of *Lactobacillus casei*, *Staphylococcus epidermidis*, *Nieseria gonorrhoeae* and *Trichomonas vaginalis*. Ethyl acetate extracts inhibited the growth of *B. coagulans* and *T. vaginalis*. | [59] |
| Antimicrobial | Disk diffusion | The methanol extract of *C. alata* leaf inhibited *Actinomycyes bovis* and *Mucor* sp. | [60] |
| Antimicrobial | Disk diffusion | The ethanol extract inhibited the growth of *Escherichia coli* bacterium and *Rhizopus* sp. | [61] |
| Antimicrobial | Agar well diffusion | The acetone extract inhibited *Proteus vulgaris* and *Bacillus subtilis*. | [62] |
| Antimicrobial | Disk diffusion | Water extract inhibited *Staphylococcus aureus* bacterium. | [63] |
| Antiviral     | *In vivo* with male white rats with various doses (100 mg/kg body weight, 300 mg/kg BW and 900 mg/kg BW) | The toxicity was measured by MTT assay. 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. The leaves extract and butanol subfraction were reported to have strong antiviral activity against DENV-2 with the IC50 0.0256 and 6.47 μg/ml and CO50 323.45 and 645.8 μg/ml, respectively. | [64, 68, 69, 70, 71, 72] |
| Antidepressant| Forced Swim Test (FST) and Tail Suspension Test (TST) | The alcoholic extract of *C. alata* leaves had been reported to have antidepressant 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 oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP), total bilirubin and gamma glutamate transpeptidas from paracetamol induced liver damage. | [65] |
Table 1 (continued)

| Part of Plant | Biological activity | Method | Result | Reference |
|--------------|--------------------|--------|--------|-----------|
| 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, paralyzation 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] |
| Antesthetic  | 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] |
| Thrombolic  |                 | 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 IC_{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        | Antimicrobial      | Disk diffusion | Methanol extract inhibited S. typhi bacterium growth. Petroleum ether extract inhibited bacterial growth of B. megaterium, Spectroccocus faecalis, S. typhi. Dichloromethane extract inhibited bacterial growth of B. coagulans. Ethyl acetate extract inhibited bacterial growth B. cereus, B. megeutarium, St. pneumoniae, K. pneumoniae, N. gonorrhoeae and S. typhi. | [59] |
| Bark        | Antimicrobial      | 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. | [46] |
| 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 freundi, 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. mirabilis. | [66] |
| 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 against carbon tetrachloride (CCL4) | After administration with CCL4, the extract more active than CCL4. In the extract, serum aspartate aminotransferease and alanine aminotransferease decreased significantly (P ≤ 0.05) in rats. | [45] |
The antioxidant IC\textsubscript{50} values of 0.33 μmol/mg, respectively. DPPH radical scavenging Methanol extract gave ED\textsubscript{50} 175.36 μg/ml, while BHT had 14.17 μg/ml. [15]

DPPH radical scavenging Aqueous extract had EC\textsubscript{50} 823 μg/ml, while BHT had 500 μg/ml. The extracts were active against S. aureus, E. coli, P. vulgaris, P. aeruginosa, S. marcescens.

In broth dilution technique the crude extract of flowers at 500 μg/mL were active against S. aureus, St. faecalis, M. luteus, B. subtilis, P. putida, S. typhi, B. egaterium, C. utilis.

In disk diffusion method, methanol extract and fraction inhibited the growth of fungi A. brevipes, S. aureus, M. canis, L. casei, S. epidermidis, B. subtilis, B. coagulans, T. vaginalis, C. alata.

The aqueous dried leaf extract of C. alata, leaves of P. versicolor has been reported for the collection of clinically effective antifungal compounds from the plant. The results of 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. tubram, 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, aloë-emodin, and rhein were reported caused subtle hepatoxenial 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**

All authors listed have significantly contributed to the development and the writing of this article.

**Funding statement**

This paper is partially funded by the Indonesian Ministry of Research, Technology and Higher Education under WCU Program managed by Institut Teknologi Bandung.

**Competing interest statement**

The authors declare no conflict of interest.

**Additional information**

No additional information is available for this paper.

**References**

[1] E.F. Gilman, D.G. Watson, *Cassia Alata Candlebrush, Southern Group of State Forests*, 1993, pp. 1–3.

[2] T.K. Lim, “Senna alata” edible medicinal and non-medicinal plants? 7 (2014) 841-859.

[3] T. Henselbelle, W. Bernard, J. Henry, S. Sevser, B. Francois, Senna alata, Fitosferapia 80 (7) (2009) 389–393.

[4] I. Reezal, M.N. Somchit, M.A. Rahim, In vitro anti-fungal properties of *Cassia alata* (Gelenggang Besar), in: The Regional Symposium on Environment and Natural Resources, 2002, pp. 654-659.

[5] N. ShkidmAllaya, A. Yasmen, K. Gopakumar, Medicobotanical survey of Kumar pavatha Kukbe Subramanya, Manglore, Karnataka, Indian J. Tradit. Knowl. 9 (2010) 96–99.

[6] C.A. Alalor, C.I. Igwilo, E. Jeroh, Evaluation of the anti-bacterial properties of aqueous and methanol extracts of *Cassia alata*, J. Pharm. Allied Health Sci. 2 (2012) 40–46.

[7] P. Monkheang, R. Sudmoon, T. Tane, et al., Species diversity, usages, molecular markers and barcode of medicinal Sesna species (Fabaceae, Caesalpinioideae) in Thailand, J. Med. Plants Res. 5 (2011) 6073–6181.

[8] S. Saito, G. Silva, R.X. Santos, G. Gosmann, C. Pungartnik, M. Bredel, Astragalin from edible medicinal and non-medicinal plants 7 (2014) 659.

[9] C.A. Pieme, V.N. Peniap, B. Nkegoum, J. Ngogang, *Cassia alata* Free Radic. Antioxidants 8 (2) (2018).

[10] D.S. Gupta, B. Jann, Structure of a galactomannan from *Cassia alata* Linn, Crude Leaf Extract, Res. J. Biol. Sci. 5 (3) (2010) 275–286.

[11] M.O. Wegwu, E.O. Ayalogu, O.J. Sule, Antioxidant protective effects of *Cassia alata* L on experimental diabetes, Br. J. Food Sci. Technol. 5 (2014) 260–270.

[12] S. Kundu, S. Roy, M.L. Lyndem, *Cassia alata* I: potential role as anthelmintic agent against Hymenolopis diminuta, Parasitol. Res. 111 (2012) 1187–1192.

[13] P. Phanyakyparkaranant, S. Kaewsawan, Bioassay-guided isolation of the antioxidant constituent from *Cassia alata* L leaves, Songklanakarin J. Sci. Technol. 26 (2004) 103–107.

[14] M.S. Rahman, A.J.M.M. Hasan, M.Y. Ali, M.U. Ali, A flavone from the leaves of *Cassia alata* Bangladesh, Cranes. Sci. Ind. Res. 41 (2006) 93–96.

[15] M.S. Rahman, M.Y. Ali, M.U. Ali, In vitro screening of two flavonoid compounds isolated from *Cassia alata* L leaves for fungicidal activities, J. Biol. Sci. 16 (2008) 142–153.

[16] M.A. Adina, M.P. Muzara, Study on *Cassia alata* and its different extracts by Fourier Transform Infrared Spectroscopy and two-dimensional correlation infrared spectroscopy, J. Mol. Struct. 991 (2011) 84–91.

[17] G.U. Igwe, F.K. Onwu, Leaf essential oil of *Senna alata* linn from south east Nigeria and its antimicrobial activity, Int. J. Pharm. Chem. 5 (1) (2015) 27–33.

[18] H. Moriyama, T. Iizuka, M. Nogai, T. Shostio, Anti-inflammatory activity of Heat-treated *Cassia alata* leaf extract and its flavonoid glycoside, Yakugaku Zasshi 123 (2003) 607–611.

[19] L. Liu, L. Xu, Y. Yang, Studies on chemical constituents from leaves of *Cassia alata*, Zhonggguo Zhongyao Zazhi 34 (7) (2009) 861–863.

[20] T. Promgoool, O. Panccharoen, S. Deochattai, Antibacterial and antiviral compounds from *Cassia alata* Linn, Songklanakarin J. Sci. Technol. 36 (4) (2014) 459–463.
S. Fatmawati et al. Heliyon 6 (2020) e04396

[54] G.K. Varghese, V.B. Lekshmi, H. Solomon, Anti-diabetic components of Cassia alata leaves: identification through α-glucosidase inhibition studies, Pharmaceut. Biol. 51 (2012) 345–349.

[55] S. Palanichamy, S. Nagara, M. Devasagayam, Effect of Cassia alata leaf extract on hyperglycemic rats, J. Ethnopharmacology 22 (1988) 81–90.

[56] I.M. Villanuera, A.P. Casan, M.P. Fasca, M.N. Sahando, L.A. Soliven, Bioactivity studies on Cassia alata Linn. leaf extracts, Phytother Res. 16 (2002) 895–896.

[57] M. Ansane, M. Traore, E. Bassene, A. Sere, Chloreltic effects of Cassia alata Linn in the rat, Dakar Med. 38 (1993) 73–77.

[58] S. Palanichamy, S. Nagarajan, Analytical activity of Cassia alata leaf extract and kaempferol 3-O-sophoroside, J. Ethnopharmacol. 29 (1990) 73–78.

[59] M.R. Khan, M. Kihara, A.D. Omoloso, Antimicrobial activity of Cassia alata, Fitoterapia 72 (2001) 561–564.

[60] A.A. Makinde, J.O. Igbe, L. Ta Ama, S.J. Shaibu, A. Garba, “Antimicrobial activity of Cassia alata”, Afr. J. Biotechnol. 6 (2007) 1509–1510.

[61] J.A. Oyowale, G.A. Olatunji, S.O. Oguntayo, Antifungal and antibacterial activities of an alcoholic extract of Senna alata leaves, J. Appl. Sci. Environ. Manag. 9 (3) (2005) 105–107.

[62] P. Sharma, D. Pandey, A.F. Rizvi, A.K. Gupta, Antimicrobial activity of Cassia alata from Raipur region against clinical and MTCC isolates, Int. J. Microbiol. Appl. Sci. 1 (1) (2015) 330–339.

[63] M.N. Somchit, I. Reezal, I.E. Nur, A.R. Mutalib, Anti-Cryptococcus activity of combination of G.K. Varghese, V.B. Lekshmi, H. Solomon, Antidiabetic components of Cassia alata leaves, J. Ethnopharmacology 45 (1995) 151–156.

[64] S. Angsuwan, S. Piromsri, A survey on the therapeutic efficacy of Cassia alata, Linn. leaf extract against Pyriyriae versicolor, J. Ethnopharmacol. 42 (1994) 19–23.

[65] M. Ouedraogo, F.L. Da, A. Fabre, K. Konate, C.I. Bibala, H. Carreyre, S. Thibaudseu, J.M. Courtard, C. Vandebrouck, J. Bescoud, R.G. Belemontsger, Evaluation of the bronchorelaxant, genotoxic, and antigenotoxic effect of Cassia alata L. Evid. base. Compil. Alternative Med. 11 (2013).

[66] A. Odale, B.A. Dairo, A.A. Eliujoba, A.O. Oyelami, “Management of superficial fungal infections with Senna alata (“alata”) soaps: a preliminary report, African J. Pharm. Pharmacol. 4 (3) (2010).

[67] A.T. Oladele, A.A. Eliujoba, A.O. Oyelami, Clinical studies of three herbal soaps in the management of superficial fungal infection, Res. J. Med. Plant 6 (1) (2012) 56–64.

[68] S.L.R. Naution, M. Putri, W. Hulo, E. Girsang, A.N. Naution, Optimization of Senna alata leaves extract for bleeding burns, J. Global Trends Pharmaceut. Sci. (2019).

[69] S. Chatterjee, S. Chatterjee, S. Dutta, A survey on VAM association in three different species of Cassia and determination of antimicrobial property of these phytoextracts, J. Med. Plants Res. 4 (2010) 286–292.

[70] D. Ibrahim, H. Osman, Antimicrobial activity of Cassia alata from Malaysia, J. Ethnopharmacol. 45 (1995) 151–156.

[71] S. Roy, B. Ukil, L.M. Lyndem, Acute and sub-acute toxicity studies on the effect of Senna alata in Swiss Albino mice, Cogent Biology 2 (2016) 1–11.

[72] A.E. Ugboegu, E. Okezie, C. Uche-Ikonne, M. Duru, O.C. Atasie, Toxicity evaluation of the aqueous stem extracts of Senna alata in wistar rats, Am. J. Biomed. Res. 4 (4) (2016) 80–86.

[73] I. Igbe, O. Edusuyi, Toxicity profile of aqueous extract of Cassia alata flower in Wistar rats, J. Pharmacy Bioresour. 13 (2) (2016) 92–102.

[74] M.T. Yasuko, I.F. Musa, Liver and kidney functional indices of pregnant rats following the administration of the crude alkaloids from Senna alata (Linn. Roxb) Leaves, Iranian J. Toxicol. 6 (16) (2012) 615–625.

[75] S.M. Yagi, S.E. Tigan, S.E. Adam, Toxicity of Senna obtusifolia fresh and fermented leaves (kawal), Senna alata leaves and some products from Senna alata on rats, Phytotherapy Res. 12 (1998) 324–330.