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RESEARCH ARTICLE

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Medicinal importance of *Cassia alata* L. (Fabaceae): A comprehensive review

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Abstract

Cassia alata included in the Fabaceae family which spread in tropical and humid areas. All part of the *C. alata* contains phytochemical so that is potential medicinal plants. Leaves extract was reported to produce flavonoids, alkaloid, tannin, and cynogenic glycoside. Stems extract contains alkaloid, flavonoid, saponin, oxalate, pheno, and tannin. Roots extract contains alkaloid, saponin, flavonoids, tannins, and phenols. Flower contains saponin, tannin, anthraquinone, flavonoid, glicoside, steroid, and volatile oil. *C. alata* has been reported to be anti-inflamatory, antioxidant, antibacterial, antifungal, antiviral, anti-parasitic, antitumor, anticancer, antidiabetic, hepatoprotective, and have a laxative effect. The aim of this study is to give a sneak peek view on *C. alata* taxonomy, distribution, phytochemical, pharmacological activities, and the toxicological effects.

Keywords: *Cassia alata*, phytochemical, pharmacology, toxicology

Introduction

Plants have long been used to treat various diseases, which are called herbal plants. Herbal plants have a long history in various countries. Herbal plants as medicinal ingredients are in great demand by the public because they are considered to have a low toxic effect when compared to synthetic drugs. *Cassia alata* has long been known as a traditional medicine in various countries, grow in tropics and humid, so that *C. alata* has a wide distribution in the world. The *C. alata* common name is candle

bush because the shape of the flower is like a candle. *C. alata* has known by different origin name, in Indonesia is known as the Ketepeng Cina. *C. alata* belongs to the Fabaceae family and has another name *Sena alata*[1]. *C. alata* has attractive flowers and all parts of the plant produce phytochemical compounds that are beneficial to human health. That's why *C. alata* is known as an ornamental and medicinal plant species in tropical countries of Africa, Asia, Oceania, and North America[2].

Research related to the potential of *C. alata* as a drug continues to be developed. C. alata has been reported to be anti-inflammatory, antioxidant, antibacterial, antifungal, dermatophytic, anticancer, hepatoprotective, anti-lipogenic, anticonvulsant, anti-diabetic, anti-hyperlipidemic, antimalarial, anthelmintic, and antiviral[3]. This is because the phytochemical that contains in *C. alata*. Analysis of *C. alata* leaf ethanolic extract identified 78 compounds including xylenes, alcohols, aldehydes, alkanes, alkenes, fatty alcohols, acetic acids, ketones, esters, saponins, alkaloids, tannins, phlobatannins, anthraquinones, cardenolides, steroid rings, and flavonoids[4]. According to its valuable properties, *C. alata* is an important medicinal plant, and this review aims to explain about the taxonomy, description, distribution, phytochemcal, pharmacological activities, and the toxicological effects who can support WHO Traditional Medicine Strategy 2014-2023[5].

Taxonomy[6,7]

Domain	:	Eukaryota
Kingdom	:	Plantae
Subkingdom	:	Tracheophyta
Phylum	:	Spermatophyta
Subphylum	:	Angiospermae
Division	:	Magnoliophyta
Class	:	Magnoliopsida/Dicotyledonane
Subclass	:	Rosidae
Order	:	Fabales
Family	:	Fabaceae/Leguminosae
Subfamily	:	Caesalpinioidinae
Genus	:	*Senna* Mill./*Cassia*/*Herpetica*
Species	:	*S. alata* (L.) Roxb./*C. alata* L./*Herpetica alata* (L.) Raf.

Morphology

C. alata is a woody shrub that grows upright up to 4 meters. It has large green compound leaves and oval-shaped leaflets with pinnate spines. Inflorescence terminal or axillary, yellow, erect, shaped like a candle, attractive and visited by different insects and pollinated by bees and wasps[2]. Flowers zygomorphic and pentamerous, 5 bright yellow ovate-orbicular petals (20 mm long by 12 wide), 5 oblong sepals, 10 stamens, bisexual, 2 fertile with elongated anthers and 8 with rudimentary anthers, elongated recursive pubescent ovary with short slender style and stigma[1,3]. Young pods are green and dark brown to black when ripe. Ripe seeds are black and triangular.

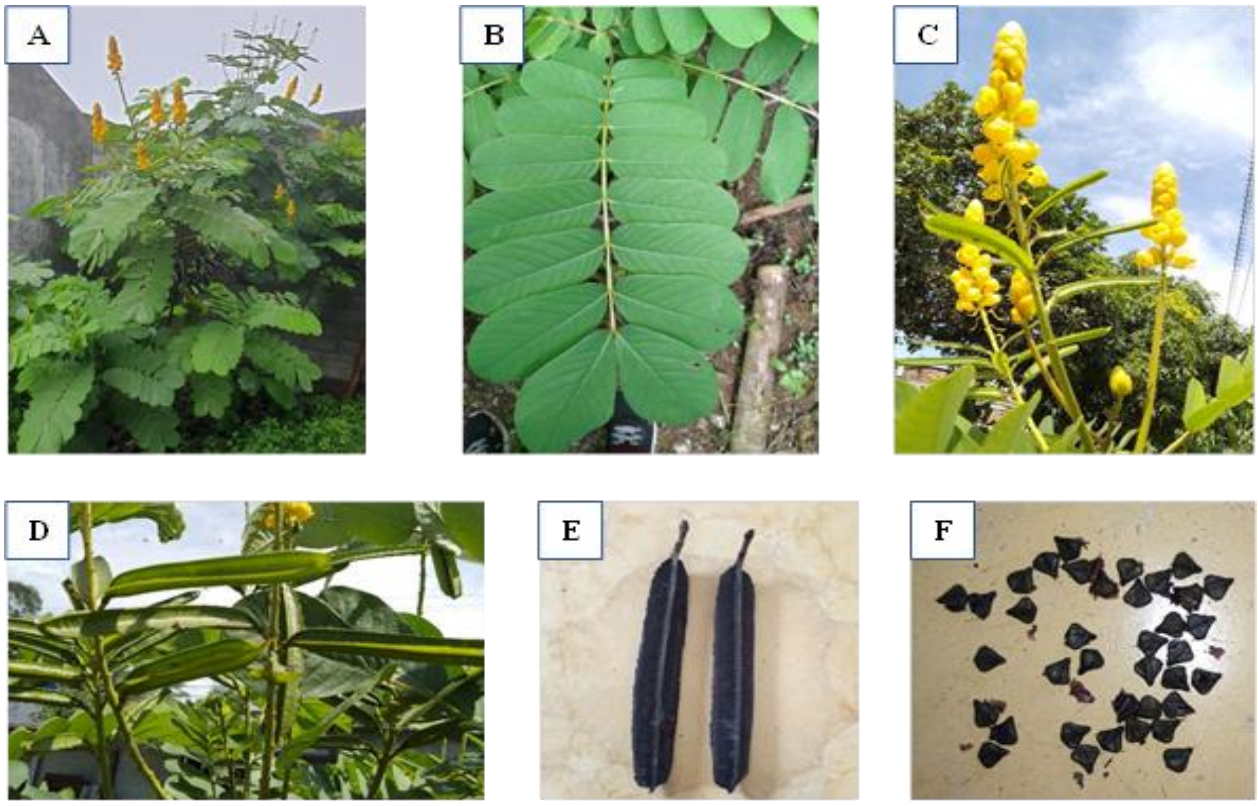

Figure 1. *Cassia alata*: A. plant, B. leaf, C. flower, E. pods, F. ripe pods, G.ripe seeds

Local Name

The common name of *C. alata* is candle bush. It is called candelabra bush[8], candelabra plant, emperor's candlesticks, candlestick senna, candle bush, roman candle tree, ringworm bush, golden candelabra tree[9] in English. In Singapore, it is known as empress candle plant, seven golden candlesticks, candlestick cassia, candlestick senna, christmas candle, ringworm cassia, ringworm bush, gelenggang, daun kurap[10]. Aside, casia de la tiña , espiga dorada, arbusto candela, candlebush, ringworm bush in Belgia[11] as well as acapulco, akapuku, andadose, candalaria, take-biha in Chamoro[9]. Andadasi (iloko), katanda (tagalog), palochina (bisaya) is the terminology uses in Philippines[12]. Ketepeng cina, ketepeng badak, ketepeng kebo, madat, acon-aconan, kupang-kupang, kupang leaves, kurap leaves, sajamera, tabankun, gelenggang, uru'kap, and ki manila in Indonesia also gelenggang in Malaysia[13] and chumhetthet in Thailand[14].

Geographical Distribution

C. alata grows in the tropics and humid area[3]. The habitat is very wide and diverse in both water and dry land, including on the banks of rivers, roadsides, fields, forests, and coasts. Grows in heavy, sandy soils, acidic to slightly alkaline, well-drained soils but thrives in deep, well-drained soils rich in organic matter with a pH range 5.5–6.51. This is causes that the C. alata to be found on several continents, namely Asia (Indonesia, Malaysia, Singapore, India, Thailand, Philipine, Korea, China, Bangladesh, Brunei, Myanmar, Japan, Vietnam), Australia, Africa (Nigeria, Cameroon, Egypt, and Burkina Faso), America (Brazil, Argentina, United States, Venezuela, and Colombia), Europe (French, Germany, Czech, and Antilles), and Papua New Guinea[3,15–17].

Phytochemical Constituents

C. alata has been widely reported to have various bioactive compounds. Functional group analysis of *C. alata* leaf ethanol extract using fourier-transform infrared spectroscopy (FTIR) showed that there are functional bioactive molecules[18]. All parts of *C. alata* produce secondary metabolites including roots, stems, leaves, flowers, and seeds[13]. Qualitative test of aquadest crude extract showed the presence of alkaloids, phenolic compounds, tannins, carbohydrates, reducing sugars, polyuronides, coumarins, saponins, steroids, triterpenoids, flavonoids, resins, cyanophores, glycosides, cardiac glycosides, fixed oils and fats, carotenoids, anthraquinones, free anthraquinones, and combine anthraquinones[19].

C. alata aquadest leaves extract was reported to produce 12.7, 1.48, 12.8, and 9.6% of flavonoids, alkaloids, tannins, and cynogenic glycoside, respectively[19]. Also, *C. alata* aquadest stems extract contains saponins, oxalates, and phenols[20]. *C. alata* methanol roots extract contains 15.89, 33.02, 36.52, 44.38, and 9.91 mg of 100 g of alkaloids, saponins, flavonoids, tannins, and phenols, respectively[21]. In another hand, the flower contains saponin, tannin, anthraquinones, flavonoids, glycosides, steroids, and volatile oils[22,23]. Research about the phytochemical of leaves has been widely reported, while details of the secondary compounds of leaves are presented in the **Table 1**[13,18,24–26].

Table 1. Phytochemical compound of C. alata leaves extract

RT (minute)	Compound	Molecular Weight	Extract/Fraction	Method
9.44	Lauric acid	120	Methanol extract	GC-MS
10.13	Methyl β-D-glucopyranoside	194	Methanol extract	GC-MS
11.03	Tetradecanal	212	Hexane extract	GC-MS
11.46	Tetradecanoic acid	228	Methanol extract	GC-MS
12.85	α-Linolenic acid	278	Hexane extract	GC-MS
13.15	Palmitic acid methyl este	270	Methanol extract	GC-MS
13.55	Palmitic acid	256	Methanol and hexane extract	GC-MS
15.23	α-Linolenic acid	278	Methanol and hexane extract	GC-MS
15.41	Stearic acid	284	Methanol extract	GC-MS
16.60	Heneicosane (isomer)	296	Hexane extract	GC-MS
17.44	Heneicosane (isomer)	296	Hexane extract	GC-MS
18.26	Heneicosane (isomer)	296	Hexane extract	GC-MS
19.03	Hexatriacontane (isomer)	506	Hexane extract	GC-MS
19.79	Tetratetracontane	618	Hexane extract	GC-MS
20.52	Hexatriacontane (isomer)	506	Hexane extract	GC-MS
21.23	Hexacosyl heptafluorobutyrate	578	Methanol extract	GC-MS
21.24	Hexatriacontane (isomer)	506	Hexane extract	GC-MS
21.93	Hexatriacontane (isomer)	506	Hexane extract	GC-MS
22.77	Hentriacontane	436	Hexane extract	GC-MS
23.01	α-Tocopherol-β-D-mannoside	592	Methanol and hexane extract	GC-MS
23.62	Dotriacontane	450	Hexane extract	GC-MS
24.24	Stigmasterol	412	Methanol extract	GC-MS
24.73	Tritriacontane	464	Hexane extract	GC-MS
24.83	1-Heptacosanol	396	Hexane extract	GC-MS

18.33	Phytol	296	Hexane extract	GC-MS
23.27	Heptacosane, 1-Chloro-	414	Hexane extract	GC-MS
26.95	14-Heptadecenal	252	Hexane extract	GC-MS
28.49	Octadecanal	268	Hexane extract	GC-MS
29.81	3-Butoxy-1,1,1,5,5,5-Hexamethyl-3-(trimethylsiloxy) trisiloxane	368	Hexane extract	GC-MS
30.86	9-Octadecene, 9-Octadecene, 1-[3-(Octadecyloxy) propoxy]-, (Z)-	578	Hexane extract	GC-MS
2.86	Propylene glycol	78	Ethanol extract	GC-MS
5.25	4-Pentadecanol	228	Ethanol extract	GC-MS
7.13	2-Hydroxyethylhydrazine	76	Ethanol extract	GC-MS
17.66	Isopropyl-5-methylcyclohexyl 3-(1-(4- Chlorophenyl)-3-Oxobutyl)-C	524	Ethanol extract	GC-MS
18.09	Hexadecanoic acid	312	Ethanol extract	GC-MS
19.56	Eicosanoic acid	312	Ethanol extract	GC-MS
21.30	Oleic acid	282	Ethanol extract	GC-MS
23.79	Pentadecanoic acid	242	Ethanol extract	GC-MS
27.96	cyclotrisiloxane, hexamethyl-	222	Ethanol extract	GC-MS
5.32	1,3,5-Triazine-2,4,6,-triamine	126.11	Ethanol extract	GC-MS
5.59	Undecane	156.31	Ethanol extract	GC-MS
7.73	Phenol,2-propyl-	136.19	Ethanol extract	GC-MS
8.52	Cycloheptasiloxane, tetradecamethyl-	519.07	Ethanol extract	GC-MS
8.72	Ethylparaben	152.15	Ethanol extract	GC-MS
8.79	Benzoic acid, 4-ethoxy, ethyl ester	194.23	Ethanol extract	GC-MS
9.00	Beta-D-Glucopyranoside, methyl	194.18	Ethanol extract	GC-MS
5.25	4-Pentadecanol	228	Ethanol extract	GC-MS
7.13	2-Hydroxyethylhydrazine	76	Ethanol extract	GC-MS
17.66	Isopropyl-5-methylcyclohexyl 3-(1-(4- Chlorophenyl)-3-Oxobutyl)-C	524	Ethanol extract	GC-MS
18.09	Hexadecanoic acid	312	Ethanol extract	GC-MS
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5.59	Undecane	156.31	Ethanol extract	GC-MS
7.73	Phenol,2-propyl-	136.19	Ethanol extract	GC-MS
8.52	Cycloheptasiloxane, tetradecamethyl-	519.07	Ethanol extract	GC-MS
8.72	Ethylparaben	152.15	Ethanol extract	GC-MS
8.79	Benzoic acid, 4-ethoxy, ethyl ester	194.23	Ethanol extract	GC-MS
9.00	Beta-D-Glucopyranoside, methyl	194.18	Ethanol extract	GC-MS
10.43	Cyclononasiloxane, octadecamethyl	667.40	Ethanol extract	GC-MS
10.96	Hexadecanoic acid, methyl ester	270.45	Ethanol extract	GC-MS
11.28	n-Hexadecanoic acid	284.47	Ethanol extract	GC-MS

11.88	Phytol	296.50	Ethanol extract	GC-MS
12.00	9,12,5-octadecatrienoic acid, methyl este	292.50	Ethanol extract	GC-MS
12.06	Octadecanoic acid	284.48	Ethanol extract	GC-MS
16.76	Octadecane	254.50	Ethanol extract	GC-MS
16.77	Eicosane	282.50	Ethanol extract	GC-MS
19.04	Beta-tocophenol	416.70	Ethanol extract	GC-MS
19.50	Eicosane	282.50	Ethanol extract	GC-MS
20.44	Vitamin E	430.71	Ethanol extract	GC-MS
24.62	Gamma.sitosterol	432.70	Ethanol extract	GC-MS
8.82	5,7,2′,5′- Tetrahidrox-flavone	287.05	Ethanol extract	LC-MS
10.86	Daturametelin H	621.31	Ethanol extract	LC-MS
5.48	Kaempferol- 3,7- diglucoside	611.16	Ethanol extract	LC-MS
7.24	5,7,2′,5′- Tetrahidrox-flavone	287.06	Ethanol extract	LC-MS
8.03	Clinopodisida F	991.55	Ethanol extract	LC-MS
8.94	Daturametelin H	621.3	n-Heksana fraction	LC-MS
6.29	Kaempferol-3,7-diglucoside	6.29	n-Heksana fraction	LC-MS
7.36	5,7,2′,5′- Tetrahidroxyflavone	287.06	n-Heksana fraction	LC-MS
7.43	Digitopurpon	271.06	Ethyl acetate fraction	LC-MS
9.88	Daturametelin H	621.3	Ethyl acetate fraction	LC-MS
6.64	Kaempferol-3,7-diglukosida 25-Dehydroxy-24-acetate	633.14	Ethyl acetate fraction	LC-MS
10.61	25-Dehydroxy-24-acetate alisol A	537.36	Ethyl acetate fraction	LC-MS
7.44	3,3′,5,5′-Tetramethoxy-trans-stilbene	301.14	Ethyl acetate fraction	LC-MS
-	5,7,2′,5′-Tetrahydroxy-flavone	287.06	Ethyl acetate fraction	LC-MS
-	Bis(2-ethylhexyl) phthalate	413.27	Butanol fraction	LC-MS
8.16	Deoxycholic acid	393.3	Butanol fraction	LC-MS
9.9	Epianhydrobelachinal	469.33	Butanol fraction	LC-MS
6.41	Kaempferol-3,7-diglucoside	611.16	Butanol fraction	LC-MS
10.62	21-O-Methyltoosenddanopentanol	521.38	Butanol fraction	LC-MS
9.9	25-Dehydroxy-24-acetate alisol A	637.36	Butanol fraction	LC-MS
7.44	3,3′,5,5′-Tetramethoxy-trans-stilbene	301.14	Water fraction	LC-MS
8.96	Bis (2-ethylhexyl) phthalate	413,27	Water fraction	LC-MS
8.16	Deoxycholic acid	393.3	Water fraction	LC-MS
6.42	Kaempferol-3,7-diglucoside	633.14	Water fraction	LC-MS

Pharmacology

C. alata has been used in various countries as traditional medicine by its secondary metabolites. This plant is used as a traditional medicine for diabetes, typhoid, asthma, malaria, tinea infections, ringworms, scabies, blotch, eczema, and herpes[3]. The previous research showed that the most suitable leaves of *C. alata* for the herbal medicines were young leaves and mature leaves with 1-6 leaf positions[14].

Anti-inflammatory activity

C. alata leaf extract can be used as an anti-inflammatory agent and may be very useful for the prevention of inflammation. When acute inflammation is occurred, macrophages/monocytes produces cytokine inflammatory, namely Tumour Necrosis Factor α (TNF-α). The leaf extract and rhein has been shown to inhibit t-BHP-induced inflammatory responses such as TNF-α and IL-8 production through suppression of ROS production[27]. *C. alata* extract has inhibitory activity on TNF- α production by immature dendritic induced Lipopolysaccharide, with inhibitory activity dependent to dose[28]. *C. alata* extract given to CFA arthritic rats significantly reduced knee swelling and decreased the number of leukocytes in the blood and synovial fluid[29]. The sun-dried aqueous extract leaves had greater inhibitory activity against cyclooxygenase-1 and -2 (COX-1 and -2), also decreased concanavalin-induced histamine release from rat peritoneal exudate cells when compared with heat-treated leaves[30].

Antioxidant

Antioxidant activity analysis is often done using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method[31]. *C. alata* ethanol leaves extract showed the highest antioxidant activities but was inhibited by the increase of temperature[32]. DPPH analysis of *C. alata* extract showed an inhibition of 61.69% at a concentration of 1000µg/ml[33]. In general, the lower the half maximal inhibitory concentration (IC50) value, the higher the antioxidant activity. Aqueous extract has a lower IC50 value (0.619) than methanol extract (0.662)[31]. *C. alata* also has the activity of superoxide radical scavenging, nitric oxide radical inhibition, hydroxyl radical inhibition, hydrogen peroxide scavenging, which is dose dependent[33]. *C. alata* significantly reduces malondialdehyde (MDA) levels and also increases antioxidant activity34. Antioxidant activity can also be seen from the reduction ability of a compound which is influenced by the number of reducing agents. Reducing agents play a role in inhibiting free radical chains by donating hydrogen ions. Methanol extract had a higher reducing ability than aqueous extract, although both increased with increasing concentration[31]. *C. alata* has greater free radical inhibitory activity when compared to synthetic drugs[18]. The highest antioxidant capacity is found in leaves that are extracted using low temperatures, so they are good for consumption[34].

Antibacterial

Antibacterial activity of *C. alata* root ethanol extract (80 °C) had the largest diameter of inhibition zone against *Staphylococcus aureus*, *Eschericia coli*, and *Salmonella enterica* serovars *Typhimurium* when compared to other parts[35]. 100 mg/mL concentration of methanol and hexane leaves extract were able to inhibit the growth of *Bacillus subtilis*, *E. coli*, *Pseudomonas aeruginosa*, and *S. aureus*[24]. The results of other studies also showed that the root and leaf extract of C. alata be able to againts *Neisseria gonorrhoeae*[36]. Silver nanoparticles (AgNPs) synthesized from *C. alata* bark extract be able to inhibit the growth of gram-negative and gram-positive bacteria[37]. The antibacterial activity was caused by the phytochemical compounds contained in the *C. alata* extract, namely saponins, flavonoids, alkaloids, phenols, and tannins[38].

Antifungal

C. alata leaf methanol extract has antifungal activity against *Saccharomyces cerevisiae*, *Candida albicans*, and *Trichophyton rubrum*[24,38]. The hexane leaves extract had a 29.3 μg/ ml minimal inhibitory concentration (MIC) and minimum fungicide concentration (MFC) on the growth of *Epidermophyton floccosum*, *Trichophyton mentagrophytes*, *Microsporum audouinii*, *T. rubrum*, and *M. canis*[25,38]. Fatty acids of *C. alata* flower were reported can inhibit to the growth of *Malassezia furfur*, while citronellols, pinitols, anthracenediones, and chrysenes on the flower has reported as a antidandruff actifity[39,40]. *C. alata* lotion 50% has the same activity as sodium thiosulfate 25%, ketoconazole cream 2% and terbinafine 1% as a treatment for superficial fungal skin infections[41].

Antiviral

C. alata contains kaempferol-3,7-diglucosyd[42]. Kaempferol and glycoside are antiviral agents used to inhibit human cytomegalovirus (HCMV)[42,43]. Aqueous and ethanol aerial part extracts had inhibitory activity to human immunodeficiency virus-1 (HIV-1) reverse transcriptase. The leaf ethanol extract was strongly able to inhibit the dengue virus (DENV) at every stage of virus replication[26]. The IC50 yield of crude ethanol leaves extract was 0.026 g/mL, with a logarithmic regression of y = 6.3628 ln (x) + 73,277, for the hexane and ethyl acetate sub-fraction the IC50 yield was <2.5 g/mL with a logarithmic regression y = -6.665 ln(x) + 14,885, buthanol sufraction was 6.47 g/mL with linear regression y = -2.5707 x + 14,885, water sub-fraction IC50 was <2.5 g/mL with logarithmic regression y = -10.85 ln(x) + 51,038. It is therefore considered that the concentration required to achieve 50% inhibition requires a much lower dose than the tested dose (IC50 is lower than the lowest tested concentration of <10 g/mL)[44]. *C. alata* extract is effective as an anti DENV-2 which is able to inhibit at small concentrations and requires high concentrations to produce toxic effects on cells[43].

Anti-parasite

40 mg/mL concentration of *C. alata* was able to immobilize and weaken *Heterakis gallinarum* (nematodes), *Catatropis sp*. (trematoda) and *R. tetragona* (cestodes) in a fairly short time in *Ascardia* gall caused paralysis 5 minutes and died 29 minutes after treatment[45]. *Hymenolepis diminuta* treated with ethanolic extract of *C. alata* showed decreased motility with increasing concentration and complete immobilization required less time than control. The anthelmintic activity is caused by its bioactive compound[46]. Tannins are one of those involved[47]. *C. alata* ethanol extract has also been shown to inhibit the growth of *Plasmodium falciparum*[48,49] via *in vitro* and *in vivo* test on mice that given various doses (50, 100, 250, 400 mg/kg wb) showed that all of them had parasite reduction activity[50].

Antitumor and anticancer

In Philippines, *C. alata* is used for anti-tumor and other therapeutic purposes[51]. The flower ethanol extract was shown to be able to inhibit colon cancer cells through its potential effect on inhibiting pro-tumorigenic inflammation and oxidative stress genes[52]. Determination of cytotoxicity activity of n-hexane *C. alata* extract with 7 concentration variations (0, 9.38, 18.75, 37, 50, 75.00, 150,00, and 300,00 g/mL) for 24, 48, and 72 hours using the sulforhodamine B (SRB) assay showed that the IC50 of breast cancer cells (MCF-7) was 0.013 g/mL (highly toxic) and was not detectable in the IC50 of normal human breast epithelial cells (MCF10A)[17]. *C. alata* flower methanol extract has anti-proliferative effect. *In vitro* studies with a concentration of 0.2 mg/ were significantly able to inhibit 50% of colon cancer cell growth HT-115 mL after 48 hours of administration and in normal cells showed growth inhibition of 4% and 5%, respectively[52].

Anti-diabetic

C. alata can be used as an alternative medicine for diabetes mellitus[53]. Kaempferol 3-O-gentiobioside was able to inhibit the α-glucosidase enzyme[54]. Acetone and hexane extract of leaves can inhibit α-glucosidase and α-amylase enzymes by competitive and non-competitive inhibitory activities[55]. *In vivo*, administration of *C. alata* ethanol extract for 21 days was shown to be able to reduce blood glucose levels, regenerate and repair pancreatic cells in alloxan-induced diabetes mellitus rats[56]. *C. alata* leaf hexane extract also reduced sucrose-induced postprandial hyperglycemic rats[55]. It can relieve hyperleptinemia, hyperinsulinemia, hyperglycemia, and adiposity by activating 5' adenosine monophosphate-activated protein kinase (AMPK), which will lead to an increase in glucose homeostasis in high fatty diet (HFD)-treated mice[57].

Hepatoprotective

C. alata alcohol extract has been shown to have hepatoprotective activity by preventing the depletion of tissue glutathione (GSH) levels[58]. *C. alata* hydroethanol extract was also able to inhibit the decrease in catalase, GSH, and GSH in streptozotocin-induced diabetic rats[53]. The extract can reduce the risk of liver injury which can be identified through several parameters, namely serum oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), total bilirubin and gamma glutamate transpeptidase (GGTP), alkaline phosphatase (ALP), and through histological examination showed the ability to protect liver damage in paracetamol-induced animals[34].

Laxative

C. alata leaves have long been used as a laxative16. It is obtained from the anthraquinone/anthrone glycosides compounds it contains[59]. Its hydroxyanthracene derivatives14 are also capable to provide a laxative effect[32]. The lactation effect can be obtained by cutting 12 pieces of fresh or dry leaves added to 2 cups of water and then boiled until the remaining one cup[60].

Cytotoxicity effects

In vitro toxicity studies were conducted on Huh7 cells treated by *C. alata* extract in ranging doses from 2.5 to 320 g/mL showed that there was no toxic effect. Cell viability is inversely proportional to the extract concentration, the higher the concentration indicates that the lower the cell viability[42]. MTT test on HepG2 cells showed significant cell cytotoxicity by 100 μg/ml concentration of *C. alata* leaf extract after 72 hours of incubation, resulting in 57% cytotoxicity[33]. The in vivo toxicity test using the brine shrimp lethality test (BSLT) method did not show cytotoxicity even at high concentrations (5,000 g/mL). The median lethal dose (LC50) for extracts of buthanol, dichloromethane, chloroform, and water was >1,000 g/mL (non-toxic)[17]. Other study was conducted on non-pregnant albino wistar rats given aqueous extract stem at various doses (250, 500, and 1000 mg/kg) and observed after 24 hours for 14 days. The treatment and control organisms showed that the acute toxicity test (LD50) with the maximum dose caused tiredness and drowsiness symptoms, but no death occurred, while the sub-acute toxicity test on the liver and kidneys (bicarbonate, urea, and creatinine parameters) did not show significant difference. Liver and kidney tissue also showed normal histopathology[20].

The administration of *C. alata* alcohol extract to Swiss strain male mice with 1,000, 2,000, and 3,000 mg/kg body weight doses, after 10 hours fasting for 15 days showed no behavioral disturbances, no changes in the skin color, eyelids, sleep, food, and water intake, no significant change in organ weight and relative organ weight of liver, kidney, and spleen, no significant difference in red blood cell (RBC),

white blood cell (WBC), hemoglobin (Hb), platelet count, serum analysis illustrated no abnormalities histology in kidney, liver, and spleen tissues[61]. In Nigeria, *C. alata* aqueous extract has long been used for abortion and to wash the uterus. Research conducted on pregnant rats given *C. alata* extract at doses of 250, 500, and 1000 mg/kg can pose a risk of systemic and cardiovascular toxicity, can cause structural and functional dysfunction in the heart, liver, and kidneys[62]. In Myanmar and Malaysia *C. alata* is usually consumed after cooking that the flowers are consumed after being boiled made into vegetables or curries. The leaves and seeds are roasted and consumed like coffee. Young pods are consumed after steaming1.

Conclusions

C. alata is an herbal plant that has various health benefits and has low toxicity but is not intended for consumption by pregnant women. The distribution is very wide and easy to live in various environmental conditions, so it has the potential to be used as medicinal ingredients. Further research is needed on the phytochemical content of *C. alata* related to its bioactivity and pathway.

Acknowledgments

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Conflicts of Interest

The authors declare no conflict of interest

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