The phytochemical and pharmacological activity of extract Kirinyuh (Chromolaena odorata L.) leaves: A Review

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ABSTRACT

C. odorata L. is considered to be a plant weed that is scattered in various climates. As a weed, this plant contains a variety of beneficial secondary metabolites. Several studies have shown the benefits of C. odorata L. leaf extract. This study reviews the metabolite content and the pharmacological activities of C. odorata L. leaf extract. A literature search was carried out to obtain various studies related to the use of this plant extract. Secondary metabolites identified in C. odorata L. are alkaloids, flavonoids, tannins, saponins, and steroids. Several reports have also shown that even though it is considered a weed, C. odorata L. leaf extract also provides many benefits due to its pharmacological activities. Various pharmacological activities include anti-inflammatory, anti-microbial, antioxidant, anti-diabetic and anti-cataract, analgesic and antipyretic, wound healing, anti-malaria, mosquito larvicidal, anti-hypercholesterolemia, and anti-fungal.

Key words: Characterization, Chromolaena odorata, kirinyuh, Pharmacological activity, Phytochemical.

INTRODUCTION

The Asteraceae plant family includes the perennial shrub Chromolaena odorata (L.) R.M. King & H. Rob., also known as Kirinyuh in the local Indonesian language. The invasive shrub C. odorata L. is native to America. In a short period, the plant spread fast to other countries in southern and western Africa, eastern and southern Asia, and Australia, where it became one of the most prevalent shrub species in agriculture.1 For instance, the second-most common invasive plant species in South Africa was C. odorata L. C. odorata L. thrives in a range of ecological conditions, including dissimilar to the plant’s original habitat. The ability of C. odorata L. is thought to be due to some characteristics, including the plant’s rapid reproduction rate, high nutrient assimilation rate, suppressive effect on other plant species, and growth adaptability under diverse soil and climatic circumstances.2

Although it can grow invasively, C. odorata L. has historically been valued for various medical qualities. Local medical professionals use the plant to treat wounds, fungal infections, coughs, headaches, toothaches, diarrhea, stomach disorders, and dysentery. The plant is said to have antibacterial, anti-inflammatory, anti-diarrhea, anti-analgesic, anti-cancer, anti-diabetic, antioxidant, wound healing, and hemostatic properties. However, some of these uses have not been scientifically proven.3,4 As a result, many chemical components that could cause the observed biological characteristics have been discovered by analyzing the plant materials extracted from C. odorata L. There are phenolics, flavonoids, saponins, terpenoids, tannins, and steroids in the leaves of C. odorata L.4 Researchers also discovered phenolic acids, such as protocatechueic acid, ferulic acid, vanillic acid, and combinations of flavonoid aglycones like sinensetin, rhamnetin, tamarixetin, and kaempferide, in column fractions of an ethanol extract of C. odorata L. leaves.5 The hydro-distilled essential oil from the root of C. odorata L. contains the sesquiterpenes himachalol, 7-isopropyl-1,4-dimethyl-2-azulenol, androencecalinol, and 2-methoxy-6-(1-methoxy-2-propenyl) naphthalene as its main bioactive components. Many chalcones, such as acacetin, luteolin, isosakuranetin, persicogenin, 5,6,7,4′-Tetramethoxyflavanone, 4′-hydroxy-5,6,7-trimethoxyflavane, and others, were also extracted from the flower’s dichloromethane extract.6 C. odorata L. may contain lead substances with noteworthy in vitro and in vivo therapeutic effects. Studies on the plant’s therapeutic efficacy have been conducted in Asia and sub-Saharan Africa. The process by which the plant exerts its pharmacological properties is still unknown.4 As a result, the purpose of this review was to provide insights into the C. odorata L. phytochemical and pharmacological.

PHARMACOGNOSY C. ODORATA L.

Description

C. odorata L. or Kirinyuh is a wild plant native to Central and South America that spreads throughout the world, especially in tropical and subtropical areas, as shown in Figure 1.7 Economically and ecologically, C. odorata L. is considered detrimental due to negative impact on agriculture, biodiversity, and livelihoods in the area.10 C. odorata L. quickly grows easily and is widespread in tropical regions, even in grasslands where grass cannot be
Different names in each area know C. Odorata L., for example, Acheampong, Jabinde, Matapa, Mighbe, Sekou Toure (Africa); Herbe du Laos (France); Siam krait (German); Kesengesil (Guam); Bagh Dhoka, Tivra Gandha (India); Grasshopper Grass, Golkar Grass, Kirinyuh, Pakoasi, White Grass (Indonesia); Japanese Grass, Main Dhoka, Tivra Gandha (India); Grasshopper Grass, Golkar Grass, du Laos (France); Siam kraut (German); Kesengesil (Guam); Bagh Acheampong, Jabinde, Matapa, Mighbe, Sekou Toure (Africa); Herbe Phacognosy Journal, Vol 14, Issue 5, Sep-Oct, 2022

Microscopic

Microscopically, Kirinyuh leaves are composed of epidermal tissue, collenchyma, sponge and trichomes, collateral vessel bundle type, and a normocytic stomata type. A palisade is located just below the epidermis, and the cuticle protects the epidermis. This plant has various collateral vascular bundles (Figure 4).13

Chemical Content of Daun Kirinyuh (C. odorata L.)

The composition of the compounds contained in Kirinyuh leaves can be seen in Table 1 below.6,17,18

Kirinyuh leaves contain a variety of potent phytochemicals that includes (a) flavonoid aglycones (flavanones, flavonols, flavones), including acacetin, chalcones, paclitaxel, luteolin, naringenin, kaempferol, quercetin, quercetagetin, and sinensetin, (b) terpenes and terpenoids, (c) essential oils, (d) alkaloids, namely pyrrolizidine, (e) saponins and tannins, (f) phenolic acids, namely ferulic acid and protocatechuic acid, and (g) phytosterane components, namely chromomic acid, as shown in Figure 5.12 Triterpenes/stereoids, monoterpenes, sesquiterpene hydrocarbons, and essential oils (geyren, bornyl acetate, and β-eubened) are also present in Kirinyuh.13

| Component | Status |
|-----------|--------|
| Alkaloids | + |
| Cyanogenic glycosides | + |
| Flavonoids | + |
| Z. Aurone | + |
| Z. ChalcDaunone | + |
| Z. Flavone | + |
| Z. Flavonol | + |
| Phytates | ++ |
| Saponins | +++ |
| Tannins | ++ |
| Steroid | + |
| Terpenoid | + |

(+) = low levels; (++) = sufficient levels; (+++) = high levels

Table 2: Phytochemical examination of methanol extract and distilled water C. odorata.

| Phytochemicals       | Methanolic extracts | Aqueous extracts |
|----------------------|---------------------|------------------|
| Alkaloids            | +                   |                  |
| Saponins             | -                   | +                |
| Tannins              | +                   | +                |
| Anthraquinones       | -                   | +                |
| Steroids             | +                   | +                |
| Terpenoids           | +                   | +                |
| Flavonoids           | +                   | +                |

(+) = Contains; (-) = Does not contain

| Component Status |
|------------------|
| Alkaloids (+)     |
| Cyanogenic glycosides (++) |
| Flavonoids (++)    |
| Z. Aurone (+)     |
| Z. ChalcDaunone (+) |
| Z. Flavone (+)    |
| Z. Flavonol (+)   |
| Phytates (++)     |
| Saponins (+++)    |
| Tannins (++)      |
| Steroid (+)       |
| Terpenoid (+)     |

(+ = Contains; (-) = Does not contain; (+++) = high levels)
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Phytochemical content contained in methanol extract and distilled water extract

A qualitative phytochemical examination of methanol extract and distilled water was carried out on *C. odorata* L., and the results obtained in Table 2 are as follows:

**Pharmacological activities of Kirinyuh (C. odorata L.) leaves**

Some of the pharmacological activities shown by Kirinyuh leaves include and as shown in Table 3:

- **Anti-inflammatory:** The flavonoid content in *C. odorata* L. leaf extract shows anti-inflammatory activity *in vitro* and *in vivo*. The aqueous extracts of *C. odorata* L. were administered to the rats implanted with a cotton pellet and showed to reduce granuloma formation. The doses of 100 and 200 mg/kg significantly decreased the formation of granulomas (P < 0.05). *C. odorata* L. leaf extract reduced chronic inflammation (expressed by the cotton pellet method) in this test with higher doses of the extract. Granulation is caused by leukocyte buildup, which is probably less effective when administered in smaller amounts. Tamarixetin and kaempferide, 4-methyl ethers of quercetin and kaempferol flavonols, may work together to reduce inflammation. Kaempferol and quercetin both showed high potency of antioxidant and anti-inflammatory effects.

- **Anti-microbial:** In the research that has been done, the pharmacological effects found in *C. odorata* L. can be helpful as an anti-microbial.
Kirinyuh extract leaf extract contains dichloromethanolic and ethanolic, which can fight 22 bacterial strains of various Gram (+) and Gram (-) bacteria. This leaf extract also shows resistance activity against Mycobacterium tuberculosis. Several studies have shown that C. odorata L. has good antifungal activity and found nematicidal activity.

One research stated that C. odorata L. extract with the active constituent of flavonoids could reduce the growth of S. aureus, which proved that the RF result in TLC was 0.9.

Antioxidants: C. odorata L. shows high antioxidant activity. Research shows that phenolic acids are present in C. odorata L. extracts, such as p-coumaric, ferulic, protocatechuic, p-hydroxybenzoic, and vanilla acid. Various hydrolobic complexes of aglycone flavonoids such as flavones, flavanones, chalcones, and flavonols are present in C. odorata L. leaves showed inhibitory activity using the DPPH method. (22) The methanol extract of C. odorata L. showed strong inhibitory activity using the DPPH method. (22)

Antidyslipidemia: The researcher stated that Kirinyuh (C. odorata L.) leaf extract contains flavonoids (79.63 ± 4.55 mg/100 g). The C. odorata L. extract significantly reduced LDL and TG levels and increased HDL concentrations in mice.

Hematologic agent: Ethanol extract of C. odorata L. and kidneys.24

Anti-dyslipidaemia: The researcher stated that Kirinyuh (C. odorata L.) leaves showed inhibitory activity using the DPPH (2,2-diphenyl-1-pircilihydrazyl) radical inhibition method with IC50 values of 63.95, 64.38, and 202.15 µg/ml, with gallic acid as control positive (5.29 µg/ml). 22

Antifungal: The most susceptible organisms to the aqueous and ethanol extracts of C. odorata L. were Aspergillus niger, Candida albicans, and Aspergillus oryzae. At the same time, Geotrichum sp. and Penicillium notatum displayed considerable resistance to bioactivity. Nevertheless, all of them were sensitive to Nystatin (10 mg/dl).

Antidiabetes and anti-cataract: When diabetic rats (administrated with STZ streptozotocin; 45 mg/kg, iv) were given an ethanol extract of C. odorata L. leaves (ACO), blood sugar levels, lipid profiles, glycogen content, glucose absorption by skeletal muscle, serum insulin, and direct bilirubin levels were lower in untreated diabetic rats than in the control group. Untreated diabetic rats had lower albumin and total and direct bilirubin levels than the control group. Treatment with extract at 300 and 600 mg/kg body weight considerably returned the AST, ALP, albumin, direct and total bilirubin, and total proteins to normal levels compared to the untreated control (P < 0.05). The increased bicarbonates, chloride, creatinine, sodium, and urea levels could not be attenuated significantly (P > 0.05).

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Table 3: Some pharmacological activities of Kirinyuh leaf extract (C. odorata L.).

| No. | Pharmacological Activities | Results | Research |
|-----|-----------------------------|---------|----------|
| 1.  | Anti-inflammatory           | The flavonoid content in Kirinyuh leaf extract shows anti-inflammatory activity. | (16) |
| 2.  | Anti-microbial              | C. odorata L. leaf extract showed resistance activity against Mycobacterium tuberculosis. | (16) |
| 3.  | Antioxidants                | Flavonoids in C. odorata L. extract can reduce the growth of S. aureus, with RF 0.9 in TLC. | (19) |
| 4.  | Antidysslipidemia           | Kirinyuh leaf extract contains flavonoids (79.63 ± 4.55 mg/100 g). The C. odorata L. extract significantly reduced LDL and TG levels and increased HDL concentrations in mice. | (22) |
| 5.  | Hematologic agent           | As a hematologic agent, the ethanol extract of C. odorata L. leaves can be useful since it shortens the bleeding period in mice (2.5 min) without producing platelet aggregation or blood clotting in vitro. Therapy for ACO reversed STZ-induced diabetes and cataract in rats and positively affected diabetes mellitus and associated complications. This study provided evidence that taken as a whole, supports the use of C. odorata L. in traditional medicine. | (24) |
| 6.  | Anti-diabetic and anti-cataract | A root extract from C. odorata L. showed anti-diabetic and hepatic impairment-preventive properties. | (26) |
| 7.  | Analgesic and anti-inflammatory | Several fractions of C.odorata L. (CDE; nBF; and EAF) showed analgesic, anti-inflammatory, and antipyretic activity. Furthermore, the nBF fraction, where this biological activity is related to flavonoids in it. | (27) |
| 8.  | Wound healing               | The use of C. odorata L. in wound healing has been established. The plant extract promotes neovascularization and cell migration, increases hemostatic activity, reduces inflammation, and stimulates cell proliferation. | (13) |
| 9.  | Anti-malaria                | Ethanol leaf extracts of C. odorata L. and Cymbopogon citratus showed blood schizontocidal activity with significant results (p < 0.05) within four days compared with the standard drug chloroquine. | (20) |
| 10. | Mosquito larvicidal          | The methanolic leaf extract of C. odorata L. has anti-larval activity against the vector, An. stephensi. Cq. quinquefasciatus and Ae. Aegypti. | (30) |
| 11. | Antihypercholesterolemia    | Ethanol extract of Kirinyuh leaves (C. odorata L.) can lower total cholesterol levels on Wistar strain male white rats given a high-fat diet, with the best (6) concentration being 60 mg/kg BW in mice. | |
| 12. | Antifungal                  | Microsporum gypseum, Cryptococcus neoformans, Trichophyton rubrum, and Trichophyton mentagrophytes are all inhibited in vitro by extract and fractions of C. odorata L., having an inhibitory concentration range for the extract of 62.5 to 500 g/ml and the fractions of 25 to 100 g/ml. | (28) |

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One research stated that C. odorata L. extract with the active constituent of flavonoids could reduce the growth of S. aureus, which proved that the RF result in TLC was 0.9.19

Antioxidants: C. odorata L. shows high antioxidant activity. Research shows that phenolic acids are present in C. odorata L. extracts, such as p-coumaric, ferulic, protocatechuic, p-hydroxybenzoic, and vanilla acid. Various hydrolobic complexes of aglycone flavonoids such as flavones, flavanones, chalcones, and flavonols are present in C. odorata L. as the primary and potent antioxidants.21 Nitric oxide (NO) is also found in Kirinyuh extract, the most abundant phenolic compound. NO in C. odorata L. is responsible for its antioxidant potential.16

The researcher stated that the methanol extract of C. odorata L. leaves showed inhibitory activity using the DPPH (2,2-diphenyl-1-pircilihydrazyl) radical inhibition method with IC50 values of 63.95, 64.38, and 202.15 µg/ml, with gallic acid as control positive (5.29 µg/ml).22

Antidysslipidemia: The researcher stated that Kirinyuh (C. odorata L.) leaf extract could reduce blood glucose levels and lipid profile concentrations, namely VLDL, LDL, Triacylglycerol, and total cholesterol in white mice. This study also found an increase in HDL levels in the blood. This study's dose of Kirinyuh leaf extract was 20 mg/kg BW.23

Hematologic agent: Ethanol extract of C. odorata L. shows an effect as a hematologic agent, namely an anticoagulant. The mechanism of this plant works on stimulation of coagulation on factor 12. However, using extracts and isolation in large doses will cause hepatotoxicity to the liver and kidneys.26

Antidiabetes and anti-cataract: When diabetic rats (administrated with STZ streptozotocin; 45 mg/kg, iv) were given an ethanol extract of C. odorata L. leaves (ACO), blood sugar levels, lipid profiles, glycogen content, glucose absorption by skeletal muscle, serum insulin, and direct bilirubin levels were lower in untreated diabetic rats than in the control group. Untreated diabetic rats had lower albumin and total and direct bilirubin levels than the control group. Treatment with extract at 300 and 600 mg/kg body weight considerably returned the AST, ALP, albumin, direct and total bilirubin, and total proteins to normal levels compared to the untreated control (P < 0.05). The increased bicarbonates, chloride, creatinine, sodium, and urea levels could not be attenuated significantly (P > 0.05).

Analgesic and Anti-pyrexia: Phytochemical examinations were carried out on several leaf fractions of C. odorata L., namely dichloromethane (DCF), ethyl acetate (EAF), and n-butanol (nBF) fractions. The results showed that the DCF fraction showed analgesic, anti-inflammatory, and antipyretic activity. Next is the nBF fraction, and finally, the EAF. This biological activity is related to the presence of flavonoids in each fraction.27
Wound healing Source: It has been established that *C. odorata* L. is generally safe for wound healing and can treat exterior and internal wounds with its wound-healing agent. By promoting TXS and inhibiting MMP-9 production, *C. odorata* L. extract stimulates hemostatic action. It also initiates the expression of HO-1 (Heme oxygenase-1) by activating the MEK, p38 MAPK, Akt, and JNK kinase pathways. Inhibiting inflammation, promoting cell growth, increasing neovascularization, and encouraging cell migration are all effects of HO-1 induction that will aid in wound healing.13

Anti-malaria: Ethanol leaf extracts of *C. odorata* L. and *Cymbopogon citratus* showed anti-plasmodial activity (*P. berghei*). Blood schizontocidal activity gave significant results (*P < 0.05*) within four days compared with the standard drug chloroquine (5 mg/kg/day).26

Antifungal: The researcher stated yeasts and filamentous fungi were used to test an aqueous ethanol extract of *C. odorata* L. leaves and some of its fractions for their antifungal capabilities. *Microsporum gypseum*, *Cryptococcus neoformans*, *Trichophyton rubrum*, and *Trichophyton mentagrophytes* are all inhibited in vitro by extract and fractions. The inhibitory concentrations ranged from 62.5 to 500 g/ml for the extract and from 25 to 100 g/ml for fractions.28

*C. odorata* L. showed that all the test fungi were vulnerable to the hot water and ethanolic extracts, which inhibited growth at 100 mg/ml and 50 mg/ml concentration. The three molds with the highest susceptibility to the aqueous and ethanol extracts were *Aspergillus niger*, *Candida albicans*, and *Aspergillus oryzae*. *Geotrichum sp.* and *Candida albicans* and *C. odorata* L. showed some resistance to the bioactivity of the hot water and ethanolic extracts, which inhibited growth at 100 mg/ml and from 25 to 100 g/ml for fractions.28

**Toxicity of *C. odorata* L.**

Administration of *C. odorata* L. leaf water extract can reduce levels of amylase, albumin and total serum protein, and Na + at doses of 538.5 mg/kg and 1077 mg/kg and can cause an increase in serum creatine kinase, AST, K +, glucose, uric acid levels, urea and creatinine.27

Long-term use and large doses of *C. odorata* L. extract (> 250 mg/kg body weight) can cause side effects on kidney function and histological changes in rat intestines.21

Pyrrolizidine alkaloids (PAs) in *C. odorata* L. may be toxic to grazing animals like cattle and goats. It has been demonstrated that pyrrolizidine alkaloids exhibit a wide range of genotoxic effects. Clinical research must be done to determine the safe dosage range for treating different diseases because PAs can be dangerous to humans and animals.21,32,33

**CONCLUSION**

In summary, Indonesia is known as megabiodiversity country with numerous medicinal plants.34,35,36,37,18,30,40 However, the leaves of kirinyuh (*Chromolaena odorata* L.) are shrubs that originated from America and spread across Indonesia, Africa, and the Pacific. Kirinyuh leaves are a medicinal plant that contains alkaloids, flavonoids, tannins, saponins, and steroids. Various pharmacological benefits include anti-inflammatory, anti-microbial, antioxidant, antidiyslipidemia, hematologic agent, anti-diabetic and anti-cataract, analgesic and antiinflammatory, wound healing, anti-malaria, mosquito larvicidal, anti-hypercholesterolemia and antifungal. From the results of this study, it can be estimated that Kirinyuh (*C. odorata* L.) has sufficient potential as a medicinal raw material. More in-depth research is needed for future development.

**CONFLICTS OF INTEREST**

There are no conflicts of interest in the preparation of this article.

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GRAPHICAL ABSTRACT

Kirinyuh (C. odorata. L.)

A phytochemical compound in C. odorata L.

Anti-inflammatory

Anti-microbial

Antioxidants

Antidyslipidemia

Hematologic agent

Anti-diabetic and anti-cataract

Analgesic and anti-pyretic

Wound healing

Anti-malaria

Mosquito larvicidal

Antihypercholesterolemia

Antifungal

Pharmacological activities of Kirinyuh leaf extract (C. odorata L.)

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