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**Original Research Article**

# *Uncaria gambir* (W. Hunter) Roxb: From phytochemical composition to pharmacological importance

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## Abstract

***Purpose:*** *To present an overview of the ethnopharmacology, phytochemistry, and pharmacological effects of the 'wonder' plant, Uncaria gambir (W. Hunter) Roxb.*
***Methods:*** *The literature search for information on phytochemical composition and pharmacological importance of U. gambir was undertaken using diverse electronic search engines, including Google, Scopus, Web of Science, scientific literature, and databases (Pubmed, Springer and Science Direct). Other relevant literature sources include books, book chapters, conference papers, theses, and other scientific publications.*
***Results:*** *Uncaria gambir Roxb possesses significant medicinal potentials as an antioxidant, anthelmintic, antibacterial, anti-diabetic, and for the management of osteoarthritis. Interest has increased among researchers for the utilization of this plant in complementary medicine, for example, to relieve sore throat, spongy gum, and dysentery, to treat atherosclerosis and obesity, and to prolong sexual intercourse.*
***Conclusion:*** *Uncaria gambir demonstrates significant pharmacological properties. This review will be useful for prospective research and development of this ethnomedicinal plant into potentially valuable health products.*

***Keywords:*** *Anthelmintic, Antibacterial,Anti-Diabetic, Osteoarthritis, Uncaria gambir*



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## INTRODUCTION

The utilization of traditional medicine has gained a lot of attention as an alternative medicine to modern treatment worldwide [1-3]. Currently, more than 2,000 species of medicinal plants with therapeutic benefits have been discovered in Malaysia [4,5]. These plants are very often used as traditional medicine and self-prescribed to relieve minor illnesses such as fevers, diarrhea, headaches, colds, coughs, and abdominal pains. Herbal medicines are also used as health supplements in improving health and maintaining physical fitness [6].

*Uncaria gambir* (W. Hunter) Roxb is a climbing

shrub, native to Southeast Asia, particularly Malaysia and Indonesia [7]. This plant belongs to the family Rubiaceae, genus *Uncaria*. This plant is also known as gambir or gambir Sarawak in Malaysia and Indonesia [8]. Indonesia contributes around 80% of the gambir export commodities in the world [9]. There are four cultivars of gambir reported in West Sumatera, Indonesia, namely shrimp gambir, mancik Riau, Riau sieve, and cubadak [10].

All cultivars are rich in flavonoids such as quercetin and catechin, which have antioxidant and anti-inflammatory properties [11]. Due to flavonoids and tannins, this plant was reported to have antioxidant properties [12].

This high-value plant has traditionally been used for various ailments, as well as being formulated as a gel for topical application on penile glans, resulting in a numb sensation to prolong sexual intercourse and alleviate premature ejaculation [10]. In this review, botany, ethnobotanical uses, chemical properties, and pharmaceutical effects of *U. gambir* will be highlighted for better understanding and exploitation of this useful plant.

## BOTANY

### Scientific name

*Uncaria gambir* (W. Hunter) Roxb

### Synonyms

*Nauclea gambir* Hunter, *Ourouparia gambir* (Hunter) Baill, *Uncaria gambir* var. latifolia S. Moore., *Uruparia gambir* (Hunter) Kuntze [13].

### Common names

In Malaysia, this plant is colloquially known as gambir or gambir Sarawak. *U. gambir* grows in abundance in Sarawak, the northwest Borneo Island. In India and Thailand, *U. gambir* is known as pale catechu, gou teng in China, and asen'yaku in Japan. In some parts of the world, *U. gambir* is also called cat's claw or *una de gato*, which are also the common names for several other plants [13,14].

### Botanical description and distribution

Gambir plants can grow approximately 2.4 m tall and about 8 to 14 cm in length, with oval or oblong leaves of 4 to 6.5 cm wide. Yellowish flowers are formed at the leaf base and each pair of leaves may have a pair of globular inflorescences [15,16]. The tubular and hairy flowers are borne in globose heads of 6 to 8 cm. The fruits are near cylindrical and less than 2 cm long [17]. As stated by Sebayang [15], gambir plants can only be grown under specific conditions in any type of soil with the pH range from 4.8 to 5.5. The plant needs to be grown at 200 to 800 meters above sea level, with high rainfall throughout the year and approximately 70-85% humidity with a land slope of 15%.

## ETHNOBOTANICAL USES

Due to its astringent properties, *U. gambir* has been traditionally used in Malaysia, Indonesia and Singapore for men to extend sexual intercourse and prevent premature ejaculation [18], as well as reducing toothache due to the numb sensation given by a polymer tanning mixture. Its content of catechin derived from the leaves can act as a natural antioxidant [19]. Additionally, gambir leaves and young shoots are also remedies for dysentery, diarrheal disease, spongy gums, sore throat, obesity, atherosclerosis, and deafness [16,17]. Moreover, chewing gambir with dried areca nut and calcium hydroxide can preserve oral hygiene and toughen teeth and gums [20]. In the nineteenth century, this plant was one of several traditional export commodities, being used as a brown dye and tanning agent [17]. To date, *U. gambir* is still used as herbal medicine and occasionally as a food additive in Malaysia [20].

## CHEMICAL COMPOSITION

Since gambir's discovery in the early 1900s, one of the breakthrough reports on its chemical composition was in 1980, in which two active polyphenols (flavonoids), (+)-catechin and (+)-epicatechin, were characterized from dried aqueous extracts [14-16]. Catechin was reported as a major bioactive compound and has been used as a metabolite biomarker to determine the quality of gambir [16]. A comprehensive study by Nonaka [22] found a new bioflavonoid compound, gambiriin. Andasuryani *et al* [23] also demonstrated catechin as the most abundant constituent in gambir besides epicatechin and gambiriin. Gambir also contains yellow-colored flavonoid quercetin [24], as well as gambirdine and isogambirdine [15]. A further study isolated (+)-catechin, (+) epicatechin, and seven dimeric flavans known as gambiriin A1, A2, B1, B2, procyanidin B1, procyanidin B3, and gambiriin C from the aqueous extracts [25]. Through rapid chromatography, four new indole alkaloids, namely gambirtannine, dihydrogambirtannine, oxogambirtannine, and neooxygambirtannine were identified from the leaf and stem aqueous extracts [26]. Table 1 shows the metabolites

identified from *U. gambir*. The chemical structures of selected metabolites in *U. gambir* are shown in Figure 1.

**Figure 1:** Chemical structure of selected metabolites in *Uncaria gambir*. A) (+)-Catechin, B) (-)-epicatechin, C) Gambirine, D) Isogambirine, E) Quercetin, F) Gambirtannine, and G) Roxburghine.

## PHARMACOLOGICAL PROPERTIES

### Antioxidant properties

Phytochemical analysis showed that the major antioxidant compound in *U. gambir* is catechin, the predominant secondary metabolite. Catechins are capable of obstructing and scavenging free radicals [11]. In general, *U. gambir* extracts have high antioxidant activities [34]. To prove the antioxidant properties in *U. gambir*, Anggraini *et al* [11] evaluated the 1,1-diphenyl-2picrylhydrazyl (DPPH) radical scavenging activity on four popular cultivars gambir extracts. The four cultivars of gambir demonstrated similar antioxidant activities with a highly significant ability to scavenge free radicals (92 – 93 %) [11]. DPPH has been commonly used to measure antioxidant activity due to its simple, rapid, sensitive, and reproducible approach [28].

A comprehensive review on the medicinal uses, phytochemistry, and pharmacology of the 19 species of plants in the genus *Uncaria* suggests that ethanol and ethyl acetate extracts of *U. gambir* dried leaves demonstrated a higher DPPH inhibitory activity ($IC_{50}$, 13.8 - 16.2 µg/mL) than the aqueous extract ($IC_{50}$ 27.4 µg/mL), due to the presence of tannins and condensed tannins [26,33]. Gambir extracts have also been shown to possess antioxidant activity (25.55 µg/mL) by comparing the value of DPPH radical scavenging activity with ascorbic acid [35]. The ethyl acetate extract showed the highest antioxidant activity of phenolics at 89%, accompanied by methanol extract (86%), both at 50 ppm concentration of aqueous extract [16]. Thus, it can be inferred that gambir extract may scavenge the radicals by other mechanisms, apart from hydrogen donation. A similar DPPH assay was applied by Anggraini *et al* [11] on four cultivars of gambir in West Sumatra, Indonesia. It was found that all four cultivars of gambir extracts manifest high antioxidant activity. The existence of catechin might be the reason for high phenolic content in gambir, which is one of the most effective antioxidants.

Antioxidant assay of gambir extracts using lipid peroxidation approach at different concentrations showed anti-lipid peroxidation against $Fe^{2+}$-induced lipid peroxidation at 250 µM concentration [34]. A study by Nordin *et al* [20] revealed that gambir extracts have higher inhibitory effects of lipid peroxidation compared to α-tocopherol. In general, the scavenging or chelating process is the mechanism of flavonoids as antioxidants [36]. However, the anti-lipid peroxidation by flavonoids works by metal ion chelation instead of radical scavenging [37].

### Anthelmintic activity

Helminth infections are frequently occurring infections in humans and more than half of the world population suffer helminthic infections [38]. Most of these infections happen mainly in tropical regions and the manifestation is catalyzed by unsanitary lifestyle, with symptoms such as anemia, eosinophilia, and pneumonia [39]. The wormicidal activity of the ethyl acetate fractions against earthworms suggests gambir as a source of natural anthelmintic and may be effective against human parasitic infections [38].

The anthelmintic potential of both the leaf and shoot extracts have been evaluated [38]. The ethyl acetate fraction of the alcoholic extract showed effective anthelmintic activity against Indian adult earthworms (*Pheretima posthuma*). The extract was assessed on Indian adult earthworms (*Pheretima posthuma*) by *in vitro* standard procedure. The increase in time of paralysis and the time of death of the worms indicate the effectiveness of *U. gambir* as a natural anthelmintic [38]. In another study, both the leaf and shoot extracts were found to possess anthelmintic properties in a dose-dependent manner [40]. Tannins have been reported to have anthelmintic properties as they can bind to free proteins in the gastrointestinal tract of hosts or glycoproteins on the cuticle of parasites resulting in their death [41,42].

### Antibacterial activity

Gambir was found to have antibacterial activity as its ethanol extract produced zones of inhibition against three different strains of *Escherichia coli* O157:H7 and other strains of Shiga-like toxin-producing strains, including *E.*

**Table 1:** Compounds isolated from *Uncaria gambir*

| Compound | Class | Extract | Plant part | Method of Identification | Reference |
|---|---|---|---|---|---|
| (+)-Catechin | Flavonoid | Aqueous | Leaf and young twig | HPLC | [21] |
| | | Aqueous | Leaf and young twig | Crystallization | [27] |
| | | Aqueous | Leaf | FT-NIR | [23] |
| | | Aqueous | Leaf | Spectroscopy | [24] |
| | | Methanol | Leaf | Colorimetric | [28] |
| (-)-epicatechin | Flavonoid | Aqueous | Leaf and young twig | Crystallization | [27] |
| | | Aqueous | Leaf and young twig | HPLC | [21] |
| Gambiriin $A_1$, $A_2$, A3, B1, $B_2$, $B_3$ | Flavonoid | Aqueous | Leaf and young twig | NMR | [22] |
| Gambiirin C | Flavonoid | Aqueous | Leaf and young twig | NMR | [22] |
| | | Aqueous | Leaf and young twig | HPLC | [21] |
| Gambiriin $A_1$, $A_2$, $B_1$, $B_2$ | Flavonoid | Aqueous | Leaf and young twig | HPLC | [25] |
| Procyanidin B1, B3 | | | | | |
| Gambirine | Flavonoid | Aqueous | Leaf and young twig | HPLC | [21] |
| | | Aqueous | Leaf | Spectroscopy | [24] |
| | | Ethanol | Leaf | NMR | [32] |
| | | Methanol | Leaf | NMR | [33] |
| Isogambirine | Flavonoid | Aqueous | Leaf and young twig | HPLC | [21] |
| | | Aqueous | Leaf | Spectroscopy | [24] |
| | | Ethanol | Leaf | NMR | [32] |
| | | Methanol | Leaf | NMR | [33] |
| | | Methanol | Leaf | Colorimetric | [28] |
| Quercetin | Flavonoid | Aqueous | Leaf | MS | [29] |
| | | Aqueous | Leaf | HPLC | [30] |
| Roxburghine A, B, C, D, E | Alkaloid | Aqueous | Leaf | NMR | [31] |
| Gambirtannine | Alkaloid | Methanol | Powdered gambir | NMR, MS | [26] |
| Dihydrogambirtannine | | | | | |
| Oxogambirtannine | | | | | |
| Neooxygambirtannine | | | | | |

*coli* O026:H11, *E. coli* O011:NM, and *E. coli* O22 [43]. Melia *et al* [35] determined the antimicrobial activities of gambir extract in their use in *Rendang*, a Malaysian traditional curry. The study found the extract exerted higher antibacterial activity against gram-negative bacteria *E. coli* and *Salmonella* sp. than *Staphylococcus aureus*, a gram-positive bacteria. Various classes of phytochemicals have been identified in *U. gambir* extract such as alkaloids, flavonoids, and tannins [28]. These secondary metabolites have been previously proven to have antibacterial activities and act as a defence mechanism *in planta* against pathogenic bacteria [44].

The antibacterial activity in gambir may be due to the attribution of some metabolic toxins such as tannin or broad-spectrum antibiotic compounds such as catechin [45]. Gambir is known for having a high amount of tannins with well-established antimicrobial properties [46]. Furthermore, flavonoids are known to have antibacterial activities against a wide range of phytopathogens [47]. The way flavonoids work is most likely due to their ability to form complexes with bacterial surface proteins, resulting in bacterial membrane dysfunction [48].

### Miscellaneous activities

Based on Widiyarti *et al* [49], gambir ethyl acetate extracts possess an inhibitory effect on α-glucosidase enzyme activity. The extracts can inhibit the hydrolysis of carbohydrates into glucose, therefore stopping the appearance of postprandial hyperglycemia. Thus, the extract might have the potential to act as a pharmacotherapeutic agent for type 2 diabetes mellitus [49].

Gambir has also been reported to possess analgesic and anti-inflammatory properties. A study reported that the mixed two standardized extracts of *U. gambir* leaf and *Morus alba* root bark with 1:1 ratio in carrageenan-induced rats produced a significant enhancement in pain resistance; while reducing paw edema and ear thickness in mice treated with the extracts [50]. The study suggests that these two plants have a prospect for symptom management of osteoarthritis.

## TOXICITY

To the best of our knowledge, there is no report on *in vitro* or *in vivo* toxicity studies of gambir. Due to this limited reported data, a wide-ranging toxicological study of gambir should be investigated in the future.

## CONCLUDING REMARKS

*U. gambir* is an indigenous plant in Southeast Asia and extensively used as an alternative medicine with diverse applications. Phytochemical and pharmacological studies have ratified its traditional and alternative uses. Phytochemical studies revealed biologically active constituents such as flavonoids, alkaloids, and tannins. As for pharmacological studies, diverse biological activities, particularly antioxidant, anti-helminthic, antibacterial, anti-diabetic, analgesic, and anti-inflammatory have been demonstrated. However, since there is no study on its toxicity, toxicological investigations are needed. The potentials of Gambir highlighted in this review should facilitate its commercialization for therapeutic applications.

## DECLARATIONS

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### *Conflicts of interest*

No conflict of interest is associated with this work.

### *Contribution of authors*

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors equally contributed to this review.



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