

## Review Article

## A Review: The Phytochemistry, Pharmacology and Traditional Use of Gambir (*Uncaria gambir* (Hunter) Roxb)

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**Abstract:** Indonesia is known as one of the countries that has a wealth of natural resources that can be used as herbal medicines. One of them is (*Uncaria gambir* (Hunter) Roxb). Gambir has been known to have many properties for various disease treatments. This article explores the traditional uses of gambir and seeks information about the phytochemical content of its pharmacological effects. In compiling this review article, tracing has been carried out in the form of national and international journals in the last 20 years (2000 - 2020). The main references used in this review article were searched through trusted websites such as ScienceDirect, ResearchGate, Google Scholar, and other published and trusted journals. Phytochemically, this plant contains catechin compounds, catechic acid, pyrocatechol, quercetin, tannins, flavonoids, gambirin alkaloid compounds, fluorescence gambir, tannin gambir, wax, rinkophylline, isorinkophylline, gambirdin, isogambirdine and auroparin. Pharmacologically, this plant has been reported to have antibacterial, anticancer, anti-inflammatory, antioxidant, anti-diabetic and hypoglycaemic effects. Traditionally, gambir is used as a mixture of medicines, namely for burns, headaches, diarrhoea, dysentery, canker sores and skin pain medication.

**Keywords:** Gambir, *Uncaria gambir*, traditional use, phytochemicals, pharmacological activity.

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### INTRODUCTION

Gambir belongs to the genus of the Rubiaceae family. Gambir in Indonesia is generally used for betel nut and is taken in large quantities for textile dyeing and extracts from printed and sun-dried sap which are commonly found in West Sumatra and Kalimantan [1]. Gambir has a scientific name: *Uncaria gambir* (Hunter) Roxb. Gambir is a hot water extract from the leaves and twigs of the gambir plant which is deposited and then milled and dried, which functions as an astringent [8]. Gambir extract is useful for the treatment of diarrhoea, headaches, dysentery, canker sores, and skin pain medications. Gambir plants usually grow at an altitude between 200-900 m above sea level [2].



**Fig-1: Gambir Plants [3, 4]**

### Classification of Plants

Kingdom	: Plantae
Division	: Magnoliophyta
Class	: Mangnoliopsida
Sub-class	: Asteridae
Order	: Rubiales
Family	: Rubiaceae
Genus	: <i>Uncaria</i>
Species	: <i>Uncaria gambir</i> (Hunter) Roxb
Synonyms	: <i>Uncaria gambir</i> Roxb. <i>Uncaria acida</i> Roxb. <i>Nauclea gambir</i> Hunt. <i>Ouroparia gambir</i> Baill.

### DATA COLLECTION

In compiling this review article, the technique used was the literature study by searching for sources or literature in the form of primary data or official books as well as national and international journals in the last 20 years (2000-2020). In making this review article, data search was carried out using online media with the keywords as follows: *Uncaria gambir*, phytochemicals, traditional use, and pharmacology. The main references used in this review article were searched through trusted websites such as ScienceDirect, ResearchGate, Google Scholar, and other published and trusted journals.

## DISCUSSION

### Traditional Use

Gambir (*Uncaria gambir*) is often used as a traditional medicine by the people of Siguntur, West Sumatra, Indonesia. Gambir water extract has been used as a traditional medicine to treat diarrhoea, and sore throat [4]. The traditional processing of gambir that is carried out by the community consists of several stages, namely by boiling fresh leaves, extracting the sap of gambir, tapping water draining, printing, and drying [6]. This traditional management was carried out in the seventeenth century in Sumatra and the Malay Peninsula [8]. Gambir extract is used for the treatment of diarrhoea, headaches, dysentery, canker sores, skin pain medication and a supplement for consuming betel [2].

### Phytochemical Review

The content of chemical compounds in plants is called phytochemicals. Plants can be a source of chemical compounds that can be used as medicine. The material used by this research is gambir leaves from Pontianak, West Kalimantan. The gambir leaves are processed into herbal tea of gambir leaves. The method used in the research was experimentation in the laboratory using qualitative phytochemical testing and total phenol testing following the procedures. The results of the study indicated that the characteristics of gambir leaf tea that approach SNI 2013 are at a temperature of 90° C with a moisture content of 14, 3223% (db), 16.8312%. Ash content 90° C 3,9326 with total phenol content contained in Gambir leaves of 3.9 mg GAE / 10 mg. The compounds contained in gambir leaves include flavonoids, tannins and saponins [10].

The extract (sap) of the leaves of gambir contains catechu tannat acid (tannin), catechin, pyrocatechol, fluorine, wax, and oil. The main components of gambir are Catechu Tannic acid (20-50%), catechins (7-73%), and pure pyrocatechol are slightly soluble in cold water but soluble in hot water, soluble in alcohol and ethyl acetate. When catechins are heated at 110 ° C or heated in an alkaline carbonate solution, they lose water molecules and turn into catechu tannic acid or tannins. The purification of catechin gambir with good quality will certainly increase the added value of the product itself. Therefore, it is necessary to find a method for catechin purification [7].

In the study, phytochemical screening and fractionation were identified on 4 types of gambir, namely the type of shrimp (U), Riau Gadang (RG), Riau mancik (RG), and the type of cubadak (C) taken in the Siguntur area. Screening aims to see if there are differences between the three types of chemical components of this gambir. Phytochemical identification includes alcoholoid testing, steroid-triterpenoid test, flavonoid test, saponins, tannins and

quinones. Chopped Sample of 10 grams, added with 20-30 ml  $\pm$  methanol and simmered for 5 minutes. The methanol extract was separated, then the solvent was evaporated until it was dry with water, so that the dregs were obtained. The dregs were boiled with water for a few minutes, then filtered under hot conditions. On the tested water phenolic fraction, flavonoids and saponins. The waste was added with chloroform while stirring, divided into two chloroform fractions:- Part 1 was tested for steroids and triterpenoids - Part 2 was added 1 drop of concentrated ammonia then concentrated sulfuric acid. The mixture was shaken and the water fraction was separated, then the water fraction was tested for alkaloids with Mayer and Dragendorff reagents and flavonoids and saponins. From the results of the qualitative analysis it is known that Gambir contains quinones, terpenoids, alkaloids, tannins, flavonoids and saponins. Whereas in the steroid gambir, there was no overall detection of steroid gambir. Alkaloids were found in most types of shrimp gambir. The highest yield fractionation was in the EtOAc fraction and BuOH fraction and the highest was in Riau for the gambir gadang type [20].

### Pharmacological Activity

#### Antibacterial

Antibacterial activity from crude extract of gambir leaves with the research method used was a randomized block design (RBD) with 2 factors, namely microwave power (320, 560 and 800 Watts) and the ratio of ingredients: solvent (1:25, 1; 35 and 1:45 (w / v)). The best results were obtained from the microwave power treatment of 560 Watt and the ratio of ingredients: solvent 1:35 (w / v) with a yield of 63.29%, total phenol 5581.58 ppm, antibacterial activity of *Escherichia coli* ATCC 25922 12.07 mm, *Salmonella typhimurium* 12.57 mm, *Staphylococcus aureus* ATCC 29213 13.99 mm and *Bacillus cereus* 14.38 mm. KHM for *Escherichia coli* ATCC 25922 100%, *Salmonella typhimurium* 90%, *Staphylococcus aureus* ATCC 29213 90% and *Bacillus cereus* 80%, while KBM has not been known [11].

#### Anticancer

This research was conducted to determine the anticancer activity of T47D breast cancer cells in vitro. 6 levels of gambir (31.25 mg / ml) were added to 96 microplate wells filled with breast cancer cells, the positive control was doxorubicin (with a concentration of 0.03- 1 mg / ml). The anticancer effect of the gambir plant was determined by MTT (3- [4,5-dimethylthiazol-2-yl] - diphenyl tetrazolium bromide 2.5). The results showed that the greatest anticancer activity was at a concentration of 500  $\mu$ g / ml with a percentage of breast cancer apoptotic cells by 20%. However, this study also found a decrease in the value of apoptosis at a concentration of 1000  $\mu$ g / ml while doxorubicin IC50 was 0.108  $\mu$ g / ml. This study concluded that the inhibition of breast cancer cell growth by gambir leaf extract was quite weak compared to doxorubicin [9].

### Anti-inflammatory

The anti-inflammatory effect test was carried out based on leg edema made to suffer inflammation by injection with caregan, this study showed that catechins isolating a dose of 10 mg / kg BW and a dose of 100 mg / kg BW have the ability to inhibit edema better than the dose of 1 mg / kg bw However, when observed from the percentage of the inhibitory dose of inflammation of 100 mg / kg bw the inhibitory power was higher by 59.19%. And a dose of 10mg / kg bw has the same ability to inhibit rat claw edema. Therefore, the conclusion is Catechin isolating gambir at a dose of 1 mg / kg bw has anti-inflammatory effects on carrageenan edema-induced claws in Wistar male rats. A dose of 10 mg / kg of catechin isolates Gambir, the best dose in reducing edema because it has almost the same edema as Na-diclofenac. The effect of an anti-inflammatory dose of 100 mg / kg bw was not a significant difference compared to a dose of 10 mg / kg bw [14].

The purpose of this study was to determine the activity of the anti-inflammatory ethyl acetate fraction of *Uncaria gambir* leaves in inhibiting the expression of edema, COX-2 and iNOS using the induction method with carrageenan in mice. This research was an experimental study using 25 Wistar white rats as test animals which were divided into 5 groups, namely the negative group (water), the positive group (diclofenac sodium 50 mg / kg bw), dose I (fraction 5 mg / kg bw). Group II (fraction 10 mg / kg bw) and III (fraction 20 mg / kg bw). Each was given orally 30 minutes before carrageenan 3% was induced. The foot volume was measured every day for seven days after injection of carrageenan using a measuring instrument. Inhibition of COX-2 and iNOS expression was determined by enzyme-linked immunosorbent assay. It was concluded that three-dose ethyl acetate has anti-inflammatory activity through edema volume reduction mechanisms, COX-2 expression and iNOS [19].

### Antioxidants

The results of this study indicated that all extracts had high activity to inhibit DPPH but moderate activity to inhibit -glucosidase in vitro. Apart from the aqueous extract, 92% DPPH inhibition by the extract could be achieved at 30 g / ml. The ethanol and ethyl acetate extracts had significantly higher DPPH inhibitory activity ( $p < 0.01$ ) compared to aqueous extracts. The IC<sub>50</sub> of the organic extract and residue ranged from 13.8 to 16.2 g / ml for DPPH inhibition whereas the aqueous extract was 27.4 g / ml. With regard to glucosidase inhibition, however, the IC<sub>50</sub> ranged between 15.2 and 49.5 g / ml. Catechins were identified as the main bioactive compounds present [5].

To test the antioxidant activity, the DPPH (1,1-diphenyl-2-picrylhydrazyl) radical method was used, because this method is quite simple, easy to work with, and does not require much time. Antioxidant activity

was measured based on the ability to scavenge DPPH radicals. The presence of antioxidants will neutralize DPPH radicals by donating electrons to DPPH, resulting in a colour change from purple to yellow. The colour removal will be proportional to the number of electrons taken up by the DPPH so that it can be measured spectrophotometrically [6].

The extraction process of the leaves and twigs of the gambir plant (*Uncaria gambir* Roxb) was carried out mechanically using traditional hydraulic presses, conventional screw presses, and modified twin-screw presses. The analysis of the antioxidant activity of the extract was also carried out using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) method and compared with vitamin C as a standard antioxidant. The analysis showed that the extract did not contain ash. While the content of catechins and extract water was approximately 50 and 13% so that the extract was classified as high quality gambir. Furthermore, analysis of the catechin and epicatechin content of the extract was carried out using HPLC and compared with the reference material showing the catechin content of the extract using traditional hydraulic presses, conventional screw presses, and modified double screw presses giving a catechin content of around 94,296-95,030%. However, epicatechin was detected. The antioxidant activity of the extract was 2.5 times stronger than the reference. The IC<sub>50</sub> value was 4.37-4.52 µg / mL and was included in the active antioxidant category [15].

The purpose of this study was to study the effect of repeated extraction of raw gambir from gambir production centres in West Sumatra Province. The results showed that antioxidant activity had a positive correlation with catechin content. Extraction using ethyl acetate produced the highest catechins (97.82 ± 2.01%) and had the potential to produce better antioxidants, which was characterized by an IC<sub>50</sub> value of 91.98 mg mL<sup>-1</sup> lower than extracted ethanol (IC<sub>50</sub> = 193.36 mg mL<sup>-1</sup> with catechin levels = 94.37 ± 0.45%). Purification using amberlite resulted in higher antioxidant activity than extraction using solvents with IC<sub>50</sub> = 87.52 mg mL<sup>-1</sup> and catechin content of 98.09 ± 1.40%. However, the purification process of catechins with amberlite absorbent is relatively complicated and expensive. Purification of catechins is suggested to be carried out by repeated extraction using ethyl acetate solvent [18].

### Antidiabetic

The purpose of this study was to determine the effect of giving gambir on blood sugar levels in type II diabetes mellitus sufferers in the Koto City Sungai Penuh Public Health Centre in 2018. The type of research used was Quasy Experiment with the Two Group Post-test Design approach which was held on July 3-11 2018. The results showed that the average blood sugar level in the intervention group that had been given gambir was 199.88 mg / dL, while in the



control group it was 326.25 mg / dL. Based on the statistical test, it was found that  $p$  value =  $0.003 \leq 0.05$ , which means that there is an effect of giving gambir and blood sugar levels. It can be concluded that there is an effect of giving gambir on reducing blood sugar levels in patients with type II diabetes mellitus. It is hoped that the results of this study will become one of the Non-Communicable Diseases programs in the Koto Baru Community Health Centre in utilizing gambir to help reduce blood sugar levels of type II diabetes mellitus patients, as well as being able to teach how to properly process and consume gambir for type II diabetes mellitus patients [13].

This study aimed to determine the effect of gambir extract on the gambir plant on levels of malondialdehyde (MDA), superoxide dismutase (SOD), and blood glucose levels (BGL) in type 2 diabetes mellitus (T2DM). Methods: This study was a randomized clinical study consisting of two groups, namely the placebo group ( $n = 10$ ) and the gambir group ( $n = 6$ ). Blood Samples were taken from veins after fasting overnight and before consuming 100 g of plain bread to measure levels of MDA, SOD, and BGL. The same procedure was carried out after fasting and 2 hours postprandial on days 1 and 14. The data obtained were analysed using Student's  $t$ -test, with a statistical significance level of  $p < 0.05$ . The results showed no change in MDA levels in the placebo group during follow-up, but a significant decrease [18].

### Hypoglycaemic

The purpose of this study was to extract gambir, to determine the hypoglycaemic activity of gambir drink in alloxan-induced rats. In this study gambir was extracted with 3 types of solvents with distilled water, ethyl acetate, and ethanol. Gambir drink was tested on 5 groups of mice consisting of 5 male mice. Group 1 was given 0.5% CMC 1% / body weight, group 2 was given metformin 65 mg / kg BW, groups 3, 4 and 5 were given gambir drink with a dose of 100, 200, and 300 mg / kg bw. The extraction results showed that using distilled water produces the best gambir drink. Gambir drink with a dose of 100, 200 and giving 300 mg / kg BW for 15 days reduced blood glucose levels by 27.69%, 38.75%, and 50.62% respectively, and increased body weight 13.14%, 10, 91%, and 10.18%, respectively. Treatment with gambir drinks was found to improve the condition of the pancreatic islets of Langerhans from alloxan-induced rats [17].

### CONCLUSIONS

Based on studies that have been conducted, Gambir (*Uncaria Gambir* Hunter (Roxb) has bioactivity as three chemical components, namely total phenolic, flavonoids and tannins that have antidiabetic activity by lowering blood sugar levels after the inhibition test was carried out through the alpha amylase enzyme and alpha glucosidase. Meanwhile, there was no overall detection

of steroid gambir. Gambir (*Uncaria gambir*) Cubadak variety is a shrub that has high levels of polyphenols, namely catechins and tannins which are antibacterial. The extraction method used is MAE (Microwave-Assisted Extraction). Anti-inflammatory activity was measured by carrageenan-induced rat foot edema test. The high content of catechins in the ethyl acetate fraction, is widely used as a wound healer, a mixture of medicinal ingredients, and for the treatment of diarrhoea by the Indonesian people. However, the mechanism of anti-inflammatory action is still unknown.

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