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Research Article

In Vitro Analysis of the Effectiveness of *Tinospora crispa* L. Plant Against *Plasmodium falciparum* FCR3

Mirnawati Dewi[1*], Defilia Anogra Riani[2], Ahmad Irawan[3], Farah Fauziyah Radhiyatulqalbi Ahmad[4], Septaria Yolan Kalalinggi[5]

[1]Biology Study Program, Faculty of Mathematics and Natural Sciences, Palangka Raya University, Palangka Raya, Central Kalimantan;
[2,3]Pharmacy Study Program, Faculty of Mathematics and Natural Sciences, University of Palangka Raya, Palangka Raya, Central Kalimantan
[4]Medical Study Program, Faculty of Medicine, University of Palangka Raya, Palangka Raya, Central Kalimantan
[5]Chemistry Study Program, Faculty of Mathematics and Natural Sciences, Palangka Raya University, Palangka Raya, Central Kalimantan
Email: mirnawatidewi22bio@mipa.upr.ac.id

ABSTRAK

Tanaman Tinospora crispa L. yang biasa disebut tanaman Penawar sampai oleh masyarakat Kalimantan Tengah. Tanaman tersebut dimanfaatkan sebagai obat malaria dengan cara batang T. crispa di rebus kemudian air rebusan diminum. Penelitian ini bertujuan untuk mengidentifikasi keberadaan beberapa senyawa biokimia dan mengevaluasi aktivitas antimalaria ekstrak etanol tanaman tersebut terhadap Plasmodium falciparum FCR3 secara in vitro. Serbuk kering batang T. crispa diekstraksi dengan teknik maserasi dengan pelarut etanol. Kemudian ekstrak kental yang diperoleh dilanjutkan dengan metode skrining fitokimia untuk mempelajari komponen senyawa aktif yang terdapat pada sampel tersebut. Sebelum dilakukan uji aktivitas antimalaria, parasite P. falciparum FCR3 telebih dahulu dibiakkan dengan metode Trager dan Jensen. Ekstrak yang akan dilakukan uji, dilarutkan terlebih dahulu dengan DMSO dan dimasukkan ke dalam microwell kemudian ditambahkan 500 µL suspensi parasit sehingga didapatkan konsentrasi bahan uji sebesar 100, 10, 1, 0,1, dan 0,01 µg/mL dan diinkubasi 48 jam. Untuk mengamati persen parasitemia dibuat preparat hapusan darah dengan pewarnaan Giemsa. Berdasarkan hasil penelitian dan pengolahan data dengan analisis probit, didapatkan ekstrak etanol batang tanaman Penawar sampai memiliki aktivitas antimalaria pada kosentrasi 10 µg/mL. Hasil uji fitokimia menunjukkan ekstrak etanol batang tanaman tersebut mengandung alkaloid, flavonoid, Fenolik, tanin, steroid, dan saponin.

Kata Kunci: Fitokimia, In vitro, P. falciparum, Malaria, Penawar Sampai

ABSTRACT

The *Tinospora crispa* L. plant, commonly called the Penawar sampai plant, has reached the people of Central Kalimantan. The plant is used as a malaria medicine by boiling the stems of *T. crispa* and then drinking the boiled water. This study aims to identify the presence of several biochemical compounds and evaluate the antimalarial activity of ethanol extracts of these plants against *Plasmodium falciparum* FCR3 *in vitro*. The dry powder of *T. crispa* stems was prepared. The extract was obtained by the maceration technique using ethanol as the solvent. Then, the viscous extract obtained was continued with the phytochemical screening method to study the components of the active compounds contained in the sample. Before conducting antimalarial activity tests, the parasite *P. falciparum* FCR3 was first bred by the Trager and Jensen methods. The extract to be tested was first dissolved with DMSO and put into a microwell, then 500 µL of parasite suspension was added so that concentrations of 100, 10, 1, 0.1, and 0.01 µg/mL were obtained and incubated for 48 hours. To observe the percentage of parasitemia, blood smear preparations were made using Giemsa staining. Based on the results of the research and data processing with probit analysis, the ethanol extract of the Penawar sampai plant stems was shown to have antimalarial activity at a concentration of 10 µg/mL. The results of the phytochemical tests showed that the ethanol extract of the plant stem contained alkaloids, flavonoids, phenolics, tannins, steroids, and saponins.

Keywords: Phytochemical, *In vitro, P. falciparum*, Malariae, Penawar Sampai Plant

I. INTRODUCTION

The use of herbal plants in various cultures and traditional medicine has been practiced for centuries based on beliefs and customs. In most of the world's populations, including in Asian and Western countries, modern medicine has taken over the lifestyle, practices, and use of herbal medicine to meet the health needs of ingredients (Pan et al., 2014). A number of isolated pure herbal compounds, such as taxol and artemisinin, are derived from plants and have gone through clinical development (Zainuddin, 2018). In general, herbal products are believed to have fewer side effects and to be less potent than synthetic and modern drugs (Netta et al., 2024; Welz et al., 2018). Studies investigating the biologically active constituents of medicinal plants have allowed the development of new drugs for medical use (Gunjan et al., 2015; Martani & Fatmaria, 2020). It is time to accept the importance of medicinal plants, such as the *Tinospora crispa* L. plant, as an alternative to herbal medicine.

Tinospora crispa L. is a native medicinal plant which belongs to the Menispermaceae family. Locally, this plant is known as Penawarti, patawali root, aliali root, bratawali, hanging root, brotowali, and seruntum root. This plant is a medicinal plant that grows wild in Asian countries, such as Indonesia. The leaves, roots, and

stems are claimed to have miraculous properties in curing various diseases. *T. crispa* is also used as an antiparasitic agent for humans and pets (Ahmad et al., 2016). The plant is capable of causing a decrease in serum glucose levels in diabetic mice, its hypoglycemic effects may be due to insulinotropic activity. The plant has also been shown to increase peripheral glucose utilization and inhibit the release of hepatic glucose. Furthermore, the antinociceptive and anti-inflammatory activities of *T. crispa* stem ethanol extract have also been proven (Barua et al., 2019; Hossain, 2023). In Indonesia, the ethanol extract of. *T. crispa* stem is used as a treatment for low back pain in Southeast Asia. In countries like Malaysia and China, the water extract of *Tinospora crispa* is taken as a diabetes treatment. Some studies abroad show that *T. crispa* crude methanol extract and its F5 fraction have strong antimalarial activity.

In Central Kalimantan, the plant has several benefits for lowering blood sugar and diabetes and has been used by the Dayak Ngaju community for generations because of its potent properties as a medicinal plant, including as an antimalarial drug (Martani & Fatmaria, 2020). So that *T. crispaa* L. has great potential to be developed into raw materials for traditional medicines and modern medicines. However, information on the content of secondary metobolites and the potential of chemical compounds for antimalarials is still limited, so this research needs to be conducted.

II. METHOD

A. Tools and Materials

Tools used in this study include, Conical tube 15 cc, Microtube 1.5 cc, Glass Object, Plate 96 well, Blue tip, Yellow tip, and Bottle of duran. While the tools used are, Material test, Sorbitol solution 5%, Giemsa Painting (Giemsa, methanol, aquadest), Dimethylssulfoxide (DMSO), Roswell Park Memorial Institute (RPMI), and Culture media (RPMI, Human serum, normal RBC).

B. Sample Preparation

T. crispa was obtained from Kalampangan village, Palangka Raya City, Central Kalimantan. The plant part used in this study was the stem *T. crispa* washed and dried aerated at room temperature. After the stem of *T. crispa* is dry, the stem is mashed with a blender to obtain a homogeneous powder of 100 g (Sumarlin et al., 2020).

C. Sample Extraction

A total of 100 grams of simplicia powder from *Tinospora crispa* is then macerated by placing it in a glass jar, soaking it with ethanol, and stirring it once every 24 hours for 3 days. It is stored in a

closed jar and protected from light. Every day, screening is carried out to separate the liquid from the residue, which is then evaporated until a viscous extract is obtained (Fadillah et al., 2024).

D. Identification of Compound Classes

1. Alkaloid test

Each 2 ml sample was taken and extracted with a solvent of water and ethanol into 2 different regeneration tubes. After that, each extract was added with 5 drops of Dragendorf reagent. If an orange color is formed, it indicates the presence of alkaloids (Sabdoningrum et al., 2021; Slamet et al., 2022)

2. Phenolic test

The extract and fraction (1 ml) are placed into a test tube, and then a 1% FeCl3 reagent is added. A positive test is indicated by the formation of a black color (Rosyidah & Andrianto, 2024; Slamet et al., 2022)

3. Flavonoid test

The extracts and fractions (2 ml) are added to hot water, then simmered for 5 minutes and filtered. To the 5 ml of filtrate, 0.05 mg of Mg powder and 1 ml of concentrated HCl are added and then shaken. A positive test is indicated by the formation of red, yellow, or orange colors (Slamet et al., 2022)

4. Saponin test

The extract and fraction (2-3 ml) are placed into a test tube, then 10 ml of hot water is added, and the mixture is cooled and shaken vigorously for 10 seconds. Next, 1 drop of 2 N HCl is added, and a positive test is indicated by the formation of a stable foam 1-10 cm high for 10 minutes (Bankole et al., 2016; Slamet et al., 2022)

5. Steroid Test

The test was carried out by taking 2 ml of each sample that had been extracted with water and ethanol solvents. After that, each extract is added with 3 drops of concentrated HCl and 1 drop of concentrated H2SO4. If each of the solutions forms a green color, then it is positive for containing steroids (Slamet et al., 2022)

6. Tannin test

The Extract and fraction (1 ml) are added with a few drops of 10% FeCl3 solution. The positive test is indicated by the formation of a greenish-black color (Slamet et al., 2022)

7. Terpenoid test

The test was carried out by taking each sample that had been extracted with a solvent of water and ethanol in the amount of 2 ml, then added 3 drops of concentrated HCl and 1 drop of concentrated H2SO4. If each solution forms a red or purple color, then it is positive for containing terpenoids (Slamet et al., 2022).

E. Anti-malaria Testing

A total of 100 µL of the sample is added to the plate (from low to high concentration) Then, add 100 µL of inoculum to all wells except the one containing distilled water (total of 200 µL) After that, place the microplate in a candle jar and incubate for 72 hours at 37°C. After 72 hours a thin swipe is made. Next, carry out the harvest. Harvesting begins with preparing tools and materials. Then the microplates are removed from the incubator and candle jar. The inoculum is transferred into a microtube. Then centrifuge the entire micro tube for 10 minutes (speed 100 rpm). Discard the supernatant and then make observations under a microscope. Observations were made from the last control group (from the lowest concentration to the highest concentration) (Utami & Febrianti, 2022) .

F. Data Analysis

Data analysis used on antiplasmodium activity *in vitro* is probit analysis *(probavility unit).*

III. RESULT AND DISCUSSION

Based on Table I below, alkaloid and steroid compounds were detected in the ethanol extract by showing consecutive color changes: orange after the addition of Dragendorff reagent, white precipitate after the addition of Mayer reagent, and brownish-orange after the addition of Wagner reagent. Meanwhile, for the steroid testing, a green color change occurred after the addition of concentrated HCl and concentrated H_2SO_4. The presence of flavonoids, phenolic, and tannins are characterized by successive discoloration of orange after the addition of concentrated HCl and Mg powder (flavonoids), greenish black after the addition of FeCl3 (tannin), and blackish after the addition of hot water and FeCl3 which indicates positive phenolics (Figure 1) (Tarukbua, 2018).

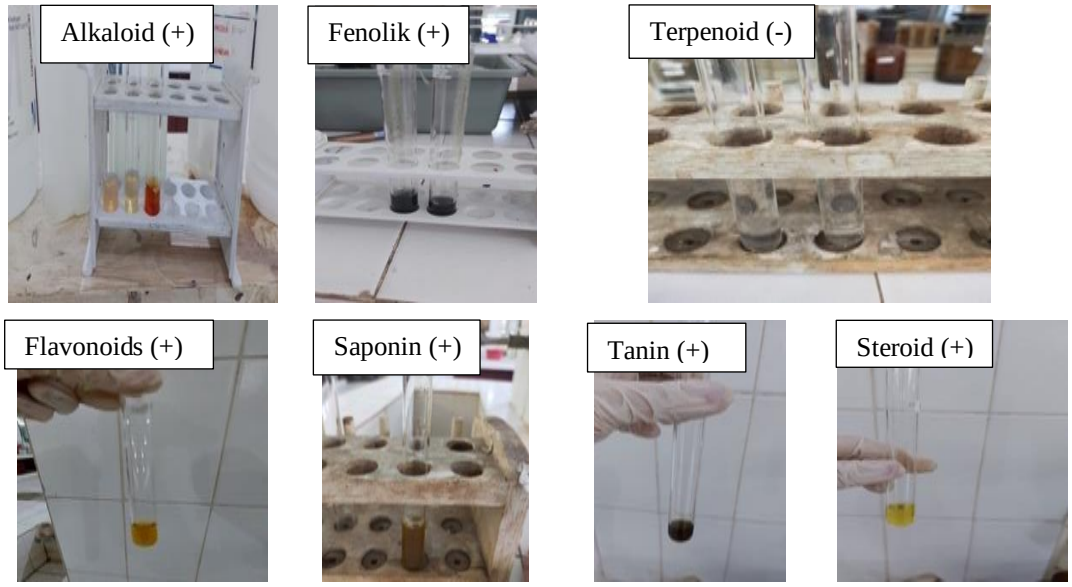
Table I. Phytochemical Screening of T. *crispa L.*

Parameters	Reagent	Test Results
Alkaloid	Dragendorff	+
	Mayer	+
	Wagner	+
Flavonoids	HCL concentrated powder Mg	+
Phenolic	$FeCl_3$	+
Tannins	Hot Water + $FeCl_3$	+
Triterpenoids	Amyl alcohol	+
Steroids	H_2SO_4 concentrated HCL + concentrated H_2SO_4	+
Saponins	The presence of foam when shaken	+

A. *In Vitro* Antimalarial Test

Inhibition of parasites by ethanol extract of the stem of the *T. crispa* plant until presented in table 2 with three

replication. Antimalarial activity *in vitro* against *Tinospora crispa* plant extracts until carried out to determine the inhibitory power of the plant on the growth of parasitemia. *P. falciparum* strain is the most dangerous strain because it causes microvascular disease that affects humans (Smith, 2014). *P. falciparum* strain FCR3 is the type of parasite used in this study. Inhibition of parasites by ethanol extracts of plant stems is presented in table II. Based on table II the percentage of inhibition of parasitemia in concentrations of 0.01 and 0.1 µg / mL is 24%.



Description: + (positive), - (negative).

Figure 1. Identification of Compound Classes

Table II. Test results of antimalarial activity of *T. crispa* L. *in vitro*

Cocentration (µg/mL)	Parasitemia Percentage (%)				SD	Inhibition Percentage (%)
	1	2	3	Average		
Control (-)	3.445	3.612	3.022	3.529	0.118	-
100	2.786	2.250	2.674	2.570	0.282	27.172
10	2.047	2.376	2.202	2.208	0.165	37.421
1	2.875	2.562	2.690	2.709	0.158	23.240
0.1	3.003	2.009	2.874	2.659	0.489	24.659

Then the percentage of inhibition increased at a concentration of 10 µg / mL which was 37% and decreased at a concentration of 100 µg / mL as 27%. The results of this study are in line with the results of research by Widyawaruyanti et

al., (2014) that the concentration of *L. rubiginosum* extract does not have a linear relationship with the percentage of inhibition of *P. falciparum*.

This may be influenced by the determination of extract concentration and improper solvent selection. In addition, according to Anisa, Wydiamala & Hayatie (2022), that the percentage of inhibition of parasitemia is not linear in each concentration and can also be caused and influenced by environmental conditions (temperature & humidity) and sensitivity of *P. falciparum* to plant ethanol extracts. Perhaps, increased concentrations and the use of appropriate solvents in the extraction will allow plants to perform better antimalarial activity (Helmi, Afriyansyah & Ekasari, 2016). On the other hand, the percentage of inhibition of this study is above 20% and new data can be calculated if the data obtained has a range of 20-80%. So that the results of this study show that the concentration of 10 µg/mL has the highest percentage of parasitemia inhibition compared to other concentrations. Previous research has also shown that *T. crispa* stem methanol extract has its ability to inhibit the growth of *P. falciparum* strain 3D7 *in vitro* (Ihwan & Koda, 2017; *Lee et al., 2020*).

According to Bankole *et al.* (2016), most compounds containing alkaloids, steroids, flavonoids, and terpenoids have the ability to inhibit plasmodium activity. An extract is classified as effective against parasitemia if it is able to reduce more than 30% of parasitemia (Utami & Febrianti, 2022). Therefore, the *T. crispa* Plant can be used to reduce parasitemia at a concentration of 10 µg/mL.

Phytochemical analysis shows that the plant extract is identified not as a triterpenoid, but it contains alkaloids, flavonoids, phenolics, tannins, steroids, and saponins. Researchers have previously reported that the compound has antimalarial activity (Bankole *et al.*, 2016). Table II shows that this extract is able to inhibit plasmodium, it is suspected that the flavonoids and terpenoids in this extract can inhibit parasites. Rudrapal & Chetia (2017) argue that flavonoids, as antioxidants, are able to ward off free radicals due to damage caused by parasite invasion. Terpenoids in some plants have potential antimalarial activity. Filtration of antimalarial terpenoid activity could be a key step in the sourcing and development of new antimalarial drugs (Helmi et al., 2016).

Remedy plant antimalarial action test showed that the level of parasitemia restraint at every fixation was not direct and the IC50 worth not set in stone (Table II), albeit the IC50 worth still up in the air, this concentrate had the option to repress *P. falciparum* (Table II). This plant has not been concentrated ideally, however demonstrated to contain alkaloids, for

example, protoberberine, furonoquinolone, and aporphine alkaloids (Arifuddin & Bone, 2020).

Alkaloids have been known as normal assets that can be utilized as medication. Quinine is one of the alkaloids that has been utilized as an antimalarial drug, created by *Cinchona succirubra* (Wijaya, 2019; Arifuddin & Bone, 2020). This will hinder intracellular choline transport so it can restrain parasite development. Other than being an alkaloid, Penabid's leaf separate contains saponins. Saponins can restrain parasite development by instigating erythrocyte lysis (Rahayu, Lucia & Inanda, 2015; Sujarwanta & Zen, 2022). Flavonoids and phenols have antimalarial activity due to their chemoprotective effects on phytoconstituent content (Sujarwanta & Zen, 2022). If the Dayak Ngaju tribal community continues to use the *T. crispa* as an alternative to antimalarial herbal medicine (Ihwan & Koda, 2017), things that must be considered are the accuracy of the dosage of use, and the accuracy of the method of use and time of use, and the right indications. The ethanol of *T. Crispa* stem is able to reduce the parasitemia of the *P. falciparum* strain FCR3 strain *in vitro* and could to be a potential candidate for anti malarias and extracted *T. crispa* tablet can be created that meets the requirements of physical qualistu test tablet (Patimah, Suriawati, & Rahmawati, 2018). The use of ethnomedicine such as herbs for the treatment of malaria varies by region, environment and population subgroups. It may be more preferred in some areas than in others (Pan et al., 2018).

The results of this preliminary study need to be followed up with further research to determine the physiological mechanism and efficacy of pure compounds as antimalarial agents and continued in vivo testing.

IV. CONCLUSION

Penawar sampai or Brotowali plant was able to inhibit *P. falciparum* FCR3 at a concentration of 10 μg / mL with percentage of inhibition 37,42%. Phytochemical test results showed that ethanol extracts of plant stems contained alkaloids, flavonoids, phenolics, tannins, steroids, and saponins.

CONFLICT OF INTEREST

All authors in this article have no conflict of interest.

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