Tombelu Extract (*Bactronophorus Sp*) Inhibits Plasmodium Falciparum Metabolism In Vitro

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Abstract. Malaria is still a serious public health problem in the world, including Indonesia, because it is found with a fairly high prevalence. Malaria is a pathological condition caused by Plasmodium which is transmitted through the bite of the Anopheles mosquito. Subjects who live in endemic areas or have had malaria can become carriers of the parasite. Tombelu (Bactronophorus sp) is believed by coastal communities to be able to increase stamina and overcome various diseases including malaria. The research objective was to determine the effectiveness of Tombelu extract (Bactronophorus sp) in inhibiting the metabolism of Plasmodium falciparum. Method: This study used a quasi-experimental in Vitro design. Plasmodium falciparum was obtained from the blood of identified symptomatic malaria patients in endemic and non-endemic areas. The treatment group was divided into a normal control group (no treatment), a negative control group: administration of distilled water, treatment F1: administration of 10% tombelu water extract, and treatment F2: administration of 100% tombelu water extract. Plasmodium readings were carried out at 100 LPB (large field of view). The research was carried out in 2018 in East Kolaka and Kendari City. The data collected was the form of Plasmodium falciparum which was identified on a microscope using the thick blood drop method. Data is processed and analyzed descriptively. Results:9 Plasmodium forms merozites, tripozoites and gametozites. Plasmodium was identified at the 12th (gametocytes), 40th (2 trophozoites), 60th (3 gametocytes), 72nd (trophozoites), and 90th (2 gametocytes) large visual fields. In negative control: Plasmodium identified 4 plasmodium tropozite and gametozite forms. Added tubeTombelu (Bactronophorus sp) at 10% and 100% dilution did not identify Plasmodium falciparum. Conclusion: Giving Tombelu aqueous extract (Bactronophorus sp) at 10% and 100% dilution can inhibit the metabolism of Plasmodium falciparum. Suggestion. It is important to carry out further research to develop the benefits of Tombelu (Bactronophorus sp) as a functional food.

Keywords: Tombelu, Bactronophorus sp, P. falciparum, anti-malaria.

1 Introduction

Tombelu *(Bactronophorus sp)* has been used by coastal communities as a food ingredient that has a physiological function. Empirically, coastal communities have

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used *Tombelu* as a food that has health benefits and is used as medicine. People who use *Tombelu* (Bactronophorus sp.) are seen as taking medicine known as Kumoro pills to cure lumbago, and infections, increase milk production and increase stamina. *Tambelo* meat is believed to be efficacious for preventing and curing lumbago, rheumatism, cough, flu, and malaria, increasing breast milk production, appetite, and male vitality by the Kamoro people of Timika district in Papua. It has been reported that coastal communities in Bira Island, Papua, have a habit of consuming *Tombelo* (Bactronophorus sp.) [1-3]. Tombelo (Bactronophorus sp.) or teredinids are found worldwide and dead or decaying mangroves. Mangrove forest is an area that grows on the edge or coast, in river estuaries and tidal areas. Indonesia has 3.7 million hectares of mangroves, which means that 25% of the world's mangroves are found in Indonesia. The preservation of mangrove forests will preserve the local wisdom of the people who live in mangrove environments, one of which is the Tombelu (Bactronophorus sp.) population, which is unique to coastal communities [2-4].

Southeast Sulawesi has a geographical location of 70% of the islands and coasts. The local wisdom of coastal communities in all regions in Indonesia and even in the world has similarities in utilizing their natural resources including food sources. Eating habits of Tombelo (*Bactronophorus sp*.) Coastal communities in Southeast Sulawesi, such as in Kolono District and Laeya Konawe Selatan District, also use Tombelo (*Bactronophorus sp*.) as a food which is believed to have properties to prevent various diseases including malaria. People in the Torobulu area which is inhabited by the Muna tribe use Tombelu (Bactronophorus sp.) as food and are believed to have health benefits, one of which is believed to be able to prevent and treat malaria. The culture of the people who live in the coastal environment will take advantage of whatever is in their environment to overcome various health problems so that they can carry out their daily activities [5-7].

Malaria is still a world health problem. Malaria has attacked 106 countries in the world including Indonesia, and there has been an increase in the number of malaria-endemic countries compared to the 2003 WHO report [8]. The global commitment to sustainable development (SDGs) includes efforts to eradicate malaria which are contained in the 3rd specific goal, namely ending the epidemics of AIDS, tuberculosis, and malaria, neglected-tropical diseases by 2030 [9]. WHO said that although the number of malaria has decreased, half the world's population is threatened by malaria. This is related to the high mobilization of people, causing migration between regions which can become the main medium for transmission of malaria between islands. Of the 400 known species of Anopheles mosquitoes, 67 species have been found to transmit malaria and 24 species have been found in Indonesia. Plasmodium falciparum is a type of malaria that is commonly found in Indonesia, including Southeast Sulawesi [10]. Southeast Sulawesi is a malaria-endemic area with a moderate category. The incidence of malaria diagnosed by health workers by paying attention to the symptoms felt, South Konawe district, which is 3.2%, is the second highest area after the Muna district, which is 3.5%, reported Southeast Sulawesi malaria prevalence of 0.22% [7,10].

The pathogenesis of malaria begins with the interaction that occurs when the bite of an Anopheles mosquito carrying the Plasmodium falciparum microorganism enters the

body through the bloodstream. Through the liver tissue, P.falcifarum releases 18-24 merozoites into the circulation. The released merozoites will enter the RES cells in the spleen and undergo phagocytosis and filtration. Merozoites that escape filtration and phagocytosis from the spleen invade the erythrocytes. The parasite then reproduces asexually in the erythrocytes. The interaction between microorganisms and the immune system will lead to a response by expressing. The clinical picture of malaria is characterized by periodic fevers, anemia, and splenomegaly. Prodromal complaints can occur before the occurrence of fever in the form of lethargy, malaise, headache, backache, feeling cold in the back, joint and bone pain, mild fever, anorexia, stomach discomfort, mild diarrhea, and sometimes cold. Malaria caused by P.falcifarum describes prodromal complaints that are not clear and even symptoms can be sudden [11-17].

Research on natural ingredients that have anti-Plasmodium falciparum potential has been widely reported as the development of natural medicines and functional foods. Natural ingredients that have anti-P.falciparum potential, such as u sea bidara wood [18], earring plant (Acalypha indica L.) [19], lime leaf plant (Harmsiopanax aculeatus) [20], watermelon rind tannins (Citrulus lanatus) [21], gempol leaves (Nauclea orientalis (L.) [22], soga wood (Strychnos ligustrida), Actinomytes marine sendiment [23], Jamblang (Syzygium Cumini); dan guava leaaf water (Psidium guajava) [24]. No study reports found Tombelu (*Bactronophorus sp*.) as an antimalarial. Chemical components that are known to have anti-parasitic properties include alkaloids. *Tombelu (Bactronophorus sp*.) has been reported to contain components of amino acids, fatty acids, vitamins B12, B6, choline, niacin, the minerals calcium, phosphorus, iron, zinc, selenium, and magnesium [1-2]. Leiwakabessy (2011) reported that tambelo meat contains 17 types of amino acids and 15 types of fatty acids, and contains alkaloids, flavonoids, steroids, triterpenoids and saponins. Furthermore, Syaputra et al. (2012) reported that the tambelo glycogen extract obtained using the hot alkaline method (40% KOH) contained about 86% glucose and the rest was residue in the form of protein and nucleic acids [25]. The role of Tombelu in malaria has not been specifically studied which is the novelty of this article. This research aimed to study Tombelu (Bactronophorus sp.) against Plasmodium malaria by in vitro method.

2 Methods

This research is an in vitro laboratory exploration. The research was conducted in 2 stages, namely obtaining the Plasmodium falciparum parasite and measuring the ability of Tombelu extract to metabolize Plasmodium falciparum. Plasmodium falciparum parasite samples were obtained from the blood of symptomatic malaria subjects in Kendari City. Parasite identified through the thick blood smear method with Giemsa staining, it was found that the subject's blood contained female falciparum gametocytes.

2.1 Material

The materials used in this study were blood containing the falciparum parasite, Tombelu water extract and distilled water.

2.2 Tool

The tools used in the research are: object glass, microscope, alcohol cotton, tourniquet, Whatman filter paper no.1, lancet and capillary tube. How to make Giemsa stock solution: Giemsa staple solution according to Garcia and Bruckner (1994): Giemsa powder 0.6 gram; Methanol absolute 50 ml; Neutral glycerin 50 ml; Grind some of the giemsa powder and glycerin in a mortar and put it in a 500 ml or 1000 ml volumetric flask until all the ingredients weighed are thoroughly mixed. Cover with cotton and wrap in thick paper, place in a 55-60ºC bath for 2 hours. Shake gently every ½ hour. Let it cool, add alcohol and store in a brown bottle. Filter before use.

2.3 Treatment

The research treatment was by administering 10% Tombelu water extract incubation 12 hours (K1.1) and 24 hours (K1.2), 100% Tombelu water extract incubation 12 hours (K2.1) and 24 hours (K2.2), control positive with the addition of distilled water incubation 12 hours (K01+) and 24 hours (K02+) and negative control (K) were samples without treatment.

2.4 Anti-parasitic test

Testing the effect of Tombelu on parasites was carried out by placing 1 ml of positive blood in a 5 ml test tube in 7 tubes that had been marked, in each tube added 1 ml of 10% Tombelu aqueous extract in tube K1.1. and K1.2; Tombelu water extract 100% tubes K2.1 and K2.2; adding distilled water to tubes K0.1 and K0.2; then each treatment was incubated for 12 hours and 24 hours and the K tube (without treatment). After incubation (except tube (K)), blood smears are made and read in 100 fields of view using WHO standards in 2000. The semi-quantitative method of counting parasites in a large field of view (LPB) according to nurain, image classification as follows:

(-) : SDr negative (no parasites found in 100 LPB)
(+) : SDr positive 1 (found 1-10 parasites in 100 LPB)
(++) : SDr positive 2 (found 11-100 parasites in 100 LPB)
(+++) : SDr positive 3 (found 1-10 parasites in 1 LPB)
(++++) : SDr positive 4 (found 11-100 parasites in 1 LPB)

3 Results

Tombelu (Bactronophorus sp.) is a type of worm that grows in decaying mangroves. Here's a picture of Tombelu

Figure 1. Tombelu(Bactronophorus sp.)

Explorations carried out on the blood of positive control group subjects (without treatment) were found from Reading Results Identified 9 plasmodium forms of merozoites, tripozoites and gametozites. It can be explained that Plasmodium was identified at the 12th (gametocytes), 40th (2 tropozites), 60th (3 gametocytes), 72nd (trophozoites) and 90th (2 gametocytes) large visual fields. Identification of various forms of P.falciparum which describes the subject being infected. The identified form of P.falciparum is shown in the following figure:

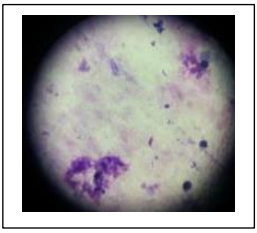

Figure 2. Plasmodium merozoites were identified in the positive control 12th field of view

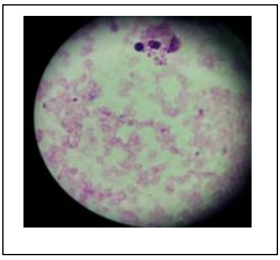

Figure 3. Plasmodium merozoites were identified in the positive control 40th visual field

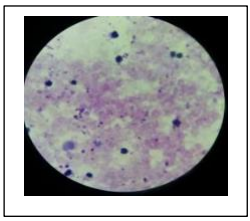

Figure 4. Plasmodium was identified in the positive control of 3 banana-shaped gametocytes at the 60th field of view

Negative Control (addition of distilled water) incubation 12 hour reading time. Plasmodium was identified on the 3rd (tropozoite), 6th (gametozite), 20th (gametozite), and 30th (tropozoite) visual fields.

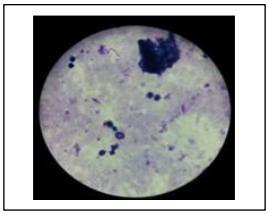

Figure 5. Plasmodium gametozite was detected in the negative control 6th visual field

Negative Control (addition of distilled water and 24 hour reading time). Identified 4 plasmodium forms of tropozite and gametozite. Plasmodium was identified on the 6th (tropozoite), 40th (gametozite), 42nd (tropozoite) and 90th (gametozite) field of view.

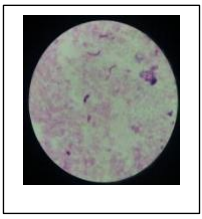

Figure 6. Tropozoid stage Plasmodium falciparum was found in the third field of view,

The addition of 10% and 100% Tambelu and a reading time of 12 to 24 hours Plasmodium was not identified in 100 fields of view.

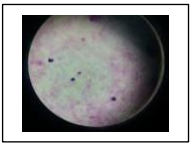

Figure 7. Plasmodium was not found in blood preparations with the addition of 10% Tombelu extract with an incubation period of 12 hours

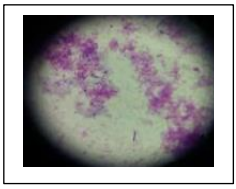

Figure 8. Plasmodium was not found in blood preparations with the addition of 10% Tombelu extract with an incubation period of 24 hours

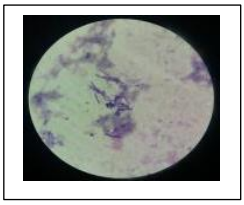

Figure 9. Plasmodium was not found in blood preparations with the addition of 100% Tombelu extract in 12 hours incubation.

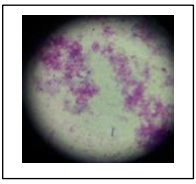

Figure 10. Plasmodium was not found in blood preparations with the addition of 100% Tombelu extract with an incubation period of 24 hours

4 Discussion

The pathogenesis of malaria begins with the interaction that occurs when the bite of an Anopheles mosquito carrying the Plasmodium falciparum microorganism enters the body through the bloodstream. Through the liver tissue, P.falcifarum releases 18-24 merozoites into the circulation. The released merozoites will enter the RES cells in the spleen and undergo phagocytosis and filtration. Merozoites that escape filtration and phagocytosis from the spleen invade the erythrocytes. Furthermore, the parasite reproduces asexually in the erythrocytes. The interaction between microorganisms and the immune system will lead to a response by expressing.

EP generally has 2 stages, namely the ring stage at 24 hours I and the mature stage at 24 II. The surface of the ring stage displays RESA antigen (Ring-erythrocyte paradise antigen) which disappears after the parasite enters the mature stage. The membrane surface of mature stage EP will be bulged and form a knob with histidine rich protein-1 (HRP-1) as the main component. Furthermore, when the EP undergoes merogony,

malaria toxin in the form of GPI is released, namely 7 glycosylphosphatidylinasitol and LPS which stimulate the release of TNF-α and interleukin-1 (IL-1) from macrophages. IL-6, IL-3, LT (lymphotoxin) and INF-γ. Therefore it is suspected that due to the role of other neurotransmitters as free-radicals in this cascade such as nictit-oxide as an important factor in the pathogenesis of severe malaria.

Malaria has the characteristic features of periodic fever, anemia and spleenomegaly. Prodromal complaints can occur before the occurrence of fever in the form of lethargy, malaise, headache, backache, feeling cold in the back, joint and bone pain, mild fever, anorexia, stomach discomfort, mild diarrhea and sometimes cold. Prodromal complaints often occur in P. vivax and Ovale, whereas in P. falcifarum and malaria the prodromal complaints are unclear and even symptoms can be sudden. The classic symptoms are the occurrence of the "malarial triad" sequentially: cold period (15-60 minutes): chills begin, the patient often wraps himself in blankets and the whole body shakes, followed by an increase in temperature; followed by a hot period: the patient has red face, rapid pulse, and fever remains high for several hours, followed by a period of sweating: the patient sweats profusely and the temperature drops and the patient feels well. The malaria triad often occurs in vivax infection, in P. falcifarum infection chills can be severe or absent. The non-heat period lasts 12 hours in P. falcifarum, 36 hours in P. vivax and ovale, 60 hours in P. Malaria. Primary attacks: ie the state starting from the end of the incubation period and the onset of paroxysmal attacks consisting of cold or chills; hot and sweaty. This paroxysmal attack can be short or long depending on the multiplication of the parasite in the patient's immunity. Latent period: the period without symptoms and without parasitemia during the course of malaria infection. It usually occurs between 2 paroxysmal states. Recrudescense: namely the recurrence of clinical symptoms or parasitemia after 24 weeks of the end of the primary attack. Relapse or rechute: is the recurrence of clinical symptoms or parasitemia that is longer than the time between periodic attacks of the primary infection, namely after a long infection from a latent period (up to 5 years), usually occurs because the infection is not cured or by forms outside of the erythrocytes (liver) in vivax or ovale malaria. This paroxysmal attack can be short or long depending on the multiplication of the parasite in the patient's immunity. Latent period: the period without symptoms and without parasitemia during the course of malaria infection. It usually occurs between 2 paroxysmal states.

Tombelu extract has potential as an anti-parasitic. In the treatment groups K1 and K2, Plasmodium falciparum cells were not found in the negative category (-), indicating that there was an inhibition of the growth of the Plasmodium falciparum parasite. The decrease in the number of parasite cells in the positive control (K0) at 12 hours and 24 hours of incubation, may have occurred due to the sample dilution factor. The control sample was categorized as positive 1 (+). Found a chemical component that also acts as an antibacterial. Qambelo has water, ash, fat, and protein content of 73.93%, 1.24%, 0.47%, and 6.22%, respectively. The yield of methanol extract was 3.12% ± 0.62, ethyl acetate: 0.68% ± 0.07, and hexane 0.41% ± 0.13. The highest antioxidant activity was in ethyl acetate extract with an IC50 value of 1072.19 μg/mL. The alpha-glucosidase inhibitory activity of the extract decreased at higher concentrations. The highest antibacterial activity was obtained in ethyl acetate extract with an inhibition zone of

10.5 mm against E. coli bacteria at a concentration of 2 mg/well. The selected extract is ethyl acetate extract which contains flavonoids, tannins, saponins and steroids. The extract is classified as toxic with an LC50 value of 425,908 μg/mL.

Different results Griffin et al. 1994 reported that a protease enzyme isolated from bacteria present in the glands of Tambelo Psiloteredo healdi Teredinidae acts as a detergent for cleaning floors, plates and glass lenses. Fresh tambelo (Teredinidae) contains 82.72±0.01% moisture, 7.21±0.31% protein, 0.28±0.04% fat, 2.07±0.27% ash, and carbohydrates (by difference) 7.72±0.62%. The dry Tambelo composition includes 6.63 ± 0.01% moisture content, 42.77 ± 2.01% protein, 14.27 ± 0.22% fat, 5.88 ± 1.04% ash, carbohydrates (by difference) 30.45±2.83%. Tombelo protein contains nine essential amino acids and eight non-essential amino acids. Tambelu contains seven saturated fatty acids and eight unsaturated fatty acids. Contains 3532.46 ppm calcium and 2363.06 ppm phosphorus. The antioxidants found were alkaloids, steroids and triterpenoids. (chemical composition & antioxidants, hardjito, linawati). Nutritional factors may play a role in determining susceptibility to severe malaria, it has been reported that severe malaria is very rare in malnourished children. Iron deficiency, riboflavin, para-amino-benzoic acid (PABA) may have a protective effect against severe malaria, because it inhibits parasite growth. Another factor that may damage the pattern of Plasmodium metabolism is a toxic compound that has antibacterial properties found in Tombelu glands which also have anti-parasitic properties.

Although there have been no reports regarding poisoning by coastal communities who consume Tombelu, choosing Tombelu as an ingredient to develop functional food, it is important to consider and carry out further analysis that the content of anti-bacterial compounds that have been reported in previous studies may be anti-parasitic, not toxic to humans. Still need to confirm the results of this study with further research to describe the role of Tombelu in malaria [26].

5 Conclusion

No Plasmodium falciparum parasite cells were found in the treatment group given Tombelu water extract (Bactronop sp) 10% with an incubation period of 12 hours. The same inhibitory ability was produced in the control by adding 100% Tombelu aqueous extract in 12-hour incubation. Tombelu water extract (Bactronop sp) at a concentration of 10% with an incubation period of 12 hours has the ability to inhibit the growth of the P.falciparum parasite.

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