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In vivo Antiplasmodial Activity of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one compound in Swiss Mice

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ABSTRACT

***Background** : Malaria is an infectious disease caused by plasmodium sp. Resistance to antimalarial drug urges the finding of new antimalarial agents. One of the potential agents is a chalcone derivate namely (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one.* ***Objective**: This study aimed to test the effect of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one on plasmodium sp infection in vivo by measuring the median effective dose (ED 50).* ***Method:** Swiss mice were divided into 6 groups consisting of control group and treatment groups receiving various doses of tested compound (10 mg, 20 mg, 40 mg, 80 mg and 160 mg /BW/day respectively). Tested compound were given for 7 consecutive days. Malaria model was made by infecting mice with 10^6 P. Berghei on day 4. Parasitemia were measured on day 5 after infection. ED50 was counted with probit analysis.* ***Result**: Probit analysis showed that the ED50 value for (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one was 17,36 mg / BW.* ***Conclusion**: (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one has a very good anti-plasmodial property.*

Keywords: Anti-plasmodium; ED50; (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one

INTRODUCTION

Malaria is a disease caused by plasmodium (Halim, 2011) which still becomes a health problem until today. This disease can cause anemia, decreases productivity, and even causes death particularly in high risk groups such as infant, toddler and pregnant women (Ministry of Health, 2011)

Parasite's resistance to commonly used anti-malarial drug has been reported worldwide. This urged the World Health Organization (WHO) to release an instruction for the use of mono-therapy and implementation of a treatment method using Arthemisin Based Combination Therapy (ACT) to reduce the mortality rate of P. Falciparum infection which is resistant to anti-malarial drug (WHO, 2013).

The occurrence Plasmodium sp resistance to existing anti-malaria agent has urged researchers to search for new anti-malarial drugs. One of the compounds that have a potential anti-malarial property is chalcone compound. Chalcone (1,3 – diaryl – 2 – propen – 1 – ones) is a secondary metabolite of flavonoid group that can be found in several kinds of plants. Chalcone and its derivatives have a variety of biological activities such as antivirus, anti-inflammation, anti-microbia, anti-tumour, cytotoxic, analgesic, anti-fungi, antioxidant, anticancer and anti-malarial properties (Sarda et al, 2009)

In his search for new anti-malarial drug, Suwito et al (2014) have succeeded in designing and synthesizing several chalcone derivates including (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one. Molecular docking of this chalcone derivate showed that it inhibited the interaction between ferredoxin (Fd) and ferredoxyn – $NADP^+$ reductase (NFR) which serves as a crucial redox system to support the life of P. Falciparum. In addition, the amino group of methoxychalcone derivate plays an important role in inhibiting the electrostatic interaction and can create a more stable complex with NFR than with Fd (Suwito, 2014)

In vitro study on (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one revealed that this compound showed good anti-plasmodial property, good selectivity index and could block the growth of plasmodium [6]. Considering previous research, this study aimed to investigate the anti-malarial effect of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one *in vivo* by measuring the effective dose in mice infected with P. berhei.

METHOD

This was an experimental study with post test only control group design aimed to determine the median effective dose of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one as anti-plasmodium in Swiss mice infected with P. Berghei.

A total of 60 Swiss mice weighed approximately 20 – 30 grams and aged 6-8 weeks were used in this study. Mice were obtained from Parasitology laboratory, Faculty of Medicine Gadjah Mada University (UGM). Mice were divided into 6 groups. Each group consisted of 5 female and 5 male mice. Group I was the negative control while group II-VI were the treatment groups.

In this study, mice were adapted for 7 days and the divided into 6 groups. Group I was the control group. Group II-VI were given (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one as the test compound with at 10 mg, 20 mg, 40 mg, 80 mg and 160 mg /BW/day respectively. Test compound were given for 3 days by intra-peritoneal injection. Mice were infected with 10^6 P. Berghei on the fourth day. Two hours after infection, treatment groups (group II-VI) were given the test compound with the same dose. Treatment with the test compound continued until four days. Parasitemia was counted on the fifth day.

Materials for the study consisted of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one, ethanol, Giemsa stain, water, RPMI 1640 medium (Sigma), and emersion oil. Instruments for the study included analytical balance, 1 ml

syringe, beaker, scissors, object glass, labeling sticker, pipette, object glass rack, light microscope, cage for mice and drinking bottle for mice.

This study was conducted in Parasitology laboratory Faculty of Medicine Gadjah Mada University on April until December 2016. The effective dose that can inhibit parasite growth up to 50% (ED50) was counted based on the correlation between dose and percentage of parasite growth inhibition by the test compound. Data were analyzed with probit analysis.

RESULT AND DISCUSSION

Anti-plasmodial activity of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one was observed with Giemsa staining. The number of erythrocyte infected with P. Berghei was counted to get the percentage of parasite growth inhibition.

Based on data calculation using probit analysis, ED value of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one was 17,36 mg / BW. ED50 states the effective dose required to inhibit 50% of the growth of P. Berghei infected to mice. Munoz et al. (2007) stated that anti-plasmodial activity in vivo of a compound is classified as very good if ED 50 is < 100 mg /BW, good if ED50 is 100 – 250 mg /BW and moderate if ED50 is > 500 mg /BW [7]. Based on this classification, anti-plasmodial activity of (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one can be classified as very good. A compound can exert an anti-plasmodial activity through several mechanisms including inhibition of heme polymerase, inhibition of folate metabolism, blocking DNA synthesis, blocking the formation of hemozoin and blocking the interaction between Fd and NFR as well as transforming erythrocyte into stomatocyte. Further research is needed to know the mechanisms of action of our test compound, (E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one.

CONCLUSION

(E) – 1 – (4 – aminophenyll) – 3 – (2,3 – dimethoxyphenyl) prop – 2 – en – 1 – one has a very good antiplasmodial activity toward P. berghei injected to Swiss mice with ED50 at 17,36 mg /BW.

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