

Research Journal of Pharmaceutical,
Biological and Chemical Sciences

(An International Research Online Journal)

ISSN:0975-8585





Search

Home

Scope

Editorial Board

Author's Guidelines

Submit Manuscript

Archives

Contact Us



Click to enable Adobe Flash Player

Invitation for Innovative Research Papers, Reviews, Mini Reviews and Short Communication

Editorial Board

Editor-in-Chief

Dr. Sridevi M

India

Associated Editor

Dr.K.Lakshmi Narayana

India

Managing Editor

Prof. Gopkumar P

India

Editorial Advisory Board Members

**Dr. Osama Mohammad Mostafa
Darwesh
Egypt**

**Prof. Jeanetta du Plessis,
South Africa**

**Prof. Dr. Qinghua Xia,
China**

**Dr.U. Michael Uwumagbe,
Nigeria**

**Prof. Dr. Suleyman Aydin,
Turkey**

**Dr. Nabil Mohie Abdel-Hamid,
Egypt**

**Dr. Aravind B,
India**

**Mrs. Sridevi G,
India**

**Dr.Amrutha Radhakrishnan,
India**

**Dr. Vandana B. Patel,
India**

**Dr. Shashikanth Pattan,
India**

**Dr. Sayeeda Sultana,
India**

**Prof.Dr.Cemil Ibis,
Turkey**

**Mr.J.S.Patil,
India**

**Prof.Dr.Liviu Mitu,
Romania**

**Dr.Zambare Vasu deo P,
USA**

**Dr.(Mrs). Sanjita Das,
India**

**Dr.Laila Abou-Zeid,
Egypt**

**Dr.Chakraborty G.S,
India**

**Dr. Kundlik Girhepunje,
India**

**Dr. Bhaskar Muzumder,
India**

**Prof.Dr. Ch.V.R.Murthy,
India**

**Dr. Subhash C. Mandal,
India**

**Dr.Prabhakar Reddy Veerareddy,
India**

**Dr. Mahesh Kumar Gupta,
India**

**Prof. Dr. Suvakanta Dash,
India**

**Dr. C.S. Shastri,
India**

**Dr. Derle DV,
India.**

**Prof. Dr. Raghavendra Kulkarni,
India**

**Dr. Saikat Dewanjee,
India**

**Dr. Shailesh T. Prajapati,
India**

**Dr.G.S.Gadaginamath,
India**

**Dr.Tanay Kesharwani,
USA**

**Dr.Pengyun Zeng,
USA**

**Dr.Yatin Shukla,
USA**

**Dr.Raviraj Kulkarni,
India**

**Dr. D.K.Sharma,
India**

**Mr.D.Nagasamy Venkatesh,
India**

**Dr.Amit G Nerkar,
India**

**Dr. Ajay Singh,
India**

**Prof. (Dr) Abdalla Shalaby,
Egypt**

**Dr. Ashok R Chandak,
India**

**Prof (Dr). Bhupen Chandra Behera,
India**

**Dr.Hiren Mehta, India,
India**

**Dr.Sitaram Bhavaraju,
Maryland**

**Dr.SP Singh,
Japan**

**Mr.Ritu mehra Gilhotra,
India**

**Mr.Devang S Patel,
India**

**Dr.Mr.Jayapal,
India**

**Prof.Dr.Ragip Adiguzel,
Turkey**

**Dr.C.Gopinath,
India**

**Dr.Arugadoss Devakumar,
USA**

**Dr.Tarek Saied Fathalla Bellal,
Egypt**

**Mr.T.Srinivasa Rao,
India**

Research Journal of Pharmaceutical, Biological and Chemical Sciences

ISSN:0975-8585

Search 

Home Scope Editorial Board Author's Guidelines Submit Manuscript Archives Contact Us

Invitation for innovative Research Papers, Reviews, Mini Reviews and Short Communication

RES J PHARM BIOL CHEM SCI

8(15), 2017 (January - February) Supplementary Issue

The Title:
Second International Seminar on Pharmaceutical Sciences and Technology 2016 (2nd ISPS12016) November 24th and 25th 2016.

Venue:
Bale Sawata, Rektorat Universitas Padjadjaran, Jl Raya Bandung Sumedang km 21.5 Jatimangor, West Java, Indonesia

Conference Special Supplementary Issue.

8(15), 2017 (January - February) Supplementary Issue

1. Effects Chitosan and Calcium Nanoparticles Mouthwash from Xylophagesideon In the Liver And Kidney Rat.

[Download PDF](#)

Ade Komariah¹, Widada A Laksono², Del A Bustam³, Bambang S Tenggono

2. Toxicity Of Selected Apocynaceae, Magnoliaceae And Simaroubaceae Of Indonesian Plants Using Brine Shrimp Lethality Bioassay.

[Download PDF](#)

Ade Zuhrotun¹, Asepangasuganda, Komar Ruslan Wirasutisna, and MartiasingihWibowo

3. Antihypertensive Activity of Ethanol Extract Of Macroalgae*GracilariaVerrucosa* (Hudson) Papenfuss. In Rats Using Non-Invasive Blood Pressure Method.

[Download PDF](#)

Ahmad Muhtadi¹, BryantariprameswarNiyomanand MoelyonoMoekoektwardoyo

4. The development and validation of RP-HPLC assay for cefotaxime sodium.

[Download PDF](#)

Alfan Denny Arbanto¹, Meva DamayantiRohayu and Susi Kuumaningrum

5. Effects of Sonicator Usage Time on Entrapment Efficiency of Liposome Magnesium Ascorbyl Phosphate Made by Thin Layer Hydration Method.

[Download PDF](#)

Ari Widayanti¹, Rahmaherliyani, and TharakaFebriyani

6. L. Ethanol Extract and Ageratum Conyzoides L Ethanol Extract as Anticancer.

[Download PDF](#)

Ari Budiman¹, Dian Lia Aulifa, Rival Ferdianesah, AnnisaNurrahmanBudiman, Alifa Nur Azizah, and Anna Yuliana.

7. In VitroAntiplasmodialActivity of Ethanol Extractor Manuran (CoptosapeltaTomentosavalaton Ex K. Heyne) Roots.

[Download PDF](#)

Arnida¹, Sutomo.

8. Antimalarial Activity and Survival Timeof AndrographispaniculataFraction (AS202-01) on Plasmodium bergheiInfected Mice.

[Download PDF](#)

Ayudyaningrum¹, Dini Astriandio, Hikmatulilmi, LidyaTunawati, DwiSetyaningrum, EndangWidhiastuti, LitaDekchayanti, Indah S Tantular.

9. In Vitro Nucleotide Sequence Editing Using Single-Primer Reactions In Parallel PCR.

[Download PDF](#)

Caturiani¹, HanahLidhidhiananta, and Debbie Soetheethonningrum.

10. Lipstick Formulation To Use A Natural Dye From Rambutan (Nepheliumlappaceum L.) Rind Extract.

[Download PDF](#)

Deny PurtyaniAzhary¹, Starikarinda, and Anis Yohana Chaerunisaa.

11. Establishment Of Hyperfemicia Mouse Model With Oxonic Acid Potassium Salt And Essence Of Chicken.

[Download PDF](#)

Dian RatihLaksmiawati¹, LiliEkNurhidayat, Nining Novita Ningith.

12. Chemical Composition and Antimicrobial Activity of Essential Oil from Aerial Parts of Pohpohan (PileaTriteriaria (Roxb.) Wight).

[Download PDF](#)

DikPrayugowibowo¹, and Ria Martani

13. Development And Validation Of A RP-HPLC Method To Determine Dehydrodissosugenol, Myristicin, And Satorol In Ethanol Extract Of Nutmeg (MyristicifragransHourst).

[Download PDF](#)

Febriana Amelia Saputri¹, Mutakin, Keri Leskari, and Juttilevita

14. Larvicidal Activity Of Curcuma heyneana Val. & V. Zipp Rhizome Against AedesAegyptiLarvae.

[Download PDF](#)

Fery Ferdiansyah Sofian¹, LamoraTambis, Yasmiwarsusilawati, Dudikunadi, Ami Tjitrasari, Zelika Mega Ramadhania, MoelyonoMoekoektwardoyo



19

SJR

Scimago Journal & Country Rank

Enter Journal Title, ISSN or Publisher Name

- Home
- Journal Rankings
- Country Rankings
- Viz Tools
- Help
- About Us

ⓘ x

Regional Science

Make an impact.

tandfonline.com


OPEN

Research Journal of Pharmaceutical, Biological and Chemical Sciences

discontinued in Scopus as of 2016

27

H Index

Country	India -  SCIMAGO INSTITUTE OF SCIENCE & TECHNOLOGY RANKINGS
Subject Area and Category	Biochemistry, Genetics and Molecular Biology Biochemistry, Genetics and Molecular Biology (miscellaneous) Pharmacology, Toxicology and Pharmaceutics Pharmacology, Toxicology and Pharmaceutics (miscellaneous)
Publisher	RJPBCS
Publication type	Journals
ISSN	09758585
Coverage	2010-2016
Scope	Information not localized

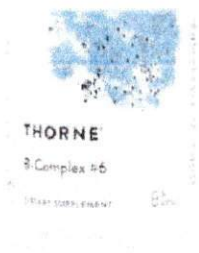
 [Join the conversation about this journal](#)

Thorne Research, B-Complex #6, 60...

IDR 278k

Gluten FreeDietary SupplementWomen's HealthFoundationalNSF
Certified SportGluten...

iHerb

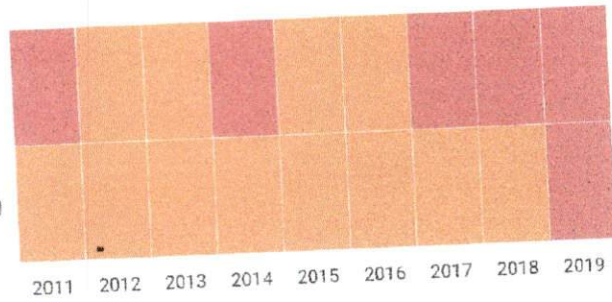


Quality Supplements at iHerb®
iHerb

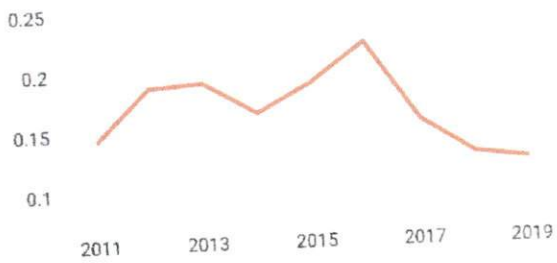
Quartiles

Biochemistry, Genetics and Molecular Biology (miscellaneous)

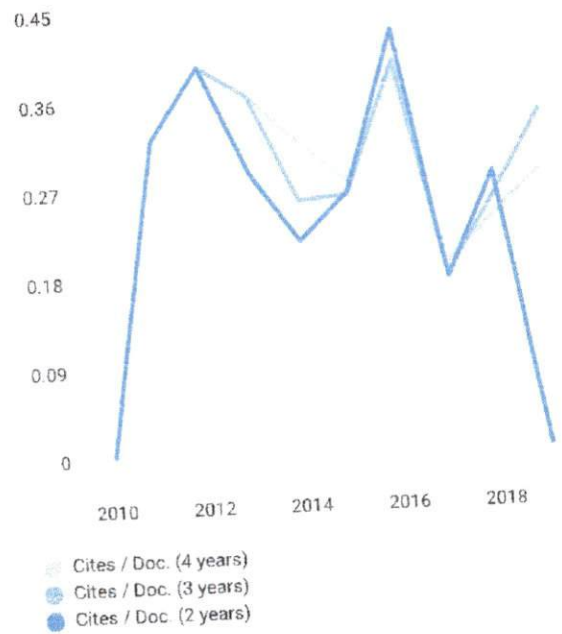
Pharmacology, Toxicology and Pharmaceutics (miscellaneous)



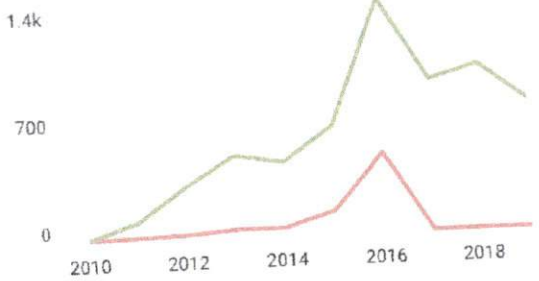
SJR



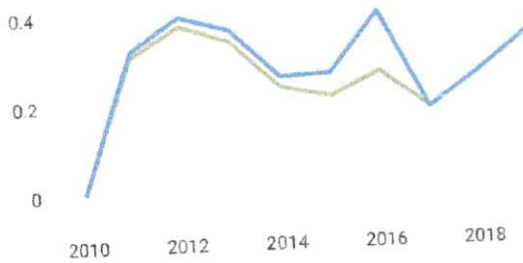
Citations per document



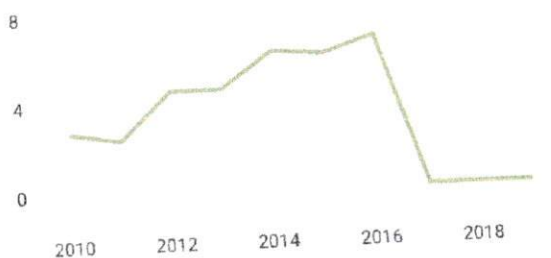
Total Cites Self-Cites



External Cites per Doc Cites per Doc



% International Collaboration

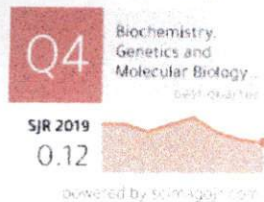


Citable documents Non-citable documents

Cited documents Uncited documents



Research Journal of
Pharmaceutical, Biological...



← Show this widget in
your own website

Just copy the code below
and paste within your html
code:

```
<a href="https://www.scimago.org/">
```



Sports Research, Collagen Peptides,...

IDR 389k Hydrolyzed Type I & III Collagen Healthy Skin & Hair Supports Bones & Joints...

iHerb

Metrics based on Scopus® data as of April 2020

Ekata kumari 3 months ago

When it is in ugc list how to prove it's in ugc list

reply



Melanie Ortiz 3 months ago

SCImago Team

Dear Ekata,

Thank you for contacting us.

SJR is a portal with scientometric indicators of journals indexed in Elsevier/Scopus. Unfortunately, we cannot help you with your request referring to the index status. We suggest you consult Scopus database (see the current status of the journal) or the mentioned database for further information. You can also check that information in the journal's website or contact directly with the editorial staff.

Best Regards, SCImago Team

Dr Nada Ahmedzeki 1 year ago

Dear,

The status of the journal says that it was cancelled, I want to know if the year 2016 is included in SJR or not. This information is quite important for a paper published in Nov.Dec. 2016.

reply

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Antimalarial Activity and Survival Time of *Andrographis paniculata* Fraction (AS202-01) on *Plasmodium berghei* Infected Mice.

Aty Widyawaruyanti^{1,3*}, Deri Astrianto², Hilkatul Ilmi³, Lidya Tumewu³, Dwi Setyawan¹, Endang Widiastuti⁵, Lilis Dachliyati⁵, Indah S Tantular^{3,4}, and Achmad Fuad Hafid^{1,3}.

¹Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Universitas Airlangga, Dharmawangsa Dalam, Surabaya-60286

²Undergraduate student of Faculty of Pharmacy, Universitas Airlangga, Dharmawangsa Dalam, Surabaya-60286

³Institute of Tropical Disease, Universitas Airlangga, C Campus Universitas Airlangga, Mulyorejo, Surabaya-60115

⁴Department of Parasitology, Faculty of Medicine, Universitas Airlangga, Mayjen. Prof. Dr. Moestopo 47, Surabaya-60131

⁵PT. Kimia Farma (Persero) Tbk., Veteran No.9, Jakarta-10110

ABSTRACT

The rapid spread of resistance encourages the search for new active compounds. *Andrographis paniculata* commonly known as sambiloto was empirically used as traditional medicine in Indonesia to cure malaria. This study aims to determine antimalarial activity and survival time of *A. paniculata* fraction from 70% ethanolic extract (namely AS202-01) on *Plasmodium berghei* infected mice. Antimalarial in vivo study was conducted based on Peter's 4-days suppressive test. Thirty healthy Balb/c male mice, divided into 6 groups (n = 5), were infected intravenously with 1×10^6 parasitized erythrocytes of *P. berghei*. Infected mice were treated at a dose of 6.25, 12.5, 25 and 50 mg/kg BW, twice a day for four days, the untreated group of mice received CMC-Na 0.5% and the control group treated with chloroquine (10 mg/kg BW). Thin blood smears giemsa staining were made every day for seven days and observed under microscope to count parasitemia and calculate inhibition of parasite's growth. Probit analysis was conducted to determine effective dose (ED₅₀) value. Observation of antimalarial effect of AS202-01 was continued until 14 days to evaluate survival time of infected mice. The results showed that AS202-01 was inhibited *P. berghei* growth with ED₅₀ value of 6.75 mg/kg BW. It was classified as a highly active antimalarial substance. The AS202-01 was also significantly able to increase survival time of infected mice compared to untreated group.

Keywords: *A. paniculata* fraction (AS202-01), antimalarial, survival time, *Plasmodium berghei*

*Corresponding author

Antimutagenic Activity and Survival Time of *Andropogon nanus* Fraction (A202-02) on Plasmid-bearing *Salmonella typhimurium* Mutated Mice

ATY Widyawati¹, Dwi Astuti², Hilda Liana³, Liana Liana⁴, Dwi Setyaningsih⁵, Endang Widiyanti⁶, Ika Diah⁷, Indriyanti⁸, and Ahmad Fadhil⁹

¹Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ²Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ³Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ⁴Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ⁵Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ⁶Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ⁷Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ⁸Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia; ⁹Department of Biotechnology, Faculty of Applied Sciences, Institut Teknologi Sepuluh Nopember (ITS), Surabaya, Indonesia

ABSTRACT

The aim of this study was to determine the antimutagenic activity of *Andropogon nanus* fraction (A202-02) on plasmid-bearing *Salmonella typhimurium* mutated mice. The study was conducted using a plasmid-bearing *Salmonella typhimurium* mutated mice model. The antimutagenic activity of A202-02 was tested by measuring the number of revertant colonies per plate (RCP) of *Salmonella typhimurium* mutated mice. The results showed that the RCP of *Salmonella typhimurium* mutated mice treated with A202-02 was significantly lower than the RCP of *Salmonella typhimurium* mutated mice treated with distilled water. The survival time of *Salmonella typhimurium* mutated mice treated with A202-02 was significantly longer than the survival time of *Salmonella typhimurium* mutated mice treated with distilled water. The results of this study indicate that A202-02 has antimutagenic activity and can increase the survival time of *Salmonella typhimurium* mutated mice.

*Corresponding author



INTRODUCTION

Malaria is one of the most important infectious diseases in the world. This disease is caused by *Plasmodium* species and transmitted by the bite of female *Anopheles* mosquito [1]. Estimated 214 million people infected malaria in the world. Despite the decrease of malaria infection about 18% from 2000 to 2015, but a new problem is antimalarial drug resistant *Plasmodium* parasites and the emergence of insecticide resistant *Anopheles* [2]. Resistant not only the spread of malaria to new areas but also its reemergence in areas where it had previously been eradicated [3]. Therefore, the search for new antimalarial, either synthetic or natural, is important for killing of malaria parasites [4].

The use of medicinal plant extract for treatment of malaria has a long and successful tradition [5]. For example, quinine was isolated from *Chinchona* species (Rubiaceae) and artemisinin from *Artemisia annua* [6]. Diterpenoids, flavonoids, saponin, polyphenols, alkaloids, kaempferol, and acetogenin from plants were known to have antimalarial activity [7, 8]. This explains why a lot of current researches focus on natural and plant-derived products as they can be sourced easily, can be locally available, and can be selected on the basis of their pharmacological use [9, 10].

Andrographis paniculata commonly known as sambiloto was empirically used as traditional medicine in Indonesia to treat people suffering from malaria. It also possesses antimicrobial effect, antiinflammatory, antioxidant, antidiabetic, antiHIV, antifungal, hepatoprotector, antifertility and anti cancer [11, 12]. The major constituents of *A. paniculata* is andrographolide, a diterpene lactone compound, which has antimalarial activity both in vitro and in vivo [13]. Andrographolide inhibited *P. berghei* growth with ED₅₀ value of 3.82 mg/kgBW [14]. The ethyl acetate fractions of *A. paniculata* from 70% ethanolic extract (AS202-01) is an andrographolide rich fraction. Previous study reported that andrographolide content of AS202-01 was higher among other extracts and fraction [15]. This study aims to determine antimalarial activity and survival time of AS202-01 on *Plasmodium berghei* infected mice.

MATERIALS AND METHODS

Plant materials:

A. paniculata dried powder with batch number PP01J1125027 was obtained from PT. Kimia Farma (Persero) Tbk, Bandung, Indonesia on February 2015

Experimental animals:

Male mice BALB/C strain were obtained from LPPT-Universitas Gajah Mada, Yogyakarta. They were weighting between 20-30 g and maintained on standard animal pellets and water ad libitum at Animal Laboratory of Institute of Tropical Disease, Universitas Airlangga. Permission and approval for animal studies were obtained from Faculty of Veterinary Medicine, Universitas Airlangga No:489-KE/2015.

Rodent malaria parasite

Plasmodium berghei ANKA strain was originally obtained from Eijkman Institute for Molecular Biology, Jakarta. The parasite has been maintained at Institute of Tropical Disease, Universitas Airlangga by a combination of passage in male BALB/C mice and cryoscopic storage.

Methods:

Procedure 1: Preparation of *A. Paniculata* fraction (AS202-01)

A. paniculata dried powder was extracted by maceration method using ethanol 70% as a solvent. Liquid ethanol extract then evaporated using rotary evaporator. The concentrated extract then further separation by liquid-liquid fractionation using ethyl acetate and water to obtain ethyl acetate fraction namely AS202-01.

Procedure 2: In vivo antimalarial activity test

In vivo antimalarial activity was performed based on Peter's test (The 4-days suppressive test) [16]. AS202-01 was tested using 30 mice which divided to 6 groups (n=5): untreated group (CMC-Na 0.5%), control group (chloroquin), AS202-01 dose of 6.25 mg/kg BW, AS202-01 dose of 12.5 mg/kg BW, AS202-01 dose of 25 mg/kg BW, AS202-01 dose of 50 mg/kg BW.

Each mice was infected intraperitoneally with 0.2 ml *P. berghei* (1×10^6). Infected mice were treated at a dose of 6.25, 12.5, 25 and 50 mg/kg BW, twice a day for four days. The untreated group of mice received CMC-Na 0.5% and control group (chloroquin at dose 10 mg/kg BW). Thin blood smears were made every day for 5 days (day-0 until day-4) and stained using 10% giemsa dye. Thin blood smear were observed under microscope to count the percentage of parasitemia and calculate inhibition of parasite's growth.

Procedure 3: Determine of mean survival time (MST)

Determination of MST was performed based on Somsak et al, 2016 [4]. The survival time of *P. berghei* infected mice was observed during 14 days (day-0 until day-13).

Data Analysis**In vivo antimalarial activity test**

Percentage of parasitemia and percentage of inhibition growth of *P. berghei* were calculated using the formula below.

Percentage of parasitemia:

$$\frac{X_e}{X_k} \times 100\%$$

Percentage of inhibition:

$$100\% - \left(\frac{X_e}{X_k} \times 100\% \right)$$

X_e: % parasitemia growth of experimental group

X_k: % parasitemia growth of untreated group

Inhibition percentage was analyzed using Probit analysis SPSS to determine Effective Dose (ED₅₀) value.

Determine of mean survival time (MST)

The mean survival time (MST) was calculated using the formula below.

$$MST = \frac{\text{Sum of survival time of all mice in a group}}{\text{Total number of mice in that group}}$$

RESULTS AND DISCUSSION**Antimalarial Activity**

Andrographis paniculata belongs to the family Acanthaceae that has been used as traditional medicine in Indonesia to cure malaria. Many reports are also available on the antimalarial activity of *A. paniculata*. Mishra (1992) was reported that crude ethanol extract and fractions of *A. Paniculata* inhibited *P.*

berghei growth. Methanol, chloroform, and petroleum ether extract of *A. paniculata* inhibited *P. falciparum* growth on gametocytes and schizont stage [17,18].

The present study assessed the antimalarial activity of AS202-01, *A. Paniculata* fraction obtained from 70% ethanol extract of *A. Paniculata*. The results showed that AS202-01 inhibited parasite (*P. berghei*) growth. The average of parasitemia percentage of infected mice which treated by AS202-01 on first-day observation until fifth day (D0-D4) tended to increase, but it was still lower than untreated group, this is showed that AS202-01 inhibited the growth of *P. berghei* (ANKA strain) in mice. The results are summarized in table 1.

Table 1. Activity of AS202-01 on *P. berghei* infected mice

Group	Dose (mg/kgBW)	% Parasitemia					% average inhibition parasite's growth
		H0	H1	H2	H3	H4	
Negative Control		0.21±0.04	2.16±1.06	5.14±1.07	7.90±1.33	10.46±2.20	-
Chloroquin	10	0.32±0.15	0.31±0.11	0.13±0.05	0.20±0.15	0.23±0.24	99.47±0.79
AS202-01	6.25	0.19±0.06	1.05±0.50	2.09±0.70	3.29±0.23	4.86±0.24	48.33±2.25
	12.5	0.30±0.11	1.26±0.40	2.19±0.61	3.07±0.44	4.24±0.26	58.46±1.27
	25	0.19±0.10	0.91±0.37	1.31±0.47	2.28±0.78	3.33±0.10	64.81±1.27
	50	0.27±0.09	0.73±0.46	1.16±0.31	1.82±0.55	2.86±0.15	70.16±0.78

AS202-01 : *A. paniculata* fraction from
H0-H4 : Day of observation

The data on table 1 showed that inhibition parasite's growth followed a dose dependent manner. The data of inhibition parasite growth was analyzed using log-probit to determine Effective Dose (ED₅₀) value. The result analysis showed that AS202-01 has ED₅₀ value of 6.75 mg/kg BW, it was highly active as an antimalarial substance based on criteria Munoz et al (2000) [19]. The period of activity of andrographolide was found evidently on the ring stage of the parasite. The point of action of this compound in the parasite life cycle corresponds with the protein and nucleic acid synthesis [13]. *A. paniculata* extract and andrographolide includes inhibition of the nuclear transcription factor-kappa B (NF-κB), making it a therapeutic target for the treatment of cancer and autoimmune diseases [20]. The role of NF-κB is also important in malaria as mentioned in a recent study [21]. Plasmodium infected erythrocytes have shown to induce NF-B (kappa) regulated inflammatory pathways in human cerebral endothelium. NF-κB is activated and translocate into nucleus, where it binds to the DNA regulatory site to regulate specific gene expression, especially cell signaling for parasite growth and development. Therefore, the inhibition of transcription factor of *A. paniculata* extract against *P. berghei* ANKA might be a critical process to inhibit blood stage propagation of parasites in vivo [12, 20].

This study results showed that chloroquine had antimalarial activity higher than AS202-01, its inhibition parasite's growth with the value of 99.47%±0.79 at a dose of 10 mg/kg BW. Meanwhile, AS202-01 at the highest dose (50 mg/kg BW) inhibited parasite's growth with the value of 70.16%±0.78. The difference of these activities might be due to the life time of Andrographolide was 2-7 hours, and rapidly elimination within 3-4 hours after administration[22], and the life time of Chloroquine was 150 hour or 6 day on healthy people.

Survival Time

The result showed AS202-01 had higher survival time than negative control. AS202-01 at all doses was capable of significantly increasing the survival time. Survival time was showed dose dependent manner. The higher of AS202-01 dose, then survival time was higher as well. The results are summarized in table 2.

The survival time longer than 12 days by the test compound is regarded as active [23]. AS202-01 at a dose of 12.5 until 50 mg/kg BW was performed survival time more than 12 days. Moreover, survival time which observed was almost as chloroquine for AS202-01 at the highest dose (50 mg/kg BW).



The present study assessed the antitumor activity of A2502-01. A Fractional Inhibition Point (FIP) value of 0.50 was observed for A2502-01, indicating that the growth of the parasite was inhibited by 50% at this concentration. The results are summarized in Table 1.

Table 1. Activity of A2502-01 on P. berghei-infected mice

Group	Dose (mg/kg BW)	% Parasitemia				% average inhibition parasite's growth
		H4	H3	H2	H1	
Negative Control	-	10.46±3.30	7.90±1.33	2.14±1.07	1.14±1.04	0
Chloroquine	10	0.28±0.24	0.20±0.10	0.19±0.08	0.31±0.11	99.47±0.29
A2502-01	6.25	4.84±0.24	3.19±0.21	2.09±0.20	1.92±0.20	98.33±0.22
	12.5	4.24±0.25	3.07±0.44	2.10±0.81	1.20±0.49	98.40±1.27
	25	4.33±0.70	3.28±0.28	1.31±0.47	0.91±0.57	94.81±1.27
	50	2.84±0.22	1.82±0.25	1.10±0.31	0.73±0.45	91.64±0.28

A2502-01: A. pentacota fraction point
H3-H4: Day of observation

The data in Table 1 showed that inhibition parasite's growth followed a dose dependent manner. The data of inhibition parasite growth was analyzed using log-probit to determine Effective Dose (ED₅₀) value. The result analysis showed that A2502-01 has ED₅₀ value of 6.25 mg/kg BW. It was highly active as an antimalarial substance based on criteria based on ED₅₀ value. The point of action of this compound in the parasite life cycle corresponds with the protein and nucleic acid synthesis [19]. A possible exact and anticancerous mechanism of inhibition of the parasite's growth is not clear. It is known that the inhibition of the parasite's growth is a critical process to inhibit blood stage propagation of parasites *in vivo* [12].

The study result showed that chloroquine had antitumor activity higher than A2502-01. Inhibition parasite's growth with the value of 99.47±0.29 at a dose of 10 mg/kg BW. Meanwhile, A2502-01 at the highest dose (50 mg/kg BW) inhibited parasite's growth with the value of 91.64±0.28. The difference of these activities might be due to the time of Anticancerous was 3-7 days and could be observed within 3-4 hours after administration [20] and the time of Chloroquine was 100 hours or 6 days of healthy people.

Survival Time

The result showed A2502-01 had higher survival time than negative control. A2502-01 at all doses was capable of significantly increasing the survival time. Survival time was showed dose dependent manner. The higher of A2502-01 dose, then survival time was higher as well. The results are summarized in Table 2.

The survival time longer than 13 days by the test compound is recorded as active [20]. A2502-01 at a dose of 12.5 until 50 mg/kg BW was performed survival time more than 13 days. Moreover, survival time which observed was almost as chloroquine for A2502-01 at the highest dose (50 mg/kg BW).

The data on table 2 also showed that the higher of inhibition parasite's growth, then survival time was higher as well. It was possible related to the immune system of infected mice. *A. paniculata* was reported as immunosuppressive agent [24]. Based on the facts, AS202-01 might play a role in immune system which inhibit parasite's growth and then the condition was associated with increased survival time.

Table 2. Survival time of AS202-01

Group	Dose (mg/kgBW)	% average Inhibition parasite's growth	Survival time (Day)
Negative control		-	9.6±2.7
Chloroquin	10	99.47±0.79	14±0
AS202-01	6.25	48.33±2.25	11.8±3.03
	12.5	58.46±1.27	12.6±2.19
	25	64.81±1.27	13.2±1.79
	50	70.16±0.78	13.8±0.45

AS202-01: *A. paniculata* fraction

CONCLUSIONS

AS202-01 was active as an antimalarial on *Plasmodium berghei* infected mice with ED₅₀ value of 6.75 mg/kg BW and classified as a highly active antimalarial substance. The AS202-01 was significantly able to increase survival time compared to negative control.

ACKNOWLEDGEMENTS

The authors acknowledge grant support from Indonesian Directorate General of Higher Education DIPA BOPTN 2016, contract no 951/UN3.14/2016.

REFERENCES

- [1] WHO. 2009. Guidelines for the treatment of malaria. Second edition. Available at: http://whqlibdoc.who.int/publications/2010/9789241547925_enf.pdf. Accessed: 1 November 2016.
- [2] WHO. 2015. World Malaria Report 2015. WHO Geneva.
- [3] Barik T. 2015. Antimalarial drug: from its development to deface, Current Drug Discovery Technologies, vol. 12, no. 4, pp. 225–228.
- [4] Somsak V., Polwiang N., Chachiyo S. 2016. In Vivo Antimalarial Activity of *Annona muricata* Leaf Extract in Mice Infected with *Plasmodium berghei*. Journal of Pathogens, 10: 1-5.
- [5] Kaur K., Jain M., Kaur T., and Jain R. 2009. Antimalarials from nature," Bioorganic & Medicinal Chemistry, vol. 17, no. 9, pp.3229–3256.
- [6] Mutabingwa T.K. 2005. Artemisinin-based combination therapies (ACTs) best hope for malaria treatment but inaccessible to the needy. Acta Trop;95:305-15.
- [7] Ginsburg H and Atamna H. 1994. The redox status of malaria infected erythrocytes: an overview with an emphasis on unresolved problems, Parasite, vol. 1, no. 1, pp. 5–13.
- [8] Barliana M.I., Suradji E.W., Abdulah R. 2014. Antiplasmodial properties of kaempferol-3-O-rhamnoside isolated from the leaves of *Schima wallichii* against chloroquine-resistant *Plasmodium falciparum*, Biomedical Reports, vol. 2, no. 4, pp. 579-583.
- [9] Negi A.S., Gupta A, and Hamid A.A. 2014. Combating malaria with plant molecules: a brief update, Current Medicinal Chemistry, vol. 21, no. 4, pp. 458–500.
- [10] Mojab F. 2012. Antimalarial natural products: a review, Avicenna Journal of Phytomedicine, no. 2, pp. 52–62.
- [11] Niranjana, Abhishek, Tewari S.K., Lehri A. 2010. Biological Activities of Kalmegh (*Andrographis paniculata* Nees) and Its Active Principle-A review. Indian Journal of Natural Products and Resources Vol 1(2): 125 – 135
- [12] Mishra K, Dash A.P., Swain B.K., Dey N. 2009. Antimalarial activities of *Andrographis paniculata* and *Hedyotis corymbosa* extracts and their combination with curcumin. Malaria Journal; 8 (26), 1-9.

- [13] Mishra K, Dash A.P., Swain B.K., Dey N. 2011. Andrographolide: A Novel Antimalarial Diterpene Lactone Compound from *Andrographis paniculata* and Its Interaction with Curcumin and Artesunate. *Journal of Tropical Medicine*, Article ID 579518.
- [14] Mahdiyanti S.M. 2004. In vivo antimalarial of *Andrographis paniculata* Nees on Plasmodium berghei infected mice. Skripsi. Fakultas Farmasi Universitas Airlangga. Surabaya. (Article in Indonesian).
- [15] Achmad Fuad Hafid A.F., Rifai B, Widiastuti E, Dachliyati L, Primaharinastiti R, Widyawaruyanti A. 2015. Andrographolide determination of *Andrographis paniculata* extracts, ethyl acetate fractions and tablets by thin layer chromatography. *Journal of chemical and pharmaceutical*; 7 (12), 557-561.
- [16] Peter W., Portus H, and Robinson L. 1995. The four-day suppressive in vivo antimalarial test. *Ann Trop Med Parasitol*, 69:155–171.
- [17] Widyawaruyanti A. 1999. Imunomodulator activity of diterpenoid compound of *Andrographis paniculata* Nees on the function of T-lymphocyte cytotoxicity (CD +8) mice. Thesis. Universitas Airlangga. (Article in Indonesian).
- [18] Widowati R, Santa IGP, Rahman A, Indah T, Widyawaruyanti A. 2003. In vitro Antimalarial of *Andrographis paniculata* isolate against *Plasmodium falciparum* on gametocyte stage. *Majalah farmasi airangga*, vol:3, no.99-102. (Article in Indonesian).
- [19] Munoz V, Sauvain M, Bourdy G, Callapa J, Bergeron S, Rojas I, *et al.* A search for natural bioactive compounds in Bolivia through a multidisciplinary approach: Part I. Evaluation of the antimalarial activity of plants used by the Chacobo Indians. *J Ethnopharmacol* 2000;69:127-37.
- [20] Luo W, Liu Y, Zhang J, Luo X, Lin C, Guo J. 2013. Andrographolide inhibits the activation of NF-kappaB and MMP-9 activity in H3255 lung cancer cells. *Exp Ther Med*. 6(3): 743-6.
- [21] Tripathi A.K., Sha W, Shulaev V, Stins M.F, Sullivan D.J. 2009. *Plasmodium falciparum*-infected erythrocytes induce NF-kappaB regulated inflammatory pathways in human cerebral endothelium. *Blood*, 114(19): 4243-52.
- [22] Panossian A, Hovhannisyan A, Mamikonyan G, Abrahamian H, Hambardzumyan E, Gabrielian E, Goukasova G, Wikman G, Wagner H. 2000. *Pharmacokinetic and Oral Bioavailability of Andrographolide from Andrographis paniculata fixed combination Kan Jang in Rats and Human*. *Phytomedicine* Vol 75.
- [23] Peter I.T and Anatoli V.K. 1998. *The Current Global Malaria Situation, Malaria parasite Biology, Pathogenesis and Protection*, ASM Press, Washington, USA.
- [24] Chao W.W, Kuo Y.H, Hsieh S.L, Lin B.F. 2011. Inhibitory effects of ethyl acetate extract of *Andrographis paniculata* on NF-kB trans-activation activity and LPS-induced acute inflammation in mice. *Evidence-based complementary and alternative medicine*, pp: -9.