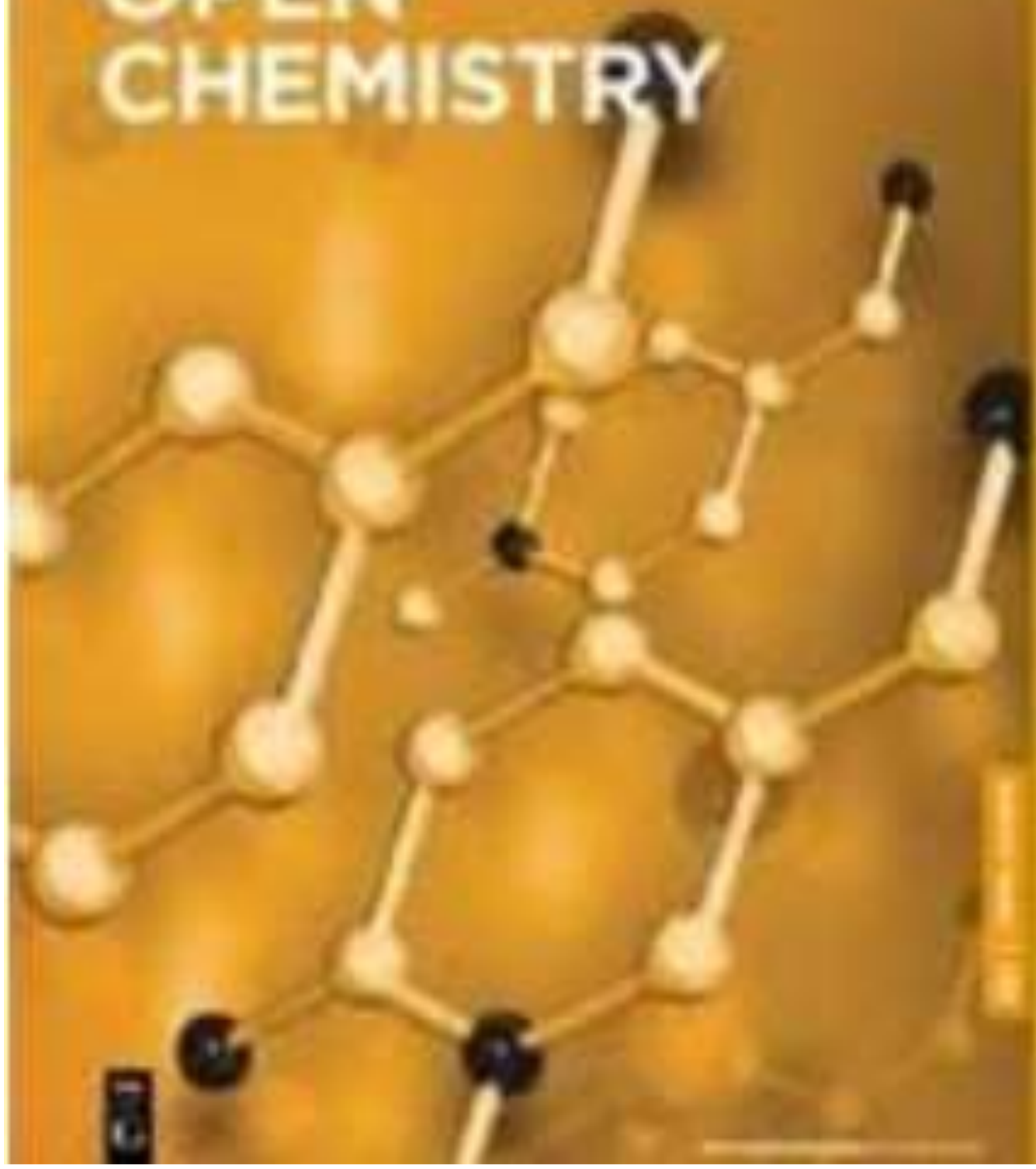


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Research Article

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Antiplasmodial Activity of Stigmastane Steroids from *Dryobalanops oblongifolia* Stem Bark

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Abstract: Three stigmastane steroids: 6-hydroxystigmast-4-en-3-one (1), stigmast-4-en-3-one (2), and 3-hydroxystigmast-5-en-7-one (3) were successfully isolated from the acetone extract of *Dryobalanops oblongifolia* stem bark. The structural determination of isolated compounds was carried out on the basis of data analysis of NMR and MS spectra. In order to identify the antiplasmodial activity, the isolated compound was put to test against *Plasmodium falciparum* 3D7. Antiplasmodial activity of the isolated compounds showed that the IC_{50} values of 6-hydroxystigmast-4-en-3-one were 37.29 $\mu\text{g/mL}$ while the IC_{50} values of stigmast-4-en-3-one were 43.54 $\mu\text{g/mL}$ and the IC_{50} values of 3-hydroxystigmast-5-en-7-one were 13.34 $\mu\text{g/mL}$ (chloroquine phosphate was used as a positive control, IC_{50} 0.006 $\mu\text{g/mL}$). Judging from the results, the isolated compounds were proven to demonstrate mediocre antiplasmodial activity. Compound (3) indicated a better antimalarial activity than compound (1) and (2), even though there was no satisfactory activity that indicated its ability to combat chloroquine. Therefore, it might not be developed as an antimalarial drug.

Keywords: Antiplasmodial; *Dryobalanops oblongifolia*; *Plasmodium falciparum*; Stigmastane steroid.

1 Introduction

Malaria is one of the infectious diseases that has become a major problem of health. It is found in nearly most of all tropics, particularly developing and poor countries. *Plasmodium*, a parasitic protozoa genus, is what causes malaria in humans. The parasite that derived from the genus namely *Plasmodium falciparum* is the lethal part that causes acute infection worldwide with an annual death toll of 1-2 million people [1, 2].

Quinine which isolated from cinchona tree has been widely used to cure malaria, yet it is still powerless to comprehensively break the life cycle of *Plasmodium* parasites [3]. Artemisinin, a sesquiterpene lactone, is reported as a potential antimalarial drug and have the ability to kill all phases of the parasites' life cycle through interaction with heme, yet animal experiment shows neurotoxic and cardiotoxic effect [4]. Development of synthesized drugs, such as chloroquin, pyrimethamine, cycloguanil, and sulfadoxine, have indicated the decline of effectivity caused by the resistance of *Plasmodium* [3,5,6,7]. Therefore, it is crucial to develop alternative medicines from plants by constituent exploration as potential antimalarial drugs.

Dryobalanops oblongifolia belongs to the family of Dipterocarpaceae and is widely found in Indonesia and Malaysia [8]. The phytochemical screening of fruit of *D. oblongifolia* revealed the presence of steroids compounds in this species [9]. *Dryobalanops* is known to produce oligostilbene constituents with various interesting activity such as antibacterial, antioxidant, antimalarial and cytotoxic [10, 11, 12, 13, 14]. In continuation for searching bioactive compounds from Indonesia's plants, a study towards *D. oblongifolia* was conducted by isolating the agents and examining the antiplasmodial activity against *Plasmodium falciparum* 3D7. Based on our knowledge this three stigmastane steroids (1-3) were first report from family Dipterocarpaceae and these isolated metabolites expressed only moderate antiplasmodial activity.

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2 Experimental section

2.1 General procedures

Firstly, CDCl_3 was used to dissolve ^1H and ^{13}C NMR and 2D NMR of stigmastane steroids spectra. While using TMS as the internal standard, JEOL J-500 spectrometer was used to record and it was utilized in CDCl_3 at 125 MHz (^{13}C) and 500 MHz (^1H). On a TSQ Quantum Access MAX Triple Quadrupole Mass Spectrometer, mass spectrometry was analyzed. Gravitation column chromatography (GCC) was conducted with Merck Si gel 60 (700-200 mesh). Vacuum liquid chromatography (VLC) and radial chromatography were conducted using Si gel 60 PF_{254} and Si gel 60 GF_{254} . The analysis of Thin Layer Chromatography (TLC) was done on Merck kieselgel 60 GF_{254} , precoated Si gel plates, with a thickness of 0.25 mm. This research used already distilled analytical and technical grade solvents.

2.2 Plant Material

Mount Mali was the place where *D. oblongifolia* Dyer stem bark was originally collected. The mount is located in Tempunak, Sintang, West Kalimantan of Indonesia. The researchers then proceeded to the identification step by sending the plant specimen to the Biological Research Center of LIPI in Bogor, Indonesia. A voucher specimen was put in safekeeping at the herbarium.

2.3 Extraction and Isolation

At room temperature, as much as 5 kg of *D. oblongifolia* stem bark powder was pulped twice in acetone. It is meant to afford the extraction of brownish gummy after the process of vacuum evaporation. The extract was subsequently separated into 2 fractions: 1 fraction is able to be dissolved in acetone – diethyl ether while the other fraction is insoluble. As much as 48 g of the soluble fraction was divided into fractions using vacuum liquid chromatography (VLC) (*n*-hexane – ethyl acetate, enhancing polarity) to give four main fractions which are fraction A-D. By using radial chromatography techniques and Gravitation Colum Chromatography (GCC), as much as 1.7 g of Fraction B was separated and purified. The process led to the production of compound **1** with a total of 6.5 mg and compound **2** with a total of 3 mg. In order to isolate both compounds and enhance the polarity, *n*-hexane and ethyl acetate mixtures were used. As

much as 1.6 g of Fraction C was separated and refined by using the same chromatography techniques and solvent mixtures, resulting in the production of compound **3** with a total of 3.4 mg.

2.3.1 In Vitro Antiplasmodial Assays

The antiplasmodial activity of compound 1-3 was determined in the Tropical Disease Institute of Universitas Airlangga, which is located in Surabaya, Indonesia. In this part, the method used was equivalent with the former method described by Widyawaruyanti et al. [15]. The dissolution of these samples was conducted in DMSO and they were stored at -20°C until use. A culture plate with 24 wells was used to cultivate the *P. falciparum* clone. The concentration range of each compound was 100, 10, 1, 0.1, and 0.01 $\mu\text{g/mL}$. As a positive control, a drug with antimalarial characteristics namely Chloroquine phosphate was used. The antiplasmodial activity measurement of compound 1-3 and chloroquine phosphate was calculated in replica. The monitoring process of parasitaemia was conducted when 48 hours had passed by firstly making a blood test fixed with MeOH and spattered with Geimsa (Merck). With the aim to determine the parasitaemia average ratio and average inhibition, the researchers calculated the total number of infected erythrocytes from originally 1000 healthy erythrocytes. The researchers used IC_{50} value to state the antiplasmodial activity of compound 1-3. IC_{50} value is the concentration of compounds that causes 50% inhibition of the parasite growth. The IC_{50} value was obtained by using probit analysis processed by the SPSS program.

Ethical approval: The conducted research is not related to either human or animal use.

3 Result and Discussion

The acetone extracted from *D. oblongifolia* stem bark was fractionated and purified using radial chromatography, gravitation column chromatography, and vacuum liquid chromatography. It was intended to produce three stigmastane steroid compounds, specifically 6-hydroxystigmast-4-en-3-one (**1**), stigmast-4-en-3-one (**2**), and 3-hydroxystigmast-5-en-7-one (**3**). The isolated compound structures were identified on the basis of ^1H - and ^{13}C -NMR spectral data, and 2D NMR experimentations and contrast with the reported data and MS spectral data.

Table 1: Average Inhibition of isolated compounds (1-3) and Chloroquine phosphate against *P. falciparum* 3D7.

No	Compound	% Average Inhibition ($\mu\text{g/mL}$)					IC ₅₀ $\mu\text{g/mL}$	IC ₅₀ μM
		100	10	1	0,1	0,01		
1	6-hydroxystigmast-4-en-3-one	60.78	35.14	18.40	10.26	1.36	37.29	86.91
2	Stigmast-4-en-3-one	58.06	34.76	20.28	11.17	1.51	43.54	105.36
3	3-hydroxystigmast-5-en-7-one	72.40	42.08	26.09	12.07	1.51	13.34	31.08
4	Chloroquine phosphate	99.13	89.38	82.01	65.73	58.55	0.006	0.01

* The IC₅₀ value was obtained by using probit analysis of SPPS program.

Compound 1 was isolated as an achromatic formless powder. C₂₉H₄₈O₂ was established as the molecular formula by means of ESI-MS ([M+H]⁺ ion at m/z 429.076). There were a total of 6 methyl groups that were found to be present according to the ¹H-NMR spectrum. They were 2 groups of tertiary methyl [δ_{H} 0.74 (H-18) and 1.38 (H-19)], 3 groups of secondary methyl [δ_{H} 0.92 (H-21), 0.81 (H-26), and 0.84 (H-27)], and 1 group of primary methyl δ_{H} 0.85 (H-29). Furthermore, 1 oxygenated methine proton was seen at δ_{H} 4.35 (H-6), while 1 sp² methine was seen at δ_{H} 5.81(H-4). Meanwhile, it appeared that there was an overlap in the proton peaks of methylene and methine groups. There were 29 carbon signals revealed by the ¹³C-NMR spectrum that contained an oxygenated secondary carbon at δ_{C} 73.3 (C-6), a carbonyl carbon at δ_{C} 200.4 (C-3), and 2 olefinic carbons [δ_{C} 126.3 (C-4) and 168.5 (C-5)]. There was an indication that the carbon signals that were present at δ_{C} 126.3, 168.5, and 200.4 signified an α,β -unsaturated carbonyl system that was present in compound **1**. It indicated a suggestion that **compound 1** was stigmastane steroid, especially when looking at the data of ¹H-NMR and ¹³C-NMR. There were many correlations that have been pointed out by the spectra of compound **1** Heteronuclear Multiple Bond Correlation (HMBC) particularly between H-21/C-17, H-21/C-20, and H-21/C-22; H-22/C-23; H-25/C-23, H-25/C-24, H-25/C-27, and H-25/C-28; H-26/C-24, H-26/C-25, and H-26/C-27; H-27/C-25 and H-27/C-26; H-29/C-28. The structure of side chain was established by these correlations. The presence of pentenoperhydrophenanthrene nucleus was indicated by the correlations between H-18/C-12, H-18/C-13, and H-18/C-14; H-19/C-1, H-19/C-5, H-19/C-9, and H-19/C-10, they signified the tetracyclic. In addition, there were indications showed by the HMBC links between H-4 / C-2, H-4 / C-6, H-4 / C-10, and H-6 / C-4, H-6 / C-8, H-6 / C-10 that there are 2 different locations for the α,β -unsaturated carbonyl system and the hydroxyl group. The location of the former is in ring A, while the latter in ring B (Table 1). Aside from the analysis of the HMBC spectrum, the determination of hydroxyl group location can also be

achieved by doing a TOCSY test. Compound **1** structure was indicated as 6-hydroxystigmast-4-en-3-one (Figure 1) [16].

Compound 2 was isolated as an achromatic formless powder with a [M+H]⁺ ion at m/z 413.244. It was isolated during ESI-MS analysis and it corresponded to C₂₉H₄₈O molecular formula. Compound **2** was discovered by the NMR data as a steroid with stigmastane skeleton. Although compound **2** has a high resemblance with compound **1** in terms of ¹H-NMR and ¹³C-NMR spectrum chemical shifts, compound **2** does not possess any hydroxyl group (Table 1). Compound **2** structure was indicated as stigmast-4-en-3-one (Figure 1) [17, 18].

Compound 3 was isolated too as an achromatic formless powder that has C₂₉H₄₈O₂ molecular formula (ESI-MS, [M+H]⁺ ion at m/z : 429.227). Compound **3** has high resemblance with compound **1** and **2** in terms of NMR spectrum chemical shifts, exposing that compound **3** was a stigmastane steroid. There were 29 carbon signals displayed by ¹³C-NMR and DEPT spectra. These carbon signals consisted of 6 methyl carbons, 10 methylene carbons, 9 methine carbons, and 3 quaternary carbons, and carbonyl ketone. The HMBC spectra proved that 1 hydroxyl group and the α,β -unsaturated carbonyl system were present with links between H-4/C-2, H-4/C-3, H-4/C-5, H-4/C-6, H-4/C-10 ; H-6/C-4, H-6/C-8, and H-6/C-10 ; H-8/ C-7, H-8/C-9. There are indications initiated by the HMBC analysis that the hydroxyl group and the α,β -unsaturated carbonyl system was located on different positions. The location of the former was at the position of C-3 in ring A, while the location of the latter was in ring B (Table 1). Compound **3** structure was identified as 3-hydroxystigmast-5-en-7-one. The confirmation can be seen through a contrast with stigmast 3-hydroxy-5-en-7-one chemical shifts, which is similar to the previously published research (Figure 1) [19, 20].

The examination of antiplasmodial activity against *P. falciparum* 3D7 was carried out by in vitro to three stigmastane steroid compounds. The test results showed

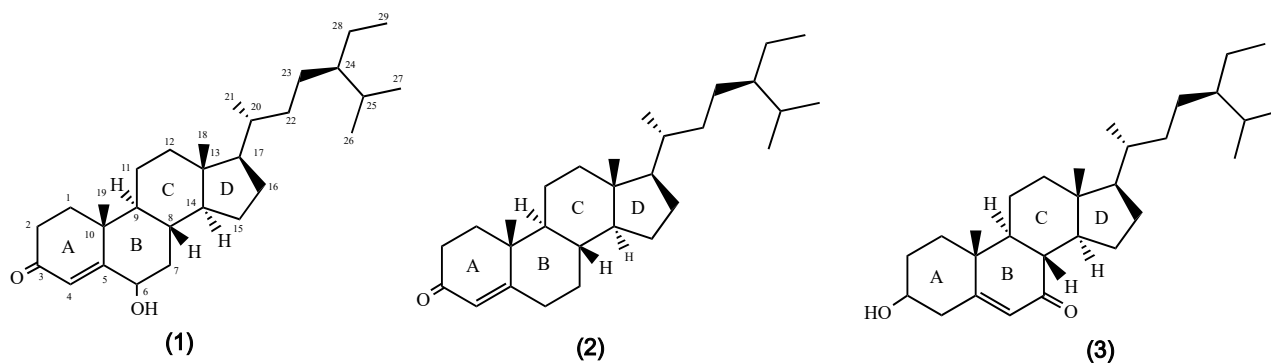


Figure 1: The structure of isolated compounds **1**, **2** and **3** from *D. oblongifolia*.

6-hydroxystigmast-4-en-3-one (**1**)

Tabel 2: Antimalarial activity of 6-hydroxystigmast-4-en-3-one against *P. falciparum* 3D7.

Dose ($\mu\text{g/ml}$)	R	% Parasitaemia		% Growth	% Inhibition	% Average Inhibition
		0 jam	48 jam			
Kontrol (-)	1	1.17	4.49	3.32	-	-
	2	1.17	4.48	3.31	-	-
100	1	1.17	2.45	1.28	61.45	60.78
	2	1.17	2.49	1.32	60.12	
10	1	1.17	3.34	2.17	34.64	35.14
	2	1.17	3.30	2.13	35.65	
1	1	1.17	3.86	2.69	18.98	18.40
	2	1.17	3.89	2.72	17.82	
0.1	1	1.17	4.15	2.98	10.24	10.26
	2	1.17	4.14	2.97	10.27	
0.01	1	1.17	4.45	3.28	1.20	1.36
	2	1.17	4.43	3.26	1.51	
IC₅₀						37.29 $\mu\text{g/mL}$

that the IC_{50} value of 6-hydroxystigmast-4-en-3-one (**1**) was as much as $37.29 \mu\text{g/mL}$. Meanwhile, for stigmast-4-en-3-one (**2**), the IC_{50} value was as much as $43.54 \mu\text{g/mL}$, whereas the IC_{50} value of 3-hydroxystigmast-5-en-7-one (**3**) was as much as $13.34 \mu\text{g/mL}$. Chloroquine phosphate was used a positive control with as much as $0.006 \mu\text{g/mL}$ IC_{50} (Table 1). Judging from the results, mediocre antiplasmodial activity was found in the three stigmastane steroid compounds [21]. Compound **3** showed better antiplasmodial activity than the others. The structure of stigmastane steroids chemical compound revealed that the presence and position of hydroxyl group can influence their antiplasmodial activity. The location of hydroxyl group in compound **3** is easier to interact with extracellular and intracellular fluids so that

it can be easily carried to target molecule [22]. However, compound **3** is considered as lacking the ability to fight against the chloroquine so it may not be promoted as an antimalarial agent.

4 Conclusion

There were three stigmastane steroids that were successfully isolated from the acetone extract derived from the stem bark of *Dryobalanops oblongifolia*. The evaluation on antiplasmodial activity was performed to all of the isolated compounds, specifically 6-hydroxystigmast-4-en-3-one (**1**), stigmast-4-en-3-one (**2**), and 3-hydroxystigmast-

Stigmast-4-en-3-one (2)**Table 3:** Antimalarial activity of sistigmast-4-en-3-one against *P. falciparum* 3D7.

Dose ($\mu\text{g/ml}$)	R	% Parasitaemia		% Growth	% Inhibition	% Avarage Inhibition
		0 jam	48 jam			
Kontrol (-)	1	1.00	4.65	3.65	-	-
	2	1.00	4.60	3.60	-	-
100	1	1.00	2.53	1.53	57.50	58.06
	2	1.00	2.49	1.49	58.61	
10	1	1.00	3.35	2.35	35.62	34.76
	2	1.00	3.38	2.38	33.89	
1	1	1.00	3.91	2.91	20.27	20,28
	2	1.00	3.87	2.87	20.28	
0.1	1	1.00	4.21	3.21	12.06	11.17
	2	1.00	4.23	3.23	10.28	
0.01	1	1.00	4.58	3.58	1.91	1.51
	2	1.00	4.56	3.56	1.11	
IC₅₀						43.54 $\mu\text{g/mL}$

3-hydroxystigmast-5-en-7-one (3)**Table 4:** Antimalarial activity of 3-hydroxystigmast-5-en-7-one against *P. falciparum* 3D7.

Dose ($\mu\text{g/ml}$)	R	% Parasitaemia		% Growth	% Inhibition	% Avarage Inhibition
		0 jam	48 jam			
Kontrol (-)	1	1.17	4.49	3.32	-	-
	2	1.17	4.48	3.31	-	-
100	1	1.17	2.09	0.92	72.29	72.40
	2	1.17	2.08	0.91	72.51	
10	1	1.17	3.08	1.91	42.47	42.08
	2	1.17	3.10	1.93	41.69	
1	1	1.17	3.64	2.47	25.60	26.09
	2	1.17	3.60	2.43	26.59	
0.1	1	1.17	4.10	2.93	11.75	12.07
	2	1.17	4.07	2.90	12.39	
0.01	1	1.17	4.44	3.27	1.51	151
	2	1.17	4.43	3.26	1.51	
IC₅₀						13.34 $\mu\text{g/mL}$

5-en-7-one (3). The antiplasmodial activity indicated that there was a total of 37.29 $\mu\text{g/mL}$ of IC₅₀ value in 6-hydroxystigmast-4-en-3-one. Meanwhile, the IC₅₀ value of stigmast-4-en-3-one was as much as 43.54 $\mu\text{g/mL}$ while as much as 13.34 $\mu\text{g/mL}$ of IC₅₀ value was found in 3-hydroxystigmast-5-en-7-one (chloroquine phosphate was

used as a positive control, IC₅₀ 0.006 $\mu\text{g/mL}$). Compound 3 was the most active isolated compounds although there was not enough activity to fight against chloroquine. As the consequence, compound 3 did not meet the standard of an antimalarial drug and may not be developed as a proper medication of the disease.

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Conflict of interest: Authors declare no conflict of interest.

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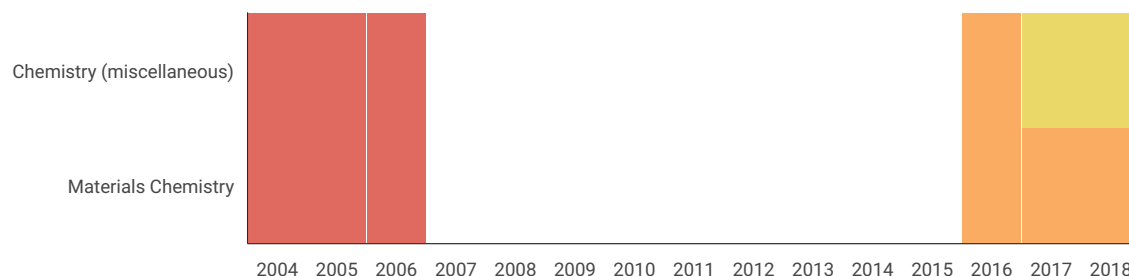
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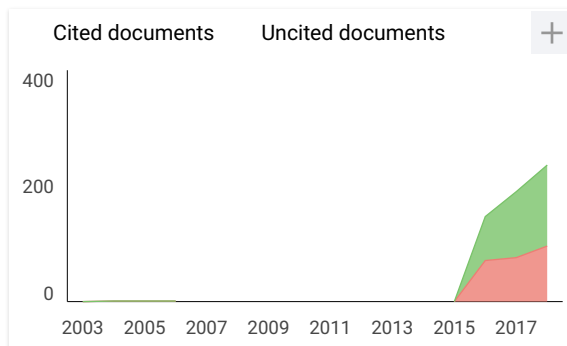
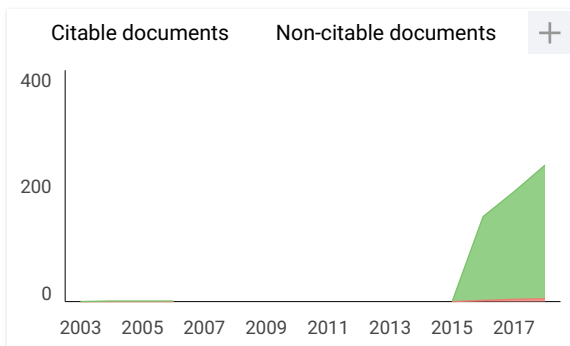
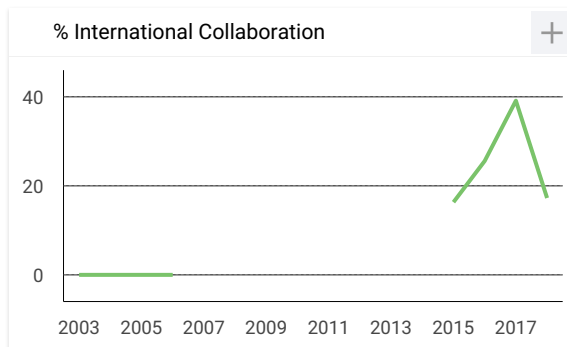
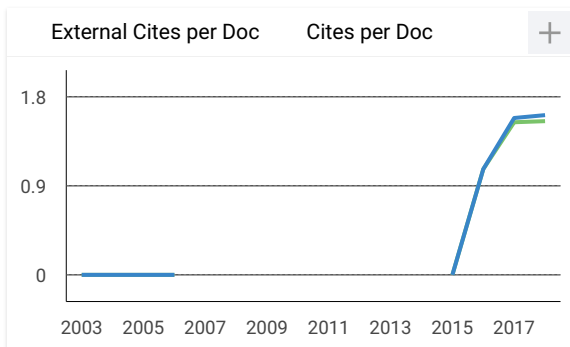
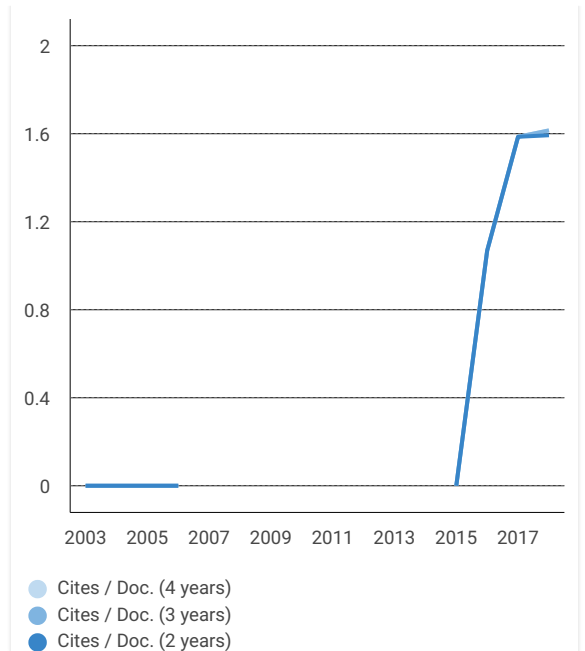
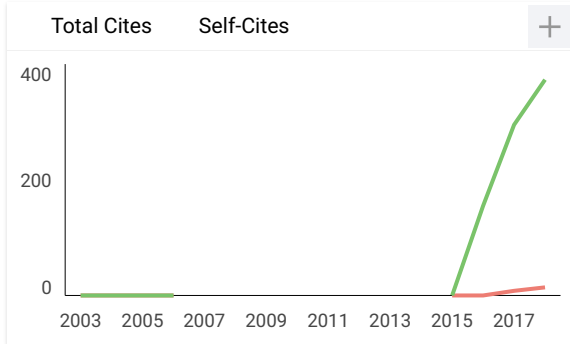
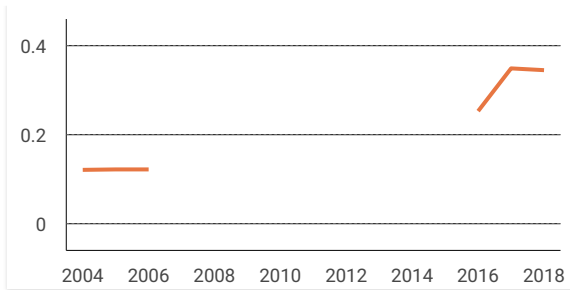


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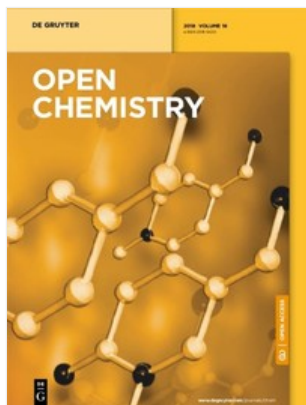


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Electrochemical antioxidant screening and evaluation based on guanine and chitosan immobilized MoS₂ nanosheet modified glassy carbon electrode (guanine/CS/MoS₂/GCE)

Ping Tang, Xiaosheng Tang, Shiyong Mei, Yixi Xie, Liangliang Liu and Licheng Ren

Pages: 1–9 | Published online: 13 Feb 2020

ABSTRACT

In this study, an electrochemical biosensor based on guanine and chitosan immobilized MoS₂ nanosheet modified glassy carbon electrode (guanine/CS/

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Kinetic models of the extraction of vanillic acid from pumpkin seeds

Milan Mitić, Sonja Janković, Pavle Mašković, Biljana Arsić, Jelena Mitić and Jovana Ickovski

Pages: 22–30 | Published online: 30 Jan 2020

ABSTRACT

Vanillic acid is used in the food industry and perfumery, and the optimization of its extraction process from the natural source is important for

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On the maximum *ABC* index of bipartite graphs without pendent vertices

Zehui Shao, Pu Wu, Huiqin Jiang, S.M. Sheikholeslami and Shaohui Wang

Pages: 39–49 | Published online: 10 Mar 2020

ABSTRACT

For a simple graph G , the atom–bond connectivity index (*ABC*) of G is defined as $ABC(G) =$

$\sum_{uv \in E(G)} d(u) + d(v) - 2d(u)d(v)$, where $d(v)$ denotes the de

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Estimation of the total antioxidant potential in the meat samples using thin-layer chromatography

Paweł Piszcz, Magdalena Tomaszewska and Bronisław K. Głód

Pages: 50–57 | Published online: 28 Feb 2020

ABSTRACT

There is limited literature on the antioxidative properties of food of animal origin. Measurements of antioxidative properties are usually performed

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Molecular dynamics simulation of sl methane hydrate under compression and tension

Qiang Wang, Qizhong Tang and Sen Tian

Pages: 69–76 | Published online: 20 Feb 2020

ABSTRACT

Molecular dynamics (MD) analysis of methane hydrate is important for the application of methane hydrate technology. This study investigated

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Spatial distribution and potential ecological risk assessment of some trace elements in sediments and grey mangrove (*Avicennia marina*) along the Arabian Gulf coast, Saudi Arabia

Hameed Alsamadany, Hassan S. Al-Zahrani, El-Metwally M. Selim and Mohsen M. El-Sherbiny

Pages: 77–96 | Published online: 10 Mar 2020

ABSTRACT

To assess trace element concentrations (Zn, Cu, Pb, Cr, Cd and Ni) in the mangrove swamps along the Saudi coast of the Arabian Gulf, thirteen sa

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Amino-functionalized graphene oxide for Cr(VI), Cu(II), Pb(II) and Cd(II) removal from industrial wastewater

Huayu Huang, Yang Wang, Yubin Zhang, Zhiying Niu and Xinli Li

Pages: 97–107 | Published online: 10 Mar 2020

ABSTRACT

Amino-functionalized graphene oxide (GO-NH₂) was synthesized by grafting (3-aminopropyl) triethoxysilane on the graphene oxide (GO) surface. The G

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Chemical composition and *in vitro* activity of *Origanum vulgare* L., *Satureja hortensis* L., *Thymus serpyllum* L. and *Thymus vulgaris* L. essential oils towards oral isolates of *Candida albicans* and *Candida glabrata*

Tomasz Baj, Anna Biernasiuk, Rafał Wróbel and Anna Malm

Pages: 108–118 | Published online: 10 Mar 2020

ABSTRACT

The purpose of this research was to investigate the chemical composition of essential oils (EOs) from: *Origanum vulgare* L., *Satureja hortensis* L.,

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Effect of excess Fluoride consumption on Urine-Serum Fluorides, Dental state and Thyroid Hormones among children in “Talab Sarai” Punjab Pakistan

Sadia Zulfiqar, Humayun Ajaz, Shafiq ur Rehman, Shan Elahi, Amer Shakeel, Farhat Yasmeen and Shehni-la Altaf

Pages: 119–128 | Published online: 18 Mar 2020

ABSTRACT

190 children aged 7-18 years from an endemic fluorotic village “Talab Sarai (n = 130) and a non-fluorotic, control, village “Ottawa” (n = 60)

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Design, Synthesis and Characterization of Novel Isoxazole Tagged Indole Hybrid Compounds

Raed A. Al-Qawasmeh, Louy A. Al-Nazer, Sarah A. Dawlat-Kari, Luay Abu-Qatouseh, Salim S. Sabri, Murad A. AlDamen and Mutasem Sinnokrot

Pages: 138–148 | Published online: 25 Mar 2020

ABSTRACT

Sixteen new isoxazole tagged indole compounds have been synthesized *via* copper (I) catalyzed click chemistry of the aryl hydroxamoyl chloride

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Comparison of kinetic and enzymatic properties of intracellular phosphoserine aminotransferases from alkaliphilic and neutrophilic bacteria

Marianne Koivulehto, Natalia Battchikova, Saara Korpela, Elvira Khalikova, Anton Zavialov and Timo Korpela

Pages: 149–164 | Published online: 24 Mar 2020

ABSTRACT

Intracellular pyridoxal 5'-phosphate (PLP) -dependent recombinant phosphoserine aminotransferases (PSATs; EC 2.6.1.52) from two alkaliphili

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Green Organic Solvent-Free Oxidation of Alkylarenes with *tert*-Butyl Hydroperoxide Catalyzed by Water-Soluble Copper Complex

Abdelaziz Nait Ajjou and Ateeq Rahman

Pages: 165–174 | Published online: 24 Mar 2020

ABSTRACT

Different benzylic compounds were efficiently oxidized to the corresponding ketones with aqueous 70% *tert*-butyl hydroperoxide (TBHP) and the catalyt

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***Ducrosia ismaelis* Asch. essential oil: chemical composition profile and anticancer, antimicrobial and antioxidant potential assessment**

Ramzi A. Mothana, Fahd A. Nasr, Jamal M. Khaled, Omar M. Noman, Nael Abutaha, Adnan J. Al-Rehaily, Omar M. Almarfadi and Mine Kurkcuoglu

Pages: 175–184 | Published online: 02 Apr 2020

ABSTRACT

The essential oil of *Ducrosia ismaelis* Asch. (Apiaceae) that grows wild in Saudi Arabia was investigated utilizing gas chromatography (GC),

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DFT calculations as an efficient tool for prediction of Raman and infra-red spectra and activities of newly synthesized cathinones

Maja Vujović, Venkatesan Ragavendran, Biljana Arsić, Emilija Kostić and Milan Mladenović

Pages: 185–195 | Published online: 07 Apr 2020

ABSTRACT

Initially made for medical treatment for Parkinsonism, obesity, and depression, cathinones have become illegal drugs for the “recreational us

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Influence of Chemical Osmosis on Solute Transport and Fluid Velocity in Clay Soils

Zhihong Zhang, Gailei Tian and Lin Han

Pages: 232–238 | Published online: 07 Apr 2020

ABSTRACT

Solute transport through the clay liner is a significant process in many waste landfills or unmanaged landfills. At present, researchers mainl

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A New fatty acid and some triterpenoids from propolis of Nkambe (North-West Region, Cameroon) and evaluation of the antiradical scavenging activity of their extracts

Abakar Ali Mahamat, Jean Noël Nyemb, Isaac Silvère Gade, Alfred Tamfu Ngenge, Emmanuel Talla, Henoumont Céline, Laurent Sophie and Joseph Tanyi Mbafor

Pages: 239–243 | Published online: 02 Apr 2020

ABSTRACT

The aim of this work was to evaluate *in vitro* antiradical scavenging activity of propolis from Nkambe (North-West, Cameroon). The polyphenol

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Antiplasmodial Activity of Stigmastane Steroids from *Dryobalanops oblongifolia* Stem Bark

Indriani Indriani, Nanik Siti Aminah and Ni Nyoman Tri Puspaningsih

Pages: 259–264 | Published online: 07 Apr 2020

ABSTRACT

Three stigmastane steroids: 6-hydroxystigmast-4-en-3-one (1), stigmast-4-en-3-one (2), and 3-hydroxystigmast-5-en-7-one (3) were successfully i

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Rapid identification of direct-acting pancreatic protectants from *Cyclocarya paliurus* leaves tea by the method of serum pharmacochimistry combined with target cell extraction

Wei-hong Chen, Zhen Luo, Zi-Wan Ning, Jiao Peng, Xiao-peng Hu, Li-xiang Zhai, Bo Wen, Hai-tao

Xiao and Zhao-xiang Bian

Pages: 265–274 | Published online: 07 Apr 2020

ABSTRACT

Extracts of *Cyclocarya paliurus* (CP) leaves, a popular sweet tea, inhibit pancreatic β cell apoptosis and have potent hypoglycemic effects, bu

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nanik

**Submission Confirmation for OPENCHEM-D-18-00482R1**

Inbox x

**Open Chemistry** <em@editorialmanager.com>

to me

Ref.: Ms. No. OPENCHEM-D-18-00482R1

Antiplasmodial activity of stigmastane steroids from *Dryobalanps oblongifolia* stem bark

Dear Dr Aminah,

Open Chemistry has received your revised submission.

You may check the status of your manuscript by logging onto Editorial Manager at (<https://www.editorialmanager.com/openchem/>). Just a reminder - we charge APC (Article Processing Charges) once article is accepted.

Kind regards,

Editorial Office
Open Chemistry

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the fol [om/openchem/login.asp?a=r](https://www.editorialmanager.com/openchem/login.asp?a=r)). Please contact the publication office if you have any questions.

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Your Submission OPENCHEM-D-18-00482R1 - Open Chemistry

10 messages

Open Chemistry <em@editorialmanager.com>

Mon, Jun 17, 2019 at 3:19 PM

Reply-To: Open Chemistry <agnieszka.topolska@degruyter.com>

To: Nanik Siti Aminah <nanik-s-a@fst.unair.ac.id>

Ref.: Ms. No. OPENCHEM-D-18-00482R1

Antiplasmodial activity of stigmastane steroids from *Dryobalanops oblongifolia* stem bark

Open Chemistry

Dear Dr Aminah,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript just a little bit more. If you are prepared to undertake the work required, I would be happy to receive your revised paper.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript.

Your revision is due by 2019/07/21.

To submit a revision, go to <https://www.editorialmanager.com/openchem/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Please, submit signed License to Publish with your revision, which can be retrieved from here - https://www.degruyter.com/view/supplement/s23915420_Open_Access_License.pdf

Yours sincerely,
Agnieszka Topolska
Managing Editor
Open Chemistry

Reviewers' comments:

Reviewer #3: After the modification, the level of the article has been improved, so I suggest it can be considered to accept.

Reviewer #4: Nanik Siti Aminah and co-workers in this manuscript describe about isolation of three known stigmastane steroids from the stem bark of the *Dryobalanops oblongifolia*. The authors were able to show a moderate anti-plasmodial activity of three isolated steroids: 6-hydroxystigmast-4-en-3-one (1), stigmast-4-en-3-one (2) and 3-hydroxystigmast-5-en-7-one (3). In general, the research presented in this manuscript is not organized well. However, I recommend this manuscript to publish after authors' address below mentioned comments.

1. Please reorganize the entire manuscript and it is difficult to follow (I feel like somehow the first version was organized better).
2. The abstract for the manuscript should be fixed and please combine everything into one like in the first version of this manuscript (Please remove all of the subheadings in abstract).
3. The authors' should discuss about known literature of these three steroids and please show the structures of chloroquine, pyrimethamine, cycloguanil, and sulfadoxine in the introduction part.
4. The authors should show correct stereochemistry for three steroids in the figure 1 and add names (please look into the literature how others' draw structures)
5. The authors should include optical rotation values for compounds (1-3).
6. Please remove the table 1 from manuscript, move it to SI and combine it with other NMR data.
7. Please cite this ref for 6 β -hydroxystigmast-4-en-3-one (1): Aguilar-Gonzalez, Amilcar R., Gonzalo J. Mena-Rejón, Nayely Padilla-Montaño, et al *Zeitschrift für Naturforschung B*. 2014, 60 (5), 577-584.
8. Ref 14 was labeled twice and please fix this.
9. Please cite this ref for Stigmast-4-en-3-one (2): A. Barla, H. Birman, S. Kultur, and S. Oksuls, *Turk. J. Chem.* 30(3), 325 (2006).

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/openchem/login.asp?a=r>). Please contact the publication office if you have any questions.

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: Tin Myo Thant <kotinkoko.kse@gmail.com>

Thu, Oct 3, 2019 at 3:14 PM

Please help to revise Ibu Indri article

The main text final is the text that the reviewer read and check.

Open che.....first is the text that the first time we send.

Thank for your kind help and cooperation.

Best regard,
Nanik

Thank you

[Quoted text hidden]

--

Dr. Nanik Siti Aminah

Assoc. Professor on Natural Product Chemistry
Dept. of Chemistry
Fac. of Science and Technology
Universitas Airlangga

Vice Dean on Research and Partnership
Faculty of Science and Technology
Universitas Airlangga
Komplek Kampu C UNAIR
Jl. Ir. Soekarno
Surabaya-East Java
Indonesia
email address : nanik-s-a@fst.unair.ac.id

2 attachments



OPENCHEM-D-18-00482-FIRST.pdf
1264K



OC-NANIK SA(Indri)-Main text-FINAL.docx
68K

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: Open Chemistry <agnieszka.topolska@degruyter.com>

Mon, Oct 28, 2019 at 3:26 AM

Dear Agnieszka Topolska

Good morning,







I have made revisions of this manuscript through the system but at the end of the process, the pdf file can not appear. Even though I have update to be pdf 10 as suggested. So I can not make approval of this revision.

Would you like to help me to put the revision of the manuscript (attach file) to the system or do you have another suggestion?

Thank you very much for your kind help.

Best regard,
[Quoted text hidden]
[Quoted text hidden]

6 attachments

-  **Cover letter-OPEN CHEMISTRY INDRI_REVISE 28 OCT 2019.docx**
69K
-  **RESPONSE TO REVEIWER COMMENT OPENCHEM.docx**
16K
-  **OC-NANIK SA(Indri)-Main text(24-Oct-2019) (1).docx**
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-  **OC-NANIK SA(Indri)_supplymentary, (24-Oct-2019).docx**
891K
-  **OC-NANIK SA(Indri)-Figure-(24-Oct-2019).docx**
51K
-  **OC-NANIK SA(Indri)-Table (24-Oct-2019).docx**
34K

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Tue, Oct 29, 2019 at 8:41 PM

Dear Nanik,

I'm sorry for my late reply. But I see that you've managed to upload all files successfully.

If we have an 'accept' decision after this round, wouldn't you mind if we publish your paper early in volume 2020 (in January)?

Also, just a reminder - the APC is 1000 EUR plus VAT (if applicable), plus money transfer charges.

Best regards,
Agnieszka

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: "Topolska, Agnieszka" <Agnieszka.Topolska@degruyter.com>

Wed, Oct 30, 2019 at 3:43 AM

Dear Agnieszka Topolska

We agree for publish in January 2020, of course we know that the APC is 1000 EUR.

Thank you very much

best regards
[Quoted text hidden]

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Wed, Oct 30, 2019 at 11:34 PM

Thank you for the confirmation Nanik!

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: Open Chemistry <agnieszka.topolska@degruyter.com>

Thu, Nov 21, 2019 at 2:49 PM

Dear
Agnieszka Topolska
Managing Editor
Open Chemistry

Good afternoon
Greeting from Universitas Airlangga

Would you like to inform the progress of our manuscript "OPENCHEM-D-18-00482R1"
We have done a revision on 2019/10/28.

Thank you for your kind help.

With best regard,

On Mon, Jun 17, 2019 at 3:19 PM Open Chemistry <em@editorialmanager.com> wrote:

[Quoted text hidden]

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: Open Chemistry <agnieszka.topolska@degruyter.com>

Thu, Nov 21, 2019 at 2:54 PM

Sorry, I mean our manuscript number " OPENCHEM-D-18-00482R2", because "OPENCHEM-D-18-00482R1" had been accepted and will publish in January 2020.

Thank you
[Quoted text hidden]

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Mon, Nov 25, 2019 at 11:37 PM

Dear Nanik,

Thank you for your email. Your submission OPENCHEM-D-18-00482R2 is being checked by the Reviewers now, so if accepted, will be published in volume 2020. But we are still waiting for the decision.

As for OPENCHEM-D-18-00445R1, I just sent you the file after language editing.
Is there any other submission you would like me to check?

Best regards,
Agnieszka

From: nanik siti aminah <nanik-s-a@fst.unair.ac.id>
Sent: Thursday, November 21, 2019 8:55 AM
To: Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
Subject: Re: Your Submission OPENCHEM-D-18-00482R1 - Open Chemistry

Sorry, I mean our manuscript number " OPENCHEM-D-18-00482R2", because "OPENCHEM-D-18-00482R1" had been accepted and will publish in January 2020.

Thank you
[Quoted text hidden]

Your Submission OPENCHEM-D-18-00482R2 - Open Chemistry

17 messages

Open Chemistry <em@editorialmanager.com>
Reply-To: Open Chemistry <agnieszka.topolska@degruyter.com>
To: Nanik Siti Aminah <nanik-s-a@fst.unair.ac.id>

Wed, Dec 11, 2019 at 3:16 AM

Ref.: Ms. No. OPENCHEM-D-18-00482R2
Antiplasmodial activity of stigmastane steroids from *Dryobalanops oblongifolia* stem bark
Open Chemistry

Dear Dr Aminah,

I am pleased to tell you that your work has now been accepted for publication in Open Chemistry.

It was accepted on 2019/12/01

In order to proceed with your publication I would like to remind you that we charge a publication fee - the APC is 1000 EUR plus VAT (if applicable), plus money transfer charges.

Thank you for submitting your work to this journal.

With kind regards,
Agnieszka Topolska
Managing Editor
Open Chemistry

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/openchem/login.asp?a=r>). Please contact the publication office if you have any questions.

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: indri.2707@gmail.com

Wed, Dec 11, 2019 at 3:27 AM

Bu Indri yang baik

Alhamdulillah artikel Bu Indri accepted di jurnal "OPEN CHEMISTRY" Q2, SJR 0,35.

Monggo Bu, ditunggu artikel Berikutnya nggih.

Terimakasih
Salam
Nanik
[Quoted text hidden]

--
Dr. Nanik Siti Aminah

Assoc. Professor on Natural Product Chemistry
Dept. of Chemistry
Fac. of Science and Technology
Universitas Airlangga

Vice Dean on Research and Partnership
Faculty of Science and Technology
Universitas Airlangga
Komplek Kampus C UNAIR
Jl. Ir. Soekarno
Surabaya-East Java
Indonesia
email address : nanik-s-a@fst.unair.ac.id

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: Open Chemistry <agnieszka.topolska@degruyter.com>

Wed, Dec 11, 2019 at 3:41 AM

Dear Agnieszka Topolska

I am glad to receive your good news that our 2nd manuscript was accepted.
We will continue the process asap.

Thank for your kind help.

Best regard,
Nanik

[Quoted text hidden]

[Quoted text hidden]

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Sat, Dec 28, 2019 at 6:30 PM

Dear Nanik,

I hope you are having a nice Holiday time.

Please, could you let me know if you have an invoice and started the payment process?

Best regards,

Agnieszka

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: "Topolska, Agnieszka" <Agnieszka.Topolska@degruyter.com>

Sat, Dec 28, 2019 at 6:55 PM

Yes, I received it, but I have meeting in Kualalumpur for a week, and after back, the bank close, We will do the payment he day after tommorow.

Thank you very much for your remaining me.

best regards

nanik

[Quoted text hidden]

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Sat, Dec 28, 2019 at 7:35 PM

Thank you Nanik.

[Quoted text hidden]

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Tue, Jan 7, 2020 at 9:41 PM

Dear Nanik, I'm afraid we still haven't received the fee payment. Please, could you check this case ASAP?

Best regards,

Agnieszka

[Quoted text hidden]

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Fri, Jan 17, 2020 at 4:35 PM

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: "Topolska, Agnieszka" <Agnieszka.Topolska@degruyter.com>

Mon, Jan 20, 2020 at 9:18 AM

Thank you for your email. I will check our payment to the bank again today.
Hope I will give you the information again soon.

Best regard,
Nanik

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id>
To: "Topolska, Agnieszka" <Agnieszka.Topolska@degruyter.com>

Wed, Jan 22, 2020 at 10:10 PM

Dear Agnieszka Topolska

Here I send the payment by credit card and also the invoice of OPENCHEM-D-18-00482.

I hope everything will doing well and our article will publish soon.


Thank you for your kind help and cooperation.

With best regard,
Nanik

[Quoted text hidden]

2 attachments

 **Invoice_OPEN CHEMISTRY_INDRI.pdf**
53K

 **PAYMENT_OPENCHEM-D-18-00482_BY CREDIT CARD.pdf**
118K

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Thu, Jan 23, 2020 at 12:03 AM

Thank you Nanik, we've received your payment and I will proceed to the production processes in coming days.

[Quoted text hidden]

Topolska, Agnieszka <Agnieszka.Topolska@degruyter.com>
To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Fri, Feb 21, 2020 at 11:19 PM

Dear Nanik,

please find attached your article after language polishing. Note to check the references list carefully (especially year of publication and the journal title - both are essential for a proper indexing), and adjust it according to our Instructions for Authors (attached) – new references style Vancouver/ICMJE https://www.nlm.nih.gov/bsd/uniform_requirements.html#journals . For any corrections use the attached version of your manuscript.

Thank you!

[Quoted text hidden]