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Synthesis and In Vitro Antimalarial Activity of Amino Chalcone Derivatives Compounds Through Inhibition of Heme Polymerization

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ABSTRACT: This study aims to investigate the potential of chalcone derivatives as antimalarial agents. The structure of the chalcone derivatives was designed by inserting amino substituents on acetophenone and methoxy variants on benzaldehyde to produce three amino chalcone derivatives (C1, C2, and C3). The synthesis was carried out by carrying out the Claisen-Schmidt condensation reaction with NaOH 40% as catalyst, resulting in compound yields ranging from 66% - 83%. The structure of the three compounds was determined by FTIR, MS, and 1H-NMR spectroscopy techniques, which confirmed that the compounds had structures that were in line with the desired molecular structure. The antimalarial activity test was carried out by inhibiting the heme polymerization process into hemozoin (β-hematin) using hydroxychloroquine sulfate as a positive control. Absorption measurements were carried out at two different wavelengths, namely 415 nm and 630 nm. The results of the IC_{50} antimalarial activity of the three compounds (C1, C2, C3) were obtained respectively at 227.61; 115.18; 260.01 µg/mL and positive control of 184.98 µg/mL. From these results, it was found that compound C2 showed better antimalarial activity compared to the other two compounds and positive control.

Keywords: **amino chalchone; synthesis; antimalarial; heme polymerization; hemozoin.**

Introduction

Malaria is a disease caused by the Plasmodium parasite, which spreads to humans through the bites of infected female Anopheles mosquitoes. There are five species of parasites that cause malaria in humans, and two of these species, *Plasmodium falciparum* and *Plasmodium vivax*, pose the greatest threat of death [1]. In 2022, malaria cases and deaths following the Covid-19 pandemic. Globally In 2022, it was estimated that there were approximately 249 million cases of malaria and 608,000 malaria-related deaths across 85 countries worldwide. In the Southeast Asia region, WHO reported that between 2021 and 2022, there was an increase in cases in Bangladesh, Indonesia, Myanmar and Thailand [2].

Currently available antimalarial drugs can be categorized into three types: aryl amino alcohol (quinine, quinidine, halofantrine, chloroquine, amodiaquine, mefloquine and cycloquine), antifolate (proguanil, pyrimethamine, trimethoprim); and artemisinin (artemisin, dihydroartemisin) [3]. Some of them are still used, and some are no longer used because of resistance. Resistance of *P. falciparum* and *P. vivax* to the antimalarial drug chloroquine (CQ) has been reported in many countries [4]. CQ is a first-line malaria drug that has been used for decades and was reported to resistancant to *P. falciparum* for the first time in East Kalimantan, Indonesia in 1973, whereas the case of resistance of the malaria parasite *P. vivax* to chloroquine was first found in 1989 in Papua [5]. Resistance to antimalarial drugs complicates disease control . Widespread and indiscriminate use of antimalaria drugs also causes malaria parasites to develop resistance mechanisms. WHO and Indonesian government through the Ministry of Health have also recommended alternative drugs to replace chloroquine and SP, namely a combination of artemisinin derivatives, known as artemisinin combination therapy (ACT) [5].

Efforts to reduce morbidity and mortality due to malaria continue in endemic countries to break the chain of malaria transmission. Various discoveries of new antimalarial drugs that can

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kill therapeutic targets without causing resistance are also being pursued. One of the compounds developed for the discovery of antimalarial drugs is chalcone. Chalcone is included in the flavonoid compound group, because it has a basic framework of C6-C3-C6 [6]. The chalcone structure consists of two aromatic rings connected to three carbons through an α,β- unsaturated carbonyl system [7]. With this structure and the presence of bound substituents, chalcone and its derivatives are known to have various therapeutic and pharmacological activities including antioxidant [8,9], anti-inflammatory [10], antiplasmodial (antimalarial) [11-14], antituberculosis [15], anti-leishmanial, antimicrobial [16] and anticancer [17,18] activities.

Chalcone derivative compounds with an N-heterocyclic framework in their structure have been reported to produce broad bioactivity, one of which is as antimalarial activity [19]. Based on the analysis of the Structure-Activity Relationship (SAR), it is known that the amine group (N) in most antimalarial drugs play an important role in antimalarial activity. Amines can form electrostatic interactions with essential amino acids in malaria parasites [20,21]. Chalcone derivatives with hydroxyl and methoxy groups can also exhibit increased antimalarial activity [22]. Therefore, it is interesting to explore the potential activity of three amino chalcone derivatives containing methoxy groups as antimalarial drug candidates.

This study presents the findings of the synthesis, structural analysis, and evaluation of the antimalarial properties of three amino chalcone derivatives. These derivatives contain methoxy substituents on aromatic ring B, positioned differently. The assessment of antimalarial activity was conducted in vitro by examining the heme polymerisation into β-hematin (hemozoin). Hemozoin is known as malaria pigment, structurally similar to beta-hematin, and functions as a biomarker in antimalarial activity [23]. The process of converting free heme to hemozoin is known as the heme polymerization reaction. Antimalarial drugs are designed to inhibit the formation of hemozoin in host cells. This method is used in antimalarial drug screening by measuring β-hematin crystals formed based on the reduction of heme absorption in the formation of β-hematin [24].

Methods

Materials

The materials used in this study were 4'-amino acetophenone (Sigma Aldrich®), 3-methoxy benzaldehyde (Sigma Aldrich®), 3,4-dimethoxy benzaldehyde (Sigma Aldrich®), 3,4,5-trimethoxy benzaldehyde (Sigma Aldrich®), HCl pa (Merck®), NaOH (Merck®), hemin (ferri protoporphyrin IX chloride) (Sigma Aldrich®), hydroxychloroquine sulfate, acetate buffer, Tween-20 (Sigma-Aldrich®), organic solvents such as absolute ethanol p.a (J.T.Baker), acetonitrile for HPLC (Merck®), DMSO (Sigma-Aldrich®), aqua DM and distilled technical solvents such as ethyl acetate, *n*-hexane, DCM and methanol.

Instruments Analysis

The purity test and reaction progress all compounds were performed by analysis using TLC on aluminium sheets silica gel 60 F254 with Camag UV lamp (eluent: *n*-hexane/ethyl acetate in 6:4 ratio) and also analysis by HPLC (Shimadzu, LC 20 AT with isocratic elution). All melting points were determined on a DMP-800 melting point device, Innotech Inc. Characterization of the compound structures was obtained from the results of ^{1}H NMR spectra taken on a Bruker Avance Neo 500 MHz Germany NMR spectrophotometer; IR spectra were obtained on a Spirit A-224158 IR spectrophotometer (Shimadzu); MS spectra were obtained on an Acquity UPLC H-Class

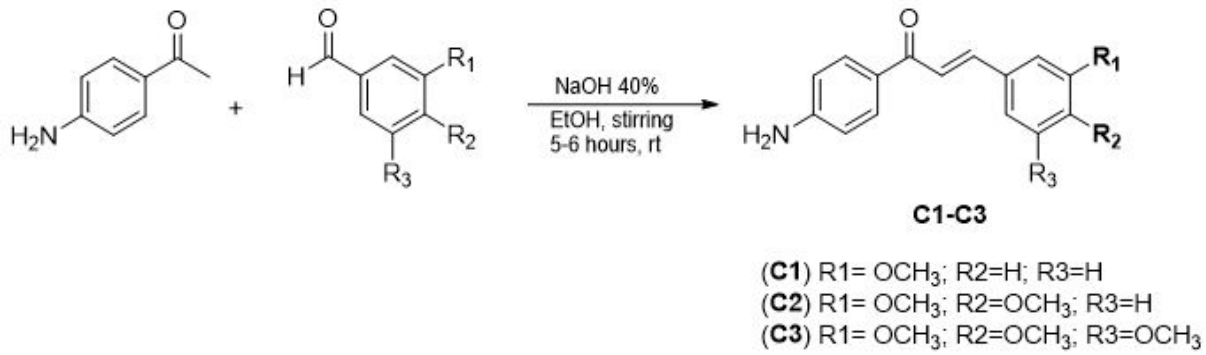

Figure 1. Synthesis route of the compounds C1, C2 and C3.

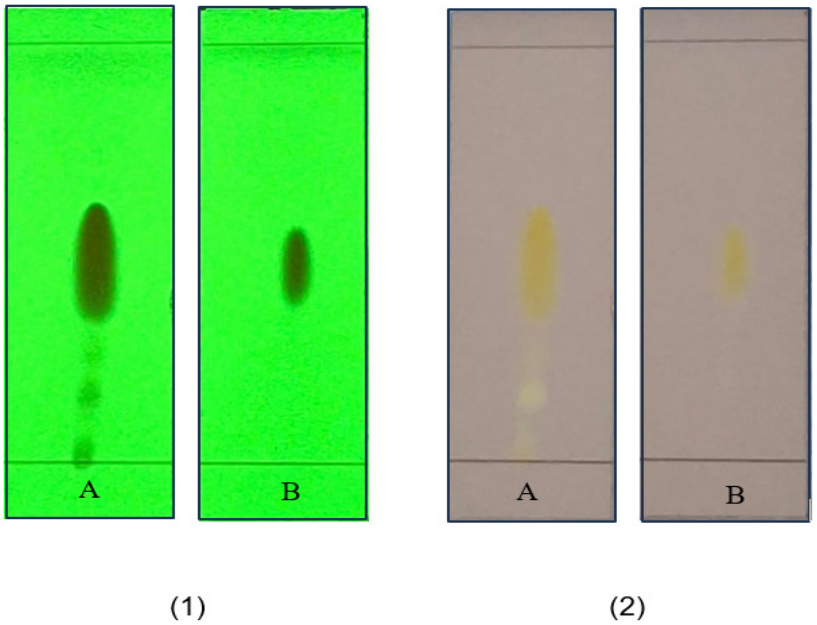

Figure 2. Visualization of TLC results of compounds before purification (A); after purification (B) viewed under UV lamps λ 254 (1) and λ 366 nm (2).

tandem Xevo TQS Micro mass spectrophotometer.

Procedures

General Method For Synthesis Of Amino Chalchone Derivatives (C1, C2 and C3)

Three target compounds of amino chalcone derivatives were designed as depicted in Figure 1 through the Claisen-Schmidt condensation reaction using NaOH 40% as base catalyst. The synthesis reaction was carried out using the stirring method. 2 mmol of 4'-amino acetophenone and 2 mmol of methoxy benzaldehyde (3-methoxy; 3,4-dimethoxy; 3,4,5-trimethoxy) were placed in a 50 mL Erlenmeyer flask, then 10 mL of absolute ethanol and 2-4 mL NaOH 40% were added and the reaction mixture was stirred at room temperature with a magnetic stirrer (speed 500 rpm) for 5-6 hours. The reaction progress was monitored by TLC using *n*-hexane: ethyl acetate (6:4) as mobile phase. Visualization method of TLC results of compounds using UV light at wavelengths of 254 and 366 nm. After the reaction was complete, 4 mL of cold aqua DM was added to the product mixture and the solution was neutralized with cold 6 N HCl gradually. The product mixture was then cooled until a precipitate formed. The precipitate formed was filtered with Whatman 40 filter paper, washed with cold aquadest and cold *n*-hexane, then allowed to dry to obtain the crude product of amino chalcone derivative compounds. For the purification of the compound was carried out through column chromatography using dichloromethane (DCM):*n*-hexane as mobile phase. The pure compound of amino chalcone derivatives (C1, C2 and C3) obtained was then weighed and its % yield was calculated. The purity and characterizations of compounds were carried out through using TLC, HPLC, melting point test, UV-Vis, FT-IR, MS, and ^{1}H-NMR.

In Vitro Antimalarial Activities Test

Antimalarial activity testing by inhibiting β-hematin polymerization in vitro by following the modified procedure of [25]. 90 µL of hemin solution was put into a 96-well plate then added the compounds **C1**, **C2**, **C3** and positive control that had been dissolved in 1 mL of DMSO, dilution was carried out with a concentration variant in the range of 50 - 350 ppm, each as much as 20 µL, then added 90 µL of Tween-20 to each well, homogenize the mixture in the well with a shaker. Incubate the sample at 37°C for 250 minutes. Perform absorbance measurements at wavelengths of 415 nm and 630 nm. The fraction of heme converted to β-hematin (f) was calculated by the following equation:

$$f = (A_{control} - A_{sample}) / (A_{control} - A_{min}) \quad \ldots\ldots\ldots\ldots (1)$$

where $A_{control}$ represents absorbance of the heme without Tween-20 and sample, A_{sample} is the absorbance of the heme in the presence of Tween 20 and sample, A_{min} is

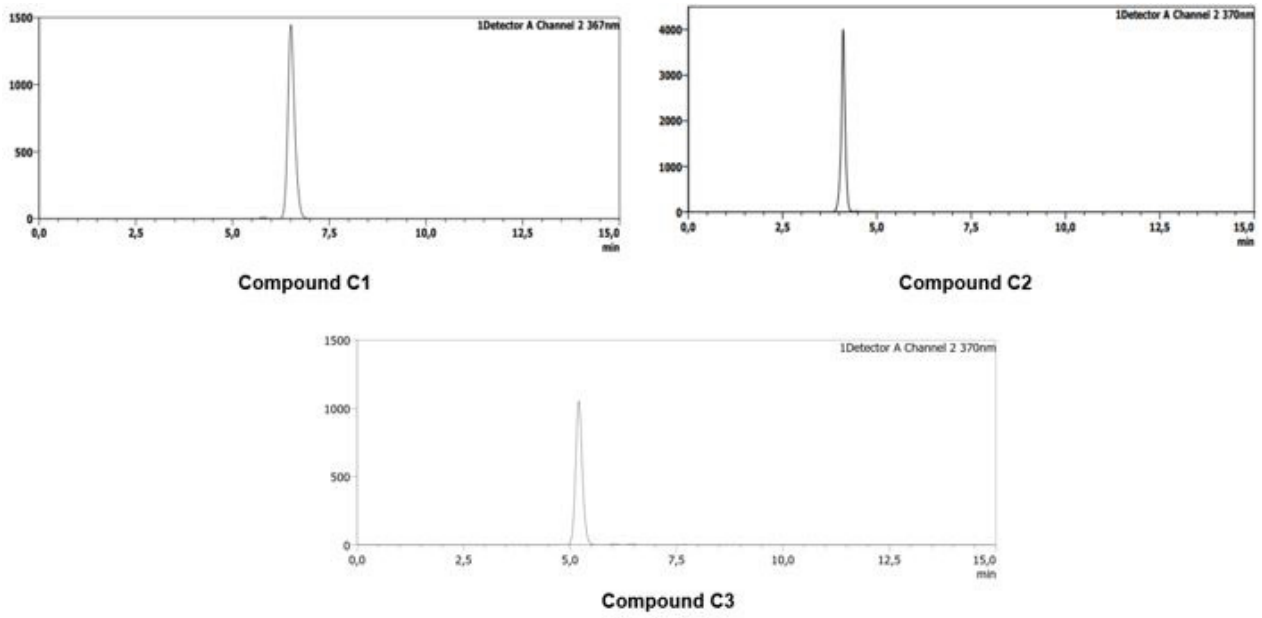

Figure 3. Chromatogram peak of the compounds C1, C2 and C3.

the absorbance of the heme in the presence of Tween 20 without sample.

The percentage of inhibition of β-hematin formation by the compound and positive control was calculated based on the equation:

% inhibition= (1-f) X 100% ……(2)

From the percentage inhibition value, the IC_{50} value of the compound is then measured using linear regression analysis.

Result and Discussion

Synthesis Compounds C1, C2 and C3

Chalcone derivative compounds 1-3 have been successfully synthesized and characterized. The result of the synthesis of C1 ((*E*)-1-(4-aminophenyl)-3-(3-methoxyphenyl) prop-2-en-1-one, molecular formula $C_{16}H_{15}NO_2$) was obtained as yellow solid with a synthesis yield crude product of 66.75 % yield. Melting point: 128-129℃. TLC analysis: R_f = 0.6 (*n*-hexane:ethyl acetate= 6:4). HPLC analysis showed a single peak at t_R = 6.507 minutes (isocratic elution, detector 367 nm). UV spectrum (in MeOH) was obtained at λ_{max} = 367 nm (absorbance= 0.535) and 251 nm (absorbance=0,320). FTIR: 3446, 3030, 2937-2960, 1643, 1579, 1255. ^{1}H-NMR (Bruker Avance Neo 500 MHz, DMSO-d_6) spectrum analysis shows 9 signals which are equivalent to 15 H atoms. These signals are found in the chemical shifts/ δ (ppm): 3,83 ppm (s, 3H, Ar-3-OCH_3); 6,15 ppm (s, 2H, -NH_2); 6,99 ppm (d, 2H, Ar-3',5'-H, *J*=3,95 Hz); 6,63 ppm (d, 1H, *J*=8,75 Hz); 7,37 ppm (m, 2H, Ar-2,6-H); 7,42 ppm (t, 1H, *J*=1,85 Hz); 7,58 ppm (d, 1Hα, *J*= 15,5 Hz); 7,86 ppm (d, 1Hβ, *J*= 15,5 Hz); 7,94 ppm (d, 2H, Ar-2',6'-H, *J*=8,7 Hz). HRMS (*m/z*) spectrum was calculated as $C_{16}H_{16}NO_2$ $[M+H]^+$ = 254.1181.

Compound C2 ((*E*)-1-(4-aminophenyl)-3-(3,4-dimethoxyphenyl) prop-2-en-1-one, molecular formula $C_{17}H_{17}NO_3$) was obtained as yellow solid with a synthesis yield crude product of 82.53 % yield. Melting point: 134-135℃. TLC analysis: R_f = 0.375 (*n*-hexane:ethyl acetate= 6:4). HPLC analysis showed a single peak at t_R = 4.104 minutes (isocratic elution, detector 370 nm). UV spectrum (in MeOH) was obtained at λ_{max} = 375 nm (absorbance of 0.648) and 255 nm (absorbance of 0.306). FTIR: 3443, 3006, 2914-2961, 1642, 1578, 1256. ^{1}H-NMR spectrum analysis shows 10 signals which are equivalent to 17 H atoms found in the chemical shifts/ δ (ppm): 3,80 ppm (s, 3H, Ar-4-OCH_3); 3,86 ppm (s, 3H, Ar-3-OCH_3); 6,10 ppm (s, 2H, -NH_2); 6,62 ppm (d, 2H, Ar-3',5'-H, *J*=8,7 Hz); 7,48 ppm (d, 1H, Ar-2-H, *J*=2 Hz); 7,31 ppm (dd, 1H, Ar-5-H, *J*=8,27 Hz,); 6,99 ppm (d, 1H, Ar-6-H, *J*=8,35 Hz); 7,57 ppm (d, 1Hα, *J*= 15,35 Hz); 7,57 ppm (d, 1Hβ, *J*= 15,5 Hz); 7,93 ppm (d, 2H, Ar-2',6'-H, *J*=8,7 Hz). HRMS (*m/z*) spectrum was calculated as $C_{16}H_{18}NO_3$ $[M+H]^+$ = 284.1294.

Table 1. IR data of compound C1, C2, C3.

Comp	Wave number of functional group (υ, cm^{-1})					
	C-H aromatic	C-H alifatic	C=C aromatic	C=O keton	C-O Eter	C-NH_2
C1	3030	1937-2960	1579	1643	1255	3446
C2	3006	2914-2961	1578	1642	1256	3443
C3	3013-3057	2973	1582	1632	1243	3443

Compound C3 ((*E*)-1-(4-aminophenyl)-3-(3,4,5-trimethoxyphenyl) prop-2-en-1-onemolecular formula $C_{18}H_{19}NO_4$) was obtained as yellow solid with a synthesis yield crude product of 79.76 % yield. Melting point: 154-155℃. TLC analysis: R_f = 0.35 (*n*-hexane:ethyl acetate= 6:4). HPLC analysis showed a single peak at t_R = 5.207 minutes (isocratic elution, detector 370 nm). UV spectrum (in MeOH) was obtained at λ_{max} = 370 nm (absorbance = 0.443) and 247 nm (absorbance = 0.234). FTIR: 3443, 3013-3057, 2973, 1632, 1582, 1243. ^{1}H-NMR spectrum analysis shows 8 signals which are equivalent to 19 H atoms found in the chemical shifts/ δ (ppm): 3,70 ppm (s, 3H, Ar-4-OCH_3); 3,86 ppm (s, 6H, Ar-3/5-OCH_3); 6,13 ppm (s, 2H, -NH_2); 6,63 ppm (d, 2H, Ar-3',5'-H, *J*=8,7 Hz); 7,16 ppm (s, 2H); 7,56 ppm (d, 1Hα, *J*= 15,4 Hz); 7,81 ppm (d, 1Hβ, *J*= 15,5 Hz); 7,94 ppm (d, 2H, Ar-2',6'-H, *J*=8,75 Hz). HRMS (*m/z*): was calculated as $C_{18}H_{20}NO_4$ $[M+H]^+$ = 314.1392.

Three amino chalcone derivative compounds (C1, C2 and C3) have been synthesised effectively utilising NaOH 40% as a base catalyst by the stirring method. The synthesis pathways of the three molecules are illustrated in Figure 1. Synthesis of compounds C1, C2 and C3 was carried out at room temperature by condensing 4'-amino acetophenone with benzaldehyde derivatives containing methoxy substituents at various locations and the number of methoxy. The synthesis resulted in a crude solid compound with a reasonably high yield ranging from 56% to 82%. The crude product of the amino chalcone analogue was purified using column chromatography. The purification process involved employing a mixture of *n*-hexane and DCM as the eluent, followed by a mixture of DCM and methanol as the mobile phase. Various comparison modifications were employed to separate the pure compounds. The purification process yielded pure compounds C1, C2 and C3 with a purity percentage ranging from 45% to 55%. The limited production of pure products in the synthesis of 4'-amino chalcone analogues is probably due to the creation of multiple unidentified by-products. The presence of these by-products is evident

Table 2. Interpretation of 1H-NMR spectroscopic data of compounds C1, C2, C3.

Atomic numbering	Chemical shift , δ_H (ppm)		
	C1	C2	C3
1	-	-	-
2	7.37 (m, 2H)	7.48 (d, 1H, J=2 Hz)	7.16 (s, 2H)
3	3.83 (s, 3H,-OCH3)	3.86 (s, 3H,-OCH_3)	3.86 (d, 3H,-OCH_3)
4	6.63 (d, 1H, J= 8,75 Hz)	3.80 (s, 3H,-OCH_3)	3.70 (d, 3H,-OCH_3)
5	7.42 (t, 1H, J= 1,85 Hz)	7.31 (dd, 1H, J= 8,27 Hz)	3.86 (d, 3H,-OCH_3)
6	7.37 (m, 2H)	6.99 (d, 1H, J= 8,35 Hz)	7.16 (s, 2H)
Hα	7.58 (d, 1H, J= 15,5 Hz)	7.57 (d, 1H, J= 15,35 Hz)	7.56 (d, 1H, J= 15,4 Hz)
Hβ	7.86 (d, 1H, J= 15,5 Hz)	7.75 (d, 1H, J= 15,5 Hz)	7.81 (d, 1H, J= 15,5 Hz)
1'	-	-	-
2'	7.94 (d, 2H, J= 8,7 Hz)	7.93 (d, 2H, J= 8,7 Hz)	7.94 (d, 2H, J= 8,75 Hz)
3'	6.99 (d, 2H, J= 3,95 Hz)	6.62 (d, 2H, J= 8,7 Hz)	6.63 (d, 2H, J= 8,7 Hz)
4'	6.15 (s, 2H,-NH_2)	6.10 (s, 2H,-NH_2)	6.13 (s, 2H,-NH_2)
5'	6.99 (d, 2H, J= 3,95 Hz)	6.62 (d, 2H, J= 8,7 Hz)	6.63 (d, 2H, J= 8,7 Hz)
6'	7.94 (d, 2H, J= 8,7 Hz)	7.93 (d, 2H, J= 8,7 Hz)	7.94 (d, 2H, J= 8,75 Hz)

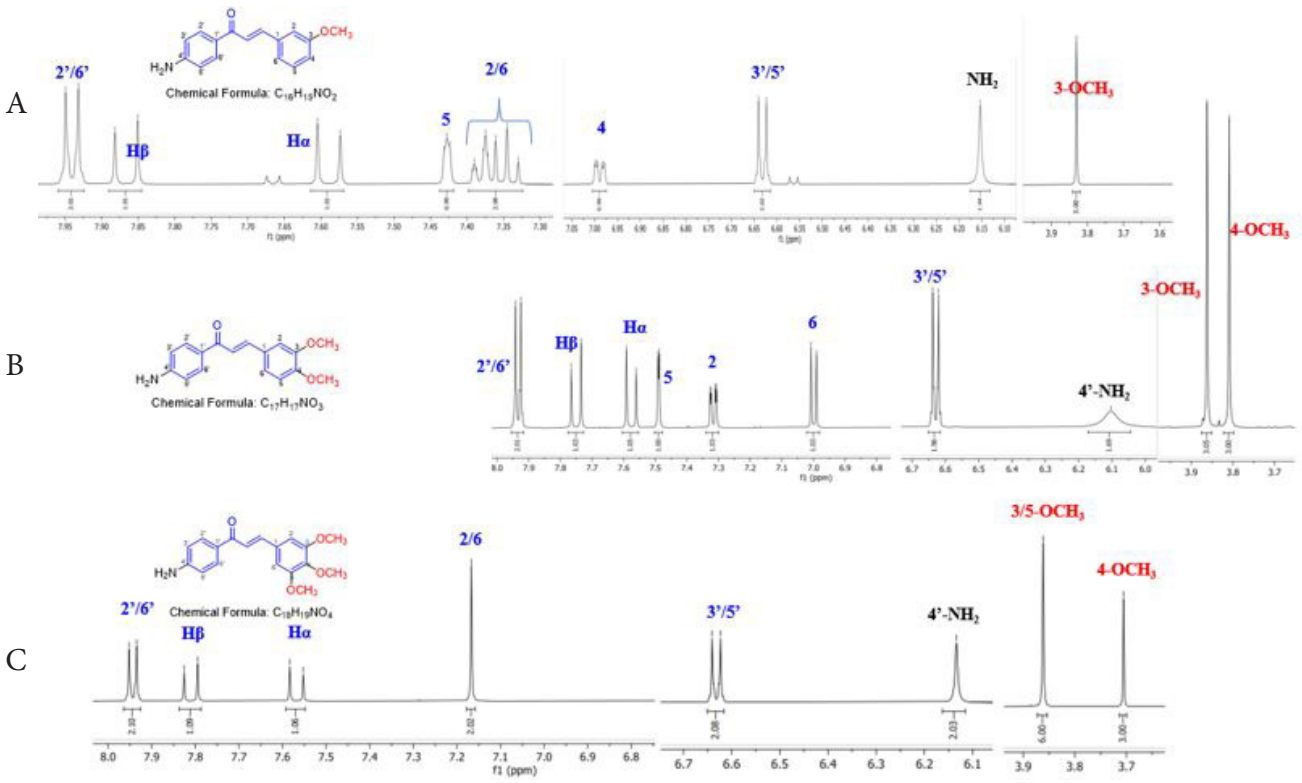

Figure 4. ^{1}H-NMR spectrum of 4'-aminochalcone analogs (C1-C3), (A) ^{1}H-NMR spectrum of compound C1, (B) ^{1}H-NMR spectrum of compound C2, (C) ^{1}H-NMR spectrum of compound C3.

from the TLC test results, which show other spots besides the desired product spots. As a consequence, not all of the intended chalcone analogue products are completely synthesised from the reaction mixture. The visualization results of the TLC profile of the compound before and after purification can be seen in Figure 2.

The purity determinations of compounds (C1, C2 and C3) was carried out by three measurements, using a silica gel GF_{254} TLC plate; analysis using HPLC and melting point measurement. The synthesized compound showed a single spot on the TLC plate eluted using *n*-hexane: ethyl acetate in 6:4 ratio as a mobile phase indicating that the compound was pure. Based on Figure 3, the purity of compounds (C1, C2 and C3) was also observed from the HPLC chromatogram results which showed one main peak, this indicates good purity of the three synthesized compounds. In the melting point measurement, it was found that the three compounds had a narrow melting point range (≤ 2 °C) which is a characteristic of pure compound solids [26]. The presence of impurities will affect the melting point of a compound, leading to a wider melting point range [27], so that the melting point of a compound can be used to tentatively identify pure compounds in solid form.

The confirmation of the structures of C1, C2, C3 were achieved through the utilisation of UV, FT-IR, H-NMR, and HRMS analysis. The UV-Vis spectrum of compounds exhibits absorption peaks at specific wavelengths, namely 367, 375, 370, 251, 255, and 247 nm. The absorption spectra of chalcone (flavonoid) compounds are characterised by two distinct bands. Band I, which occurs in the range of 300-400 nm, corresponds to the conjugated double bonds in the cinnamoyl conjugation system. Band II, on the other hand, falls within the range of 240-285 nm and is associated with the benzoyl conjugation system. [28]. The subsequent structural analysis involves the measurement of the FT-IR spectrum. By analysing the FT-IR spectrum data presented in Table 1, it is evident that the compounds exhibit similar characteristics, as indicated by the presence of absorption bands corresponding to aromatic C-H bonds, aliphatic C-H bonds, aromatic C=C bonds, conjugated C=O bonds, ether C-O bonds (methoxy), and amine C-N bonds. The identification of the ether C-O group (methoxy) in compounds C1, C2 and C3 is confirmed by the detection of absorption bands at wave numbers 1255, 1256, and 1243 cm-1 within the range of 1270-1230 cm-1 [29]. The presence of an amine group (NH_2) in the compound appears at wave numbers 3446

Table 3. In vitro antimalarial activities of compounds C1, C2, and C3.

No	Compounds	Concentration (µg/mL)	Inhibition of β-hematin (%)	IC_{50} (µg/mL)
1	C1	300	70.91	227.61
		250	59.02	
		200	42.36	
		150	23.59	
		100	11.36	
2	C2	150	71.33	115.18
		125	59.02	
		100	33.92	
		75	30.89	
		50	7.54	
3	C3	350	81.30	260.01
		300	66.62	
		250	46.58	
		200	26.73	
		150	10.59	
4	Positive Control (Hydroxychloroquine sulphate)	1000	99.68	184.98
		500	69.74	
		250	54.60	
		125	47.09	
		62.5	41.06	

and 3443 cm^{-1} (range 3500-3300 cm^{-1} based on [29]). The C=O ketone group in the three compounds is seen at wave numbers 1643, 1642 and 1632 cm^{-1} (range 1650-1600 cm^{-1} based on [29]).

Additional ^{1}H-NMR spectrum measurements were conducted on the compounds, as depicted in Figure 3, confirming the correct number of protons in the desired target molecular structure. Table 2 and Figure 4 presents the results of the ^{1}H-NMR spectrum analysis for the compounds C1, C2 and C3. The study revealed that compound 1 exhibited a total of fifteen protons, compound C2 exhibited a total of seventeen protons, and compound C3 exhibited a total of nineteen protons. The ^{1}H-NMR spectra three of compounds exhibited distinct signals corresponding to methoxy groups, with chemical shifts ranging from 3.70-3.86 ppm (s, 3H). Additionally, other characteristic signals indicated the presence of amino groups, with chemical shifts ranging from 6.10-6.15 ppm. The structure of C1, C2 and C3 exhibits an amino group that is detected as a singlet signal (2H) with a chemical shift of 6.10, 6.13, and 6.15 ppm, respectively. The general chalcone compounds exhibit α and β proton signals that appear as two doublet signals (1 H) with a trans proton configuration and a coupling constant of 15-16 Hz. [30]. In compounds C1, C2, C3, the Hα and Hβ signals appear at a coupling constants value (*J*) of 15.35-15.5 Hz. From all the characterizations above, it can be concluded that the three compounds were successfully synthesized and have a structure according to the target molecule.

Antimalarial Assay

In this study, the antimalarial activity was assessed by inhibiting heme polymerization using a modified version of the method from [25]. Compounds C1, C2 and C3, along with a positive control (hydroxychloroquine sulphate) at different concentrations, hemin chloride solution, and tween 20, were divided into control and sample groups. The mixtures were then incubated at a temperature of 37°C for a duration of 250 minutes. The absorbance was measured using a microplate reader at wavelengths of 415 and 630 nm. Hemin chloride and β-hematin crystals give different maximum absorbance [23]. Measurement at a wavelength of 415 is used to see the absorbance of hemin chloride, while a wavelength of 630 nm is used to see the maximum absorbance of β-hematin. The inhibition of heme polymerisation is quantified as the IC_{50} value, which is provided in Table 3. The study revealed that compound C2 exhibited a lower IC_{50} value (115.18 ppm) compared

to compound C1 (227.61 ppm), C3 (260.01 ppm), and the positive control (184.98 ppm). The variation in the ability to inhibit heme polymerisation observed in these findings is most likely attributed to the quantity and location of substituents attached to the test compound. It has never been reported in previous studies regarding this antimalarial test method in identifying the antimalarial bioactivity of chalcone compounds bound to methoxy and amino acids. The presence of two methoxy substituents attached to compound C2 results in distinct inhibition compared to the presence of one methoxy substituent and three methoxy substituents attached to the aromatic ring. Chalcone compounds exhibit a wide range of bioactivity. The bioactivity of chalcone compounds can vary due to the substituents attached to the aromatic ring and the presence of α,β-unsaturated carbonyl. [19]. The amine group bound to the compound also affects antimalarial activity. Most of the antimalarial drugs that are already on the market have an amine group (N). The amine group plays a role in antimalarial activity by forming electrostatic interactions with essential amino acids of Plasmodium falciparum [21].

Conclusion

A set of amino chalcone derivatives with varying amounts and positions of methoxy substituents were synthesised using the stirring method. These compounds have also been reported to exhibit in vitro antimalarial activity by inhibiting heme polymerisation. The compound C2, which is a chalcone with methoxy substitutions at positions 3 and 4 on the B ring, exhibited the highest antimalarial activity. These findings are applicable for additional investigation in the development and identification of potential antimalarial drugs.

Conflict of Interest

The authors declare no conflict of interest.

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