Synthesis and Anti-Inflammatory Activity of 1-(2,5-Dihydroxyphenyl)-3-Pyridine-2-Yl-Prophenone (AEW-1) Compound

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ABSTRACT

Chalcone compounds and some n-hydroxychalcone compounds exhibit anti-inflammatory activity. A chalcone derivative, 1-(2,5-dihydroxyphenyl)-3-pyridine-2-il-propenone showed a stronger bond to the COX-2 enzyme than 1-(2,4-dihydroxyphenyl)-3-pyridine-2-il-propenone, 2′,5′-dihydroxychalcone, 4-chloro-2′, 4'-dihydroxichalcone, and several NSAIDs when they were tested with molecular docking computation using MOE software. The result suggested that compound 1-(2,5-dihydroxyphenyl)-3-pyridine-2-il-propenone computationally has better anti-inflammatory activity. Synthesis of the compound was carried out by reacting 2,5-dihydroxyacetophenone and pyridincarbaldehyde (without solvent, K2CO3 catalyst) under microwave radiation (radiation strength of P6 41oC) within 4 minutes. The purification used ethanol washing: aquadest (10:90) and ethanol recrystallization. The structure of the synthesized compound was determined by mass spectroscopy, ultraviolet and visible (UV-Vis), infrared (IR), 1H-NMR, 13C-NMR, DEPT, and 2-dimensional NMR spectroscopy (HMHC, COSY, and HMBC). An anti-inflammatory activity test was performed using the rat foot edema method, which was induced by carrageenan. The structural elucidation showed that the compound synthesized was 1-(2,5-dihydroxyphenyl)-3-pyridine-2-il-propenone. The compound had a red color, a melting point of 190oC, and a purity of 94% by liquid chromatography. The percentage of % DAI of the synthesized compound was determined by mass spectroscopy, ultraviolet and visible (UV-Vis), infrared (IR), 1H-NMR, 13C-NMR, DEPT, and 2-dimensional NMR spectroscopy (HMHC, COSY, and HMBC). An anti-inflammatory activity test was performed using the rat foot edema method, which was induced by carrageenan. The structural elucidation showed that the compound synthesized was 1-(2,5-dihydroxyphenyl)-3-pyridine-2-il-propenone. The compound had a red color, a melting point of 190oC, and a purity of 94% by liquid chromatography.

Key words: chalcone, n-hydroxychalcone, microwave, K2CO3, anti-inflammatory

INTRODUCTION

The majority of countries including Indonesia use anti-inflammatory drugs, such as NSAIDs for symptoms related to arthritis (Soleha, et al., 2018). Non-selective NSAIDs which have a long T1/2 such as naproxen and piroxicam can cause hypertension, gastrointestinal bleeding, and heart failure if used for a long time at maximum doses (Tjay and Rahardja, 2015). Therefore, children and elderly people need special attention for having different metabolism compared to adults.

With the discovery of the compound 1-(2,5-dihydroxyphenyl) - (3-pyridine-2-il) -propenone, the higher anti-inflammatory effect is more preferable with fewer side effects than NSAIDs and thus the compound can be widely used in the community. Chalcone compound (A) is a C6C3C6 frame compound, where two aromatic rings are connected by three carbon atoms. The three connecting carbon atoms are reactive ketoe thylene (–CO-CH = CH-) groups. However, several studies have shown that modification of this group does not produce a better effect (Mandge et al., 2007). Pharmacological research on chalcone compounds and their derivatives shows that there is an anti-inflammatory activity through inhibiting COX-2 activity and some of them, in addition to inhibiting COX-2 activity, also have other anti-inflammatory mechanisms, namely inhibiting the
production of nitric oxide and TNF-α (Suzuki et al., 2005. Sogawa et al., 1993) tested various derivatives of 3’, 4’-dihydroxyxycalcaline which are potent in their action as inhibitors of 5-lipoxygenase and COX-2 enzymes.

The chalcone and n’-hydroxyxcalcaline compounds show their anti-inflammatory activities. The 2’-hydroxyxcalcaline compound was able to inhibit the production of prostaglandin E2 in RAW 264 cells by 60.32% (Dao et al., 2008). 4-chloro-2’, 4’-dihydroxyxcalcaline compounds showed the highest activity (68%) compared to other 2’, 4’-dihydroxyxcalcaline derivatives even higher than ibuprofen (53%) (Zhang et al., 2010). The compound 2’, 5’-dihydroxyxcalcaline has also been synthesized by Lin et al. (1997) and is proven as a potent COX inhibitor with IC50 of 37.5μM. In the same study, it was mentioned that this compound was better than the compound 2’, 4’-dihydroxyxcalcaline (IC50 = 280μM); 2’, 6’-dihydroxyxcalcaline (IC50 = 221μM); 4’-hydroxyxcalcaline (IC50 > 100μM); and 2’-hydroxyxcalcalone (IC > 100μM).

1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compound is a 2’, 5’-dihydroxyxcalcaline derivative in which the B ring is replaced by the 2-pyridine ring. Molecular docking test with MOE software against COX-2 enzyme showed the strongest bond interaction (-13.3162) compared to 1-(2,4-dihydroxyphenyl)-3-pyridine-2-il-propenone (-13.0570); 4-chloro-2’, 4’-dihydroxyxcalcalone (-12, 7338); 2’, 5’-dihydroxyxcalcalone (-12, 3194); mefenamic acid (-10, 9498), ibuprofen (10, 7394), naproxifen (-12, 3161), and aspirin (-10, 7311) (Wibowo, 2013).

The method of chalcone compound synthesis having more than one hydroxy group is usually carried out with the protection of a hydroxy group or acid catalyst. Hydroxy group protection methods require more types of reagents, three stages of synthesis, and are less economical (Patil et al., 2009; Jayapal et al., 2010). The purpose of this study is to synthesize 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compounds and test their anti-inflammatory activity.

**MATERIAL AND METHODS**

In this research, synthesis and testing of anti-inflammatory activity of 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compound were carried out. The synthesis was carried out by microwave radiation with K₂CO₃ catalyst and anti-inflammatory activity test through measurement of carrageenan-induced rat foot edema volume. This research is useful to provide information on the synthesis of chalcone-derived compound having more than one hydroxy group, namely 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone with microwave radiation which is more economical and efficient than the other methods and to find new compounds that have better anti-inflammatory activity than those already available on the market.

**Synthesis of 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone**

Zero point seventh five 0.75g (5mmol) of 2,5-dihydroxyacetophenone (E.Merck) and 0.69g of K₂CO₃ (Sigma) were mixed in the mortar until the mixture was homogeneous. 1mL (2mmol) of the pyridine-2-carbaldehyde (Sigma) was added, then the mixture was stirred in a mortar to form a brownish-yellow paste. The mixture was reacted with microwave radiation (Sigmatic SMO-20WGD) in power 6 (temperature equivalent to 41°C) for 4min. The reaction result was washed with cold ethanol: water (10:90) repeatedly. The solid was recrystallized from ethanol: water (90:10) and filtered. The melting point of the compound was determined by the Buchi instrument. Thin-layer chromatography (TLC) experiment was performed by using Silica Gel 60 GF254 (Merck) and mobile phase chloroform with detection by UV light. The structure elucidation was carried out by using 1H NMR, 13C NMR (JEOL DELTA 500MHz), and 2D-NMR method (DEPT, COSY, HMQC, and HMBC). IR spectrophotometry (Perkin-Elmer), and LC-MS (Shimadzu).

**Anti-inflammatory Activity Assay**

Anti-inflammatory activity assay was performed by volume measurement of carrageenan-induced rat paw edema (Chattopadhyay et al. (2012). The test animals were male white rats (Rattus norvegicus L.) 15 Wistar lines, 2 months old, and weighed between 140-200g which were obtained from the Integrated
Research and Testing Laboratory Pre-Clinical Research and Experimental Animal Development Services (LPPTLP3HP) UGM Yogyakarta. Anti-inflammatory activity testing was carried out based on a method by Wijaya (2012). The rats were divided into five groups (positive control, negative control, and three treated groups, each group contained six animals). The positive control was given ibuprofen 200mg/kg BW, the negative control was given 0.5% CMC-Na and the treatment groups were given the tested compounds at a dose of 200mg/kg BW. All compounds were suspended in 0.5% CMC-Na.

The tested compounds, ibuprofen, and 0.5% CMC-Na were injected into the rats orally an hour before 1% carrageenan-induced sub-plantar on the left paw. Rat paw edema volume measurement was performed every hour for 8h with a plethysmograph. Edema volume data were used to calculate the AUC to obtain the percentage of anti-inflammatory activity. Then, the results were analyzed by an independent t-test with a 95% confidence level to determine significant differences.

RESULT AND DISCUSSION

Synthesis of 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compound which used acid catalyst resulting from the reaction of thionyl chloride and ethanol at room temperature had been carried out. The attempt was unsuccessful in synthesizing the target compound because the acid condition was thought to affect the reactivity of pyridine-2-carbaldehyde so that it did not react with 2,5-dihydroxycacetophenone. Synthesis with ethanol solvent & base catalyst was not carried out because the base catalyst caused delocalization of anions from the starting material of 2,5-dihydroxycacetophenone (Jayapal et al., 2010).

Synthesis without solvents with microwave radiation catalyst of K₂CO₃ was considered to be a more profitable alternative because the technique is greener, economical, and only involves one reaction step. K₂CO₃ catalyst is a non-toxic, inexpensive, and easy to use catalyst (Srivastava, 2011). K₂CO₃ catalyst is a catalyst that is non-toxic, inexpensive, and easy to handle (Ravichandran et al., 2006). The optimization of reaction time was carried out by reacting a mixture of 2,5-dihydroxycacetophenone, pyridine-2-carbaldehyde, and K₂CO₃ in a P6 power microwave (temperature equivalent to 41°C) for 5min. The synthesis and mechanism reaction via aldol condensation (Figure 14).

The solid as a result of the reaction has the characteristics of a solid reddish-brown, sticky, and has a strong odor. The solid was titrated in chloroform: hexane (1:1) twice. This titration functions to remove the starting material 2,5-dihydroxycacetophenone. After being crushed, the solid was then washed using water several times until a dark red solid was obtained. Washing using water was carried out to remove the starting material of pyridine-2-carbaldehyde and K₂CO₃. The dark red solid was recrystallized from ethanol to give amorphous crystals. The yield obtained was 54%. The red solid is practically insoluble in water, rather difficult to dissolve in ethanol, and readily dissolves in DMSO.

The synthesis of 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compound using the microwave method was carried out by reacting the pyridine-2-carbaldehyde and 2,5-dihydroxyacetophenone without a solvent with K₂CO₃ catalyst in the microwave. The advantages of this method are shorter reaction time, easy handling, and no solvents required (Srivastava et al., 2011). K₂CO₃ catalyst is a catalyst that is non-toxic, inexpensive, and easy to handle (Srivastava, 2006). The optimization of reaction time was carried out by reacting a mixture of 2,5-dihydroxycacetophenone, pyridine-2-carbaldehyde, and K₂CO₃ in a P6 power microwave (temperature equivalent to 41°C) for 5min. The synthesis and mechanism reaction via aldol condensation (Figure 14).

Red crystals (Figure 2) have 190°C, with sharp melting points. Thin-layer chromatography (TLC) results showed the compound had one spot when eluted with three different mobile phases (Figure 3). The purity test with silica stationary phase TLC of Silica GF 254 showed one yellow spot at different mobile phases. The compound is confirmed to be pure by melting point and TLC tests.
Activity of 1-(2,5-Dihydroxyphenyl)-3-Pyridine-2-Yl-Propenone (AEW-1)

Figure 3. TLC results at three different mobile phases: Ethanol: hexane (2: 1) (A); chloroform (B); hexane: ethanol (10: 1) (C).

Figure 4. Liquid Chromatography profile of AEW-1.

Liquid Chromatogram (Figure 4) shows one sharp peak with a retention time of 2.1 min. The sample was run on C18 with mobile phase methanol: water (95:5) with a UV detector at 254 nm wavelength. The data provided information that the synthesized compound had a high purity (94%).

The mass spectrum of the red product suggests AEW-1 (MR 241) recorded by the Electro Spray Ionization (ESI) method of the positive ion model showed a high-intensity peak at m/z 242 (M+H)+ and a low-intensity peak at m/z 264 (M+Na)+ (Figure 5). 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone with the molecular formula C14H11O3N have molecular weights of 241 g/mol and have one nitrogen atom and therefore they follow the nitrogen rule where compounds that have an odd nitrogen atom have odd molecular weights. Thus, it can be seen that the molecular weight of the synthesized compound is the same as the molecular weight of 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone.

Figure 5. Mass spectrum of red product suggest AEW-1 (Mr 241) with Electro Spray ionization (ESI) method, positive ion mode. The spectrum showed m/z 242[M+H]+.

The UV-Vis spectrum of the compound synthesized (Figure 6) in ethanol (c=4.15 x 10-5 M; b = 1 cm) showed two absorption bands with a maximum wavelength (λmax) of 308.5 nm (ε=20.891) and 411.5 (ε=3.734). A total of 1 mg of compound (molecular weight 241) was dissolved in 10 mL of 95% ethanol. The absorbance measurement was performed after the solution was diluted 1:1000. It is in accordance with the structure of 1- (2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compound which has two benzoyl chromophore systems and 3-pyridine-2-il-acrylic.

Figure 6. (A) The UV-Vis spectrum of the synthesis compound. (B) Chromophore system of AEW-1

1-(2,5-dihydroxyphenyl)-3-pyridine-2-il-propenone has aromatic rings (phenyl and pyridyl) connected with conjugated carbonyl α, β. The compound also has a hydroxyl (OH) group attached to the phenyl ring at the positions of 2 and 5. The IR spectrum of the synthesized compound (Figure 7) shows a wide absorption band of OH at wave number 3412 cm⁻¹.

Figure 7. IR spectrum of the synthesized compound of AEW-1
The existence of this OH group is also strengthened by the presence of the C-O band at 1285 cm\(^{-1}\). Bands with weak intensity at around 3057 cm\(^{-1}\) are aromatic or olefinic C-H stretching vibrations. The band that appears at 1651 cm\(^{-1}\) corresponds to the absorption conjugated carbonyl ketone band. Normal ketones generally appear at 1715 cm\(^{-1}\) (Fleming et al., 1996). The existence of conjugation will shift the absorption band of the carbonyl ketone to the lower wavenumber. The bands that appear in 1587 cm\(^{-1}\) and 1491 cm\(^{-1}\) are characteristic of the aromatic vibrational range of C=C bonds. The IR data shows the suitability of the functional group of the synthesized compound with that of the 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compound.
Figure 9. C-NMR spektrum

Figure 10. The COZY spectrum
The identification of the synthesis results was performed by one-dimensional NMR spectroscopy (1H-NMR, 13C-NMR, DEPT) and two dimensional NMR (HMBC, COZY, and HMQC). The 1H-NMR spectrum (Figure 8) shows 11 proton resonance peaks with an integral of one hydrogen each corresponding to the number of hydrogen atoms of 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)propenone. Two resonant signals in the form of a slightly widening singlet appear at δ 11.42 and 9.25 respectively representing hydroxy protons (OH) at the positions of 2' and 5' ring A (Benzene). Hydroxy protons at the position of 2' appear at a higher chemical shift than at the position 5' due to the intramolecular hydrogen bonding between the hydroxy proton and the carbonyl group. The existence of hydrogen bonds will make these protons become increasingly unprotected (unshielded).

The signal in the form of a doublet with a coupling constant (J) of 8.45 Hz at 6.86 is a resonant benzene proton (ring A) at the position of 3' (H3') which holds an ortho coupling with H4'. Meanwhile, the doublet (J = 2.60 Hz) at δ 7.35 is an H6 'resonance signal which holds a meta coupling with H4'. Signal H4' appears at δ 7.02 in the form of doublet of doublets (J = 8.45 and 2.60 Hz) due to an ortho coupling with H3' and a meta coupling with H6'. A doublet (J = 4.55 Hz) that appears at δ 8.69 is a pyridine ring proton resonance signal at the position of 3'' (H3'') which makes a coupling with H4''. The doublet signal looks broad because the proton is expected to also hold a coupling with H5'' with a smaller constant coupling (meta coupling). Signals that are quite complex (doublet of doublets = ddd) at δ 7.45 are derived from H4''.

This proton holds an ortho coupling with H3'' (J = 4.55 Hz) and with H5'' (J = 7.15 Hz). It holds a meta coupling with H6'' (J = 1.30 Hz). The signal in the form of a triplet of doublets (td) at δ 7.90 with a coupling constant (J) of 7.15 and 1.3 Hz is a resonance of H5''. The reason is that because it holds an ortho coupling with H4'' and H6'' with a coupling constant that the same as holding a meta coupling with H3''. The signal in the form of a doublet that widens at 7.85 is an H6 resonance that holds an ortho coupling with H5 (J = 7.15 Hz), and it is also possible to hold a meta coupling with H4'' (overlapping). Two doublets at δ 8.16 Hz and 7.74 Hz are respectively the olefinic proton resonance signals 2 and 3 in the α, β-unsaturated carbonyl structure that connects the benzene ring at position1' and pyridine ring at the position of 1''. Both doublets have a coupling constant of 15.55Hz which indicates that the double bond has a trans configuration (Fleming et al., 1996). From the 1H-NMR spectrum, it can be concluded that the compound has 2 phenolic hydroxyl (OH) protons, 4 pyridine protons, 3 benzene protons, and 2 conjugated alkene protons in accordance with the structure of 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone.

The 13C-NMR spectrum (Figure 9, A) shows 14 resonance peaks of carbon atoms, of which 9 are carbon methane (CH) as shown in the DEPT 900 spectrum (Figure 9, B). In the 13C-NMR spectrum, the signal that appears most downfield at δ 192.8 is the resonance of the conjugated ketone carbonyl group (C1). The signal at δ 150.1; 125.0; 137.3; and 125.5 respectively represent carbon resonance at positions 3', 4', 5'', and 6'' pyridine ring, while signals 118, 15; 124.4; and 114.5 are benzene carbon at the positions of 3', 4', and 6'. Olefinic carbon 2 and 3 respectively appear at δ 125.7 and 142.7. The suitability of carbon with the proton binds can be seen in the HMCO spectrum (Figure 12).

The COZY spectrum (Figure 10) shows the correlation between protons - protons in the molecule reinforcing the truth that the structure of compounds 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone exists. In this spectrum, there is a cross-peak between the signals H3'' and H4'', H4'' with H5'', and H5'' with H6 '' in the pyridine ring. The correlation between benzene protons is shown by the cross-peak between the resonance of signals H3' with H4' and H4' with H6'. The spectrum also shows a correlation between olefinic protons 2 and 3.

Further confirmation of the 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone structure is carried out based on HMBC spectrum data (Figure 11). Proton H3'' correlates with C4'', C1'', and C5''; H4'' with C3'' and C6''; H5'' with C1'' and C3''; while H6'' with C1'', C4'', and C3. The correlation between H2 with C= O and C3 and H3 with C2 and C1'' confirms the presence of the unsaturated carbonyl α, β structure, where C3 is bound to the C1'' pyridine ring. In the HMBC spectrum, it is also seen that H3' is correlated with C4' and C1'; H4' with C3', C5', C2' and C6'; H6' with C5', C2', C4', and C = O. The 1H-13C correlation does not only confirm the presence of three benzene protons in the positions of 3', 4' and 6', but it also provides information on the connection between C1' benzene and C=O. Proton 2'-OH appears to correlate with C1 'and C3', while 5'-OH correlates with C4' and C6'.
Figure 11. HMBC spectrum

Figure 12. HMQC spectrum
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Table I. Spectra H NMR, 13 NMR, DEPT, COSY, HMBC

| C/H | δC (ppm) (DEPT) | δH (ppm) (nH; J Hz) | COSY | 1H-13C HMBC |
|-----|----------------|---------------------|------|-------------|
| Ketone | 192.8 (Cq) | - | - | - |
| A | 125.7 (CH) | 8.16 (1H; d; 15.15) | Hβ Ketone, β | C1 |
| B | 142.7 (CH) | 7.74 (1H; d; 15.15) | Ha C1, α Ketone |
| 1 | 152.5 (Cq) | - | - | - |
| 2 (N) | - | - | - | - |
| 3 | 150.1 (CH) | 8.68 (1H; dd; 4.55; -) | H4 C4, C1, 5 |
| 4 | 125.0 (CH) | 7.45 (1H; dd; 6.8; 4.55; 1.3) | H3/H5 C3 C6 |
| 5 | 137.3 (CH) | 7.90 (1H; dt; 7.7; 1.3) | H4 C1, 3 |
| 6 | 125.5 (CH) | 7.85 (1H; dd; 7.75; -) | - C1 Cβ, 4 |
| 1′ | 121.4 (Cq) | - | - | - |
| 2′-OH | 149.6 (Cq) | 11.4165 (1H; s) | - C1′, 3′ - |
| 3′ | 118.5 (CH) | 6.86 (1H; d; 8.45) | H4′ C4′ C1′ |
| 4′ | 124.4 (CH) | 7.02 (1H; dd; 8.45; 2.6) | H3′/H6′ C5′, 3′ C6′, 2′ |
| 5′-OH | 154.1 (Cq) | 9.2478 (1H; s) | - C4′, 6′ - |
| 6′ | 114.5 (CH) | 7.35 (1H; d; 3.25) | H4′ C5′ C4′, 2′, ketone |

Table II. NMR spectra data 1- (2,5-dihydroxyphenyl) - (3-pyridine-2-il) -propenone

| C/H | δC (ppm) (DEPT) | δH (ppm) (nH; J Hz) | COSY | 1H-13C HMBC |
|-----|----------------|---------------------|------|-------------|
| 1 | 152.5 (Cq) | - | - | - |
| 2 (N) | - | - | - | - |
| 3 | 150.1 (CH) | 8.68 (1H; dd; 4.55; -) | H4 C4, C1, 5 |
| 4 | 125.0 (CH) | 7.45 (1H; dd; 6.8; 4.55; 1.3) | H3/H5 C3 C6 |
| 5 | 137.3 (CH) | 7.90 (1H; dt; 7.7; 1.3) | H4 C1, 3 |
| 6 | 125.5 (CH) | 7.85 (1H; dd; 7.75; -) | - C1 Cβ, 4 |
| 1′ | 121.4 (Cq) | - | - | - |
| 2′ | 149.6 (Cq) | - | - | - |
| 3′ | 118.5 (CH) | 6.86 (1H; d; 8.45) | H4′ C4′ C1′ |
| 4′ | 124.4 (CH) | 7.02 (1H; dd; 8.45; 2.6) | H3′/H6′ C5′, 3′ C6′, 2′ |
| 5′ | 154.1 (Cq) | - | - | - |
| 6′ | 114.5 (CH) | 7.35 (1H; d; 3.25) | H4′ C5′ C4′, 6′, C2′, C6′ |
| C=O | 192.8 (Cq) | - | - | - |
| α | 125.7 (CH) | 8.16 (1H; d; 15.15) | Hβ C=O, Cβ C1 |
| β | 142.7 (CH) | 7.74 (1H; d; 15.15) | Ha C1, Ca C=O |
| 2′-OH | - | 11.42 (1H; s) | - C1′, 3′ - |
| 5′-OH | - | 9.25 (1H; s) | - C4′, C6′ |

δC = quarterary carbon, J = Coupling constant, nH = number of protons

All 1H-13C correlations as far as two (2J) or three (3J) bonds in the spectrum (Table I and Figure 12). Based on the analysis of all spectra above as a whole (Table II), it can be concluded that the synthesized compound is 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone.

The synthesized compound has been shown to be 1- (2,5-dihydroxyphenyl) - (3-pyridine-2-il) -propenone compound. To determine the anti-inflammatory activity of this compound, an in vivo anti-inflammatory activity test was carried out by measuring the volume of carrageenan-induced rat foot edema. This method is often used for acute anti-inflammatory testing. The dosage of the compound 1- (2,5-dihydroxyphenyl) - (3-pyridine-2-il) -propenone is 200mg/kg given one hour orally before the sub-plantar injection of 1% carrageenan suspension.
Anti-inflammatory power is measured by Area Under Curve (AUC) of edema volume reduction in the minutes of 0 to 240 after injection of carrageenan versus time. The smaller the AUC value is, the lower the edema is. The negative control group (solution of 0, 5% Na-CMC) has the greatest AUC value considered as uninhibited edema. Both the positive control group of ibuprofen and the treatment group of the compound of 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone (200 mg/kgBW).
pyridine-2-il) propenone showed a smaller AUC value compared to the AUC value of the negative control group.

The AUC data were used to calculate the percentage of anti-inflammatory activity (% DAI) of ibuprofen and 1- (2,5-dihydroxiphenyl) - (3-pyridine-2-il) - propenone. The greater the value of % DAI, the greater the effect of inhibiting edema on rat feet, and the lower the value the smaller the inhibitory effect. The results of the independent T-test between the positive control group for ibuprofen and the treatment group for compound 1- (2,5-dihydroxiphenyl) - (3-pyridine-2-yl) - propenone showed a significance value (2-tailed) of 0.552 (p>0.05 ). This shows that ibuprofen and 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il) propenone have insignificantly different activity anti-inflammatory. Ibuprofen is able to inhibit inflammation with a DAI percentage of 57.22±20.134 while 1-(2,5-dihydroxifenyl)-(3-pyridine-2-il)-propenone has a DAI percentage of 50.05±16.244.

CONCLUSION
The 1-(2,5-dihydroxyphenyl)-(3-pyridine-2-il)-propenone compounds were successfully synthesized from 2,5-dihydroxyacetophenone and pyridine-2-carbaldehyde using the microwave radiation method and K2CO3 catalyst. The compound has an anti-inflammatory activity of 50.05±16.244% and is not significantly different from the anti-inflammatory activity of ibuprofen (57.22±20.134%) in male carrageen-induced rats.

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