SYNTHESIS OF CINNAMIC ACID BASED ON PERKIN REACTION USING SONOCHEMICAL METHOD AND ITS POTENTIAL AS PHOTOPROTECTIVE AGENT

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SYNTHESIS OF CINNAMIC ACID BASED ON PERKIN REACTION USING SONOCHEMICAL METHOD AND ITS POTENTIAL AS PHOTOPROTECTIVE AGENT

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ABSTRACT

Cinnamic acid plays a vital role in the synthesis of other important compounds and as a precursor for the synthesis of commercial cinnamon esters used in perfumery, cosmetics, and pharmaceutical industries. The aim of this research is to synthesize cinnamic acid using sonochemical methods. Cinnamic acid was synthesized using Perkin reaction by reacting 0.05 mole of benzaldehyde with 0.073 mole of acetic acid anhydride and 0.03 mole of sodium acetate as catalyst in the Erlenmeyer flask and then the mixture was put in a sonicator for 60 minutes at 70 °C. The synthesized compound was tested organoleptic properties, and the melting point was measured. The chemical structure was elucidated using FT-IR, H-NMR, and ^{13}C-NMR. The photoprotective activity was examined from its antioxidant and SPF values. The synthesized compound was found in the form of a shiny white fine crystal which had distinctive odor with a yield of 4.98% and the melting point was found at 133 °C. In the structure elucidation using FT-IR (the aromatic ring absorption at the wave number 1580 cm^{-1} - 1600 cm^{-1}. The wave number 1625 $cm^{-1}$is an aromatic conjugated alkene group, while wave number 1689.4 cm^{-1} is a carbonyl group. The wave number 2500 cm^{-1} – 3250 cm^{-1} is an OH carboxylic acid group) , H-NMR (7.410 (*m*, 5H, Ar-H); 7.425(*t*, 1H); 7.572 (*d*, 1H); 8.057 (d, 1H,C=CH) and ^{13}C-NMR (129.309 ppm; 130.998 ppm; 134.58 ppm; 170.017 ppm) showed that when compared with the standard compound as the reference, the synthesized compound was confirmed to be cinnamic acid. The antioxidant activity test showed that at the concentration of 20 ppm the synthesized compound was able to reduce free radicals by 46.69%. This finding showed that the synthesized compound had antioxidant activity.

Keywords: *Cinnamic acid, Perkin Reaction, Photoprotective, Sonochemistry, Structure elucidation*

INTRODUCTION

Cinnamic acids compose a relatively large family of organic. The cinnamic acids are used in macromolecular synthesis as very important building blocks for various classes of polymers, having attractive properties, especially a high photoreactivity due to the presence, in the main or side chains, of the cinnamoyl group, well known as photoresponsive unit. In Pharmaceutical industries, they are used as parfume that have have antibacterial, antifungal and antiparasitical activities [1].

Cinnamic acid belongs to the group of aromatic carboxylic acids with a C6-C3 structure. This compound is naturally found

in plants [2] The biochemical process produces lignin into plant cell walls [3] Cinnamic acid is formed in the biosynthetic pathway leading to phenylpropanoids, coumarins, lignin, isoflavonoids, flavonoids, stilbene, auron, anthocyanins, spermidine and tannin [4] Cinnamic acid is an organic acid which has low toxicity, has extensive biological activity, has several active compounds that can be derivatized to new compounds, and can be developed into new drug compounds. Many derivatives of cinnamic acid have health benefits as antioxidants and free radical scavengers. Derivatives of cinnamic acid also have anti- bacterial, antiviral, and anti-fungal properties [5]

Cinnamic acid is easily obtained by Perkin synthesis using benzaldehyde in acetic acid anhydride in the presence of weak bases such as acetate salts from alkali metals [6-7]. Perkin reaction is the method most frequently used for the synthesis of cinnamic acid and its derivatives . But the main shortcoming of this method is the reactions of aldehydes in the basic environment results in side products. Moreover, this reaction requires a long time between 4-10 hours in high temperatures [6].

Sonochemistry is becoming increasingly important for various organic synthesis reactions, by utilizing ultrasonic waves as an energy source to produce radicals and start the process of electron transfer, to affect the rate of chemical reactions and the yield. Various types of ultrasonic wave-assisted organic synthesis reactions have been reported such as synthesis of thiodiazole [8], N- alkilbenzimidaxole [9], and arylthioamide [10]. Sonochemistry has also been used for condensation reactions, such as synthesis of chalcones using Claisen condensation[11] and in Knoevenagel condensation for synthesizing coumarins [12]. Sonochemistry has also been successfully applied to reactions in aqueous media [13] Cinnamic acid and its derivatives show high antioxidant activity, due to the presence of vinyl groups in it. However, the antioxidant activity is strongly influenced by the presence of substituents in various positions in the aromatic core. [14]. Cinnamic acid can be used as a sunscreen. Hammer, in 1891, created the first sunscreen in history, using benzyl salicylate class, a derivative of p-amino benzoic acid, cinnamic acid, and benzophenon [15]. Cinnamic acid and its derivatives are a class of active sunscreen substances. This group of compounds has chromophore groups which absorb ultraviolet radiation. The photoprotective activity of plant extracts and isolated compounds is evaluated through many reports and research, which shows that there is a correlation between photoprotective activity and antioxidant activity. This is something that is especially interesting for the cosmetics industries for its usage in sunscreens, such as the flavonoids and cinnamic acid derivatives. [15]. Based on these descriptions, this study seeks to develop a simple sonochemical approach to the synthesis of cinnamic acid and its potential as a photoprotectives.

METHODS

1. Instrumentation

The equipments and instruments used in this study werere glasswares, analytical

balance, plastic basin, sonicator, FT-IR spectrometer (Agilent technologies), H-NMR and C-NMR spectroscopes, melting point apparatus, sets of distillation apparatus, Buchner funnel, and silica TLC plates.

2. Materials

The materials used in this study were benzaldehyde (pa), acetic acid anhydride (pa), sodium acetate (pa), concentrated hydrochloric acid, ethanol, and sodium bicarbonate.

3. Cinnamic acid synthesis

The cinnamic acid synthesis used the procedure based on [7] with slight modification. 0.05 mole of benzaldehyde was reacted with 0.073 mole of acetic acid anhydride with 0.03 mole of sodium acetate as a catalyst in the Erlenmeyer flask and put in a sonicator with varied temperatures and time.

The reaction was monitored by TLC to find out the endpoint of the reaction. To separate cinnamic acid, the reaction mixture was added with 25 mL of distilled water in a round bottom flask, then a saturated sodium bicarbonate solution was added until it reached basic pH. The solution was then distilled until there is no benzaldehyde found in the mixture. The residue obtained was cooled and then filtered with a vacuum pump. The filtrate was acidified by adding concentrated hydrochloric acid slowly with stirring. After the mixture was cold, the cinnamic acid solid then was filtered with a vacuum pump and rinsed with distilled water. The solids obtained were recrystallized using a mixture of distilled water: ethanol in 3:1. The melting point of the obtained compound was tested using melting point apparatus. The structure of the compound then was elucidated using IR and H-NMR and C-NMR spectroscopy.

4. Antioxidant activity test

The antioxidant activity of the synthesized cinnamic acid was determined using DPPH (1,1-diphenyl-1-1- picrylhydrazyl) according to the method in [8] with slight modification. The synthesized cinnamic acid was dissolved in ethanol in the concentration of 1000 ppm, From this solution, a series of solutions were made in the concentration of 20 ppm, 40 ppm, 60 ppm, 80 ppm, and 100 ppm. From each series of solution, 1 mL was taken and were added with 1 mL of 0.1 mM DPPH (1,1- diphenyl-1-1-picrylhydrazyl) solution. The mixture was incubated for 30 minutes in a dark room and its absorbance was measured at 515 nm. The blanks were measured at the same wavelength as the sample by removing the sample from the measurement. The positive control used was a routine standard solution with a concentration of 2-10 ppm. Absorbance obtained from measurements was analyzed by the percentage of antioxidant activity using equation 1.

$$\%inhibition = \frac{A_{blank} - A_{smpl}}{A_{blank}} x\ 100\% \qquad (1)$$

5 µg/ml to 30 µg/ml. Then the absorbance was measured at 200 nm to 400 nm. [17]. Measurements were taken 3 times and the SPF . The data obtained then were made into a linear regression equation which states the relationship between the concentrations of the tested compound (x) with the percentage of the antioxidant

activities. From the linear regression equation, IC50 value of the sample will be known, which is the value describing the concentration of the tested compound which was able to capture 50% of DPPH (2,2-difenil-1-pikrilhidrazil) free radicals [16].

5. Photoprotective activity test

The determination of photoprotective activity was done by determining the in vitro SPF value using spectrophotometric methods. The synthesized compound is dissolved in ethanol with concentration from value was calculated based on the Mansur equation [18].

$$SPF = CF \times \sum_{290}^{320} EE\ (\lambda) \times I\ (\lambda) \times Abs\ (\lambda) \qquad (2)$$

SPF : Sun Protection Factor, EE : Erythema effect spektrum, Abs : Absorbance, CF : Correction factor (10). The value of EE x I is a constant that shows the value of wavelengths from 290 to 320 nm and in the scale of 5 nm [18].

RESULTS AND DISCUSSION

The synthesis of cinnamic acid in this study was based on the Perkin reaction between benzaldehyde and acetic acid anhydride using anhydrous sodium acetate as the catalyst [6-7] Perkin reaction occurs through aldol condensation between benzaldehyde and acetic anhydride in the presence of sodium acetate salt which acts as a catalyst [1] to accelerate the course of the reaction. The Perkin reaction can be seen in Figure 1.

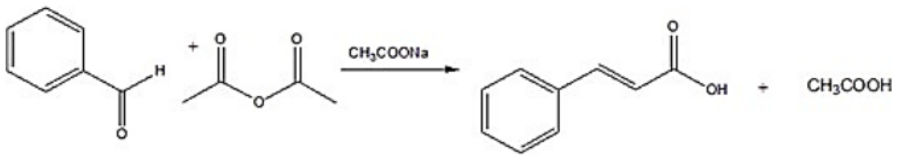

Figure 1. Synthesis of cinnamic acid through Perkin reaction

Condensation occurs between the carbonyl group of benzaldehyde and the activated methyl group of acetic anhydride. The activation of the methyl group as nucleophilic is carried out by the addition of a basic catalyst [6].

The use of sonochemical methods in organic synthesis offers a shorter reaction time, higher yield [9], and it's more environmentally friendly because it minimizes waste and energy use [10]. Ultrasonic wave assisted synthesis of cinnamic acid required 60 minutes of contact time at 70°C. The compound obtained then was crystallized using cold water to form fine crystals. The synthesized compound obtained has a yield of 4.98%.The yield of 4.98% is greater than the amount of cinnamic acid obtained from cinnamon bark isolation, which is 2.20% yield [19]. Factors that influence the small yield produced was the use of anhydrous sodium acetate catalyst. Aldehydes in the presence of bases will produce undesirable side products [6]. From this study, the use of anhydrous sodium acetate as a catalyst can be concluded to be less effective. For future research, it is better to use another acetate salt catalyst, for example potassium acetate [1].

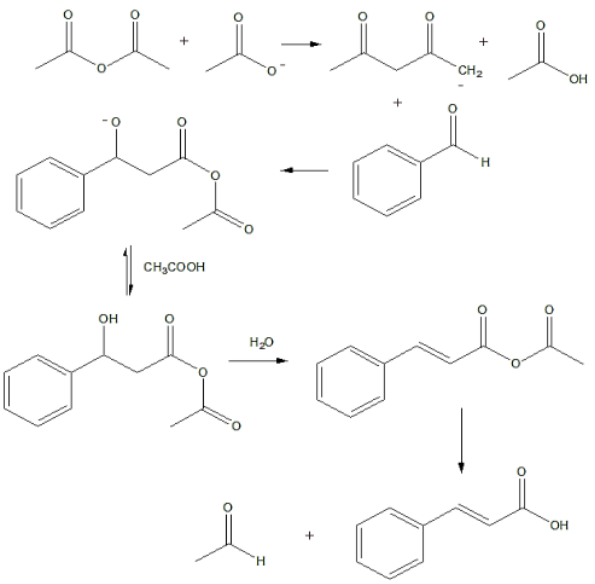

Figure 2. Cinnamic acid synthesis mechanism

Organoleptic test results showed that the compound produced was in the form of a fine shiny white crystal with a characteristic odor. When compared with the cinnamic acid standard, the synthesized compound had the same melting point of 133°C. The result of structure elucidation using FT-IR spectrophotometry can be seen in Figure 3.

The FT-IR spectrum resulting from synthesis and cinnamic acid standard shows the aromatic ring absorption at the wave number 1580 cm^{-1} – 1600 cm-1. The wave number 1625 cm^{-1} is an aromatic conjugated alkene group, while wave number 1689.4

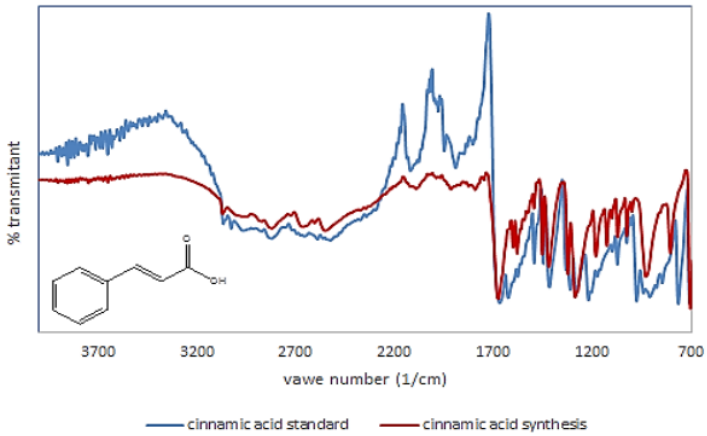

Figure 3. The IR spectrum of the synthesized compound

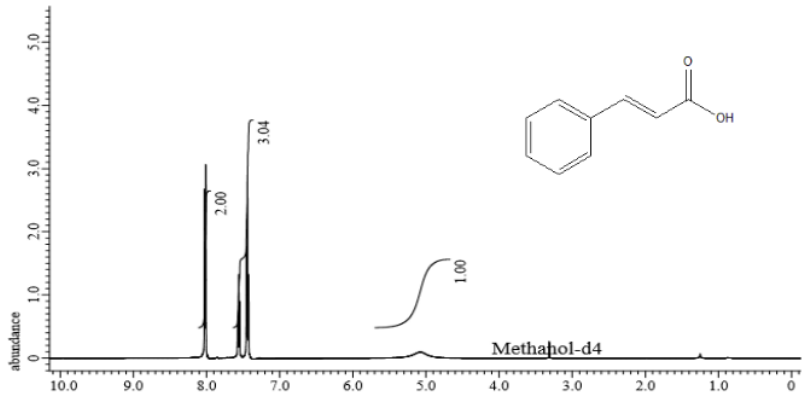

Figure 4. The H-NMR spectra of the synthesized compound

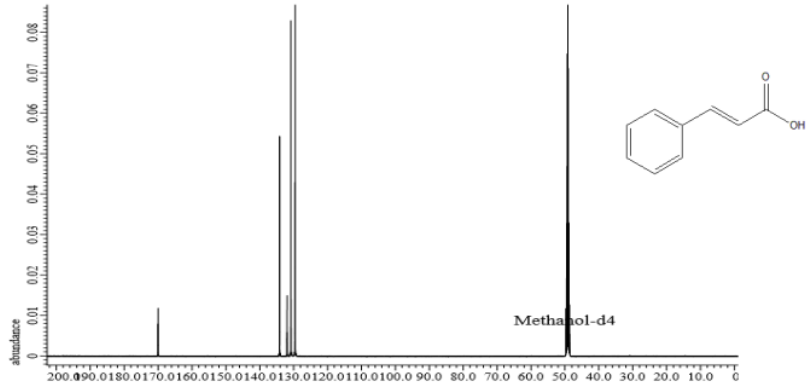

Figure 5. The ^{13}C-NMR spectra of the synthesized compound

The results of the 1H-NMR and ^{13}C-NMR spectroscopy of the synthesized compound in methanol can be seen in Figure 4 and Figure 5. The NMR spectra showed that there were chemical shifts. The 1H-NMR spectra (Metanol,δ ppm) was found at 7,410 (m, 5H, Ar-H); 7,425(t, 1H); 7,572 (d, 1H); 8,057 (d, 1H,C=CH)[20]; and spectra ^{13}C-NMR on 129,309 ppm; 130,998 ppm; 134,58 ppm; 170,017 ppm. The ^{1}H- NMR and ^{13}C-NMR spectra of cinnamic acid above show some peaks in chemical shifts in the area δH = 7.42 - 7.57 ppm which indicates the presence of protons of aromatic compounds and was reinforced with the area of δC =134.2 - 128.6 ppm and the doublet signal on the area around δH = 6.49 & 7.58 ppm. The position of carbon and proton showed that the synthesized compound was cinnamic acid.

The photoprotective activity of synthesized compounds was measured using visible spectrophotometry. This activity was seen from its antioxidant properties and SPF value. The principle of this method is the capture of hydrogen from antioxidants by free radical DPPH. The occurring mechanism is the reaction of hydrogen capture from anti-oxidants by the purple free radical DPPH (1,1-

diphenyl-1-picrylhydrazyl) which is changed to yellow DPPH (1,1- diphenyl-1-1-picrylhydrazyl). The color fading results in decrease of the absorbance.

Color changes which occured in the reaction between DPPH and antioxidants Ade Measures Bay visible spectrophotometry at its maximum wavelength. In this study, the maximum wavelength of DPPH (1,1-diphenyl -1-1- picrylhydrazyl) was obtained at 516 nm. The results of antioxidant activity tests on the synthesized compounds showed that at a concentration of 20 ppm the sample was able to reduce free radicals by 46.69%. From these results it could be concluded that the synthesized compounds could function as antioxidants.

Determination of sunscreen activity was done by determining the SPF value in vitro by the spectrophotometric method. The results of the SPF test found that at a concentration of 800 ppm, the obtained SPF value was 1.33. This shows that there is a need for further purification of the synthesized compound to then be retested its Photo-protective ability.

CONCLUSIONS

In this research cinnamic acid was able to be synthesized through Perkin reaction using sonochemical methods. The Photo-protective activity test showed that the synthesized compound at the concentration of 20 ppm was able to reduce free radicals by 46.69%. This resulst has shown that the synthesized compound can be used as an antioxidant. The H-NMR and C-NMR tests also confirmed that the synthesized compound was cinnamic acid with a yield of 4.98%.

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REFERENCES

[1] C. I. Chiriac, F. Tanasa, & M. Onciu, "A novel approach in cinnamic acid synthesis: Direct synthesis of cinnamic acids from aromatic aldehydes and aliphatic carboxylic acids in the presence of boron tribromide," *Molecules*, vol. 10, no. 2, pp. 481–487, 2005. DOI: 10.3390/10020481

[2] Z. Xu, D. Zhang, J. Hu, X. Zhou, X. Ye, K. L Reichel, & W. Shi "Comparative genome analysis of lignin biosynthesis gene families across the plant kingdom," *BMC Bioinformatics*, vol. 10, no. SUPPL. 11, pp. 1–15, 2009. DOI: 10.1186/1471-2105-10-S11-S3

[3] J. D. Guzman, "Natural cinnamic acids, synthetic derivatives and hybrids with antimicrobial activity," *Molecules*, vol. 19, no. 12, 2014. DOI : 10.3390/molecules191219292

[4] T. Vogt, "Phenylpropanoidbiosynthesis," *Mol. Plant*, vol. 3, no. 1, pp. 2–20, 2010. DOI:10.1093/mp/ssp106

[5] L. Kovanda, W. Zhang, X. Wei, J. Luo, J.X. Wu, E.R. Atwill, S. Vaessen, X. Li, & Y. Liu, "In Vitro Antimicrobial Activities of Organic Acids and Their Derivatives on Several Species of Gram-Negative and Gram-Positive Bacteria". *Molecules*, vol. 24, no. 20, 2019. DOI: 10.3390/molecules24203770

[6] D. Pal, A. Mazumder, & R. Mazumder," Synthesis of Cinnamanilide Derivatives and Their Antioxidant & Antimicrobial Activity. *J.Chem*,vol. 2015, 2015. *DOI*:10.1155/2015/208910

[7] S. L. Wang, C. Cheng, F. Y. Wu, B. Jiang, F. Shi, S. J. Tu, T. Rajale, & G. Lib," Microwave-assisted multicomponent

reaction in water leading to highly regioselective formation of benzo [f]azulen-1-ones", *Tetrahedron.* vol. 67, no. 25, pp. 4485–4493,2011. DOI:10.1016/j.tet.2011.05.002

[8] G. Dilek, B. Demirata, & R. Apak. "Determination of total antioxidant capacity by a new spectrophotometric method based on Ce (IV) reducing capacity measurement." *Talanta*, vol. 71, no. 3, pp. 1155-1165, 2007. DOI:10.1016/j.talanta.2006.06.015

[9] P. N. K. Babu, B. R. Devi, & P. K. Dubey, "Ultrasound assisted convenient, rapid and environmentally benign synthesis of N-alkylbenzimidazoles," *Der Chem. Sin.*, vol. 4, no. 1, pp. 105–110, 2013.

[10] S. Raucher & P. Klein, "Ultrasound in heterogeneous organic reactions. Improved procedure for the synthesis of thioamides," . *Org. Chem.*, vol. 46, no.17, pp.3558-3559,1981 DOI:10.1021/jo00330a041

[11] V. Calvino, M. Picallo, A. J. López-Peinado, R. M. Martín-Aranda, & C. J. Durán-Valle, "Ultrasound accelerated Claisen-Schmidt condensation: A green route to chalcones," *Appl. Surf. Sci.*, vol. 252, no. 17, pp. 6071–6074, 2006. DOI:10.1016/j.apsusc.2005.11.006

[12] J. S. Ghomi & Z. Akbarzadeh, "Ultrasonic accelerated Knoevenagel condensation by magnetically recoverable MgFe2O4 nanocatalyst: A rapid and green synthesis of coumarins under solvent-free conditions," Ultrason. *Sonochem.*, vol. 40, pp. 78–83, 2018. DOI: 10.1016/j.ultsonch.2017.06.022

[13] G. Cravotto, E. Borretto, M. Oliverio, A. Procopio & A. Penoni, "Organic reactions in water or biphasic aqueous Systems under onochemical conditions. A review on catalytic effects," *Catal. Commun.*, vol. 63, pp. 2–9, 2015. DOI:10.1016/j.catcom.2014.12.014

[14] N. N. Bogdashev, "Physicochemical Characterization of Cinnamic Acid Activity and Physicochemical Properties. AGf ~," *Pharmaceutical Chemistry Journal,* vol. 32, no. 2, pp. 86–88, 1999. DOI:10.1007/BF02471887

[15] A. R. Nunes, Í. G. P Vieira, D.B. Queiroz, A. L. A. B. Leal, S. M. Morais, D. F. Muniz , J. T. Calixto-Junior, & H. D. M. Coutinho. "Use of Flavonoids and Cinnamates, the Main Photoprotectors with Natural Origin," *Adv. Pharmacol. Sci.*, vol. 2018, 2018. DOI:10.1155/2018/5341487

[16] H. Hamidian & A. M. Tikdari, "Synthesis of unsaturated 5(4H)- oxazolone derivatives in the presence of antimony pentafluoride as catalyst," *Asian J. Chem.,* vol. 19, no. 2, pp. 970–974, 2007.

[17] A. Anggadita, Ismiyarto & Ngadiwiyana, "Amil Sinamat dari Sinamaldehid dan Uji Aktivitas," *J. Kim. Sains dan Apl.* vol. 11, no. 113, pp. 52–56, 2008. DOI:10.14710/jksa.11.3.52-56

[18] M. M. Donglikar & S. L. Deore, "Development and evaluation of herbal sunscreen," *Pharmacogn. J.,* vol. 9, no. 1, pp. 83–97, 2017. DOI:10.5530/pj.2017.1.15

[19] J. Julianus, "Sintesis Asam Sinamat dari Benzaldehid dan Asam Malonat dengan Katalis Dietilamina," *J. Chem. Inf. Model.,* 2013. DOI:10.24071/jpsc.11161

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