Synthesis 2-(3-Phenylallylidenamino) Pentanedioic Acid by Condensation of Cinnamaldehyde with Glutamic Acid and the Activity Test as Antibacterial

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Abstract: 2-(3- Phenylallyldenamino) Pentanedioic Acid as Schiff base has been synthesize by condensation between cinnamaldehyde and glutamic acid as the source of primary amine. Condensation between cinnamaldehyde and glutamic acid is in reflux condition by using ethanol as a solvent for 5 hours. The yield's percentage of reaction is 49.39%. The formed Schiff base is proven by FT-IR spectrum with the appearance of a vibration peak at wave number in 1627 cm^{-1} as the sign of C=N functional group. UV-Vis spectrum showed the change of cinnamaldehyde maximum wave number in 238 nm become Schiff base in 321 nm. The result of research also show that the Schiff base has strong antibacterial activity for *S. aureus* by obstacle zone 13.3 mm and weak antibacterial activity for *E. coli* by obstacle zone 6.6 mm.

1 INTRODUCTION

Condensation between primary amine with carbonyl from ketone and aldehyde in organic compounds in special condition will produce Schiff base (Cimerman et al. 1997, da Silva, et al, 2011). Schiff base is known structurally as azometine (-CH=N-) and one of organic compound with many uses like as pigment and dye, catalyst, intermediary in organic synthesize, and polymer stabilizer (Dhar and Taploo, 1982). Schiff base also has biology activity such as antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammation, antivirus, and antipyretic (Dhar and Taploo, 1982, Przybylski, et al, 2009). The different use of Schiff base is based on basic material from aliphatic, aromatic, heterocyclic of primary amine and the source of carbonyl in use (da Siva, et al, 2011).

Many researches also prove that Schiff base is very effective as corrosion inhibitor for metal by form a layer to protect material environmentally (Li et al. 1999, Munir, at al, 1985). The former researcher also tested Schiff base from cinnamaldehyde, 2-aminophenol condensation as corrosion inhibitor for iron in HCl 0.5 N with inhibitor efficiency 92% (Qasim, 2011). Schiff base from cinnamaldehyde as the source of carbonyl and ethylenediamine as the source of amine also can be used as corrosion inhibitor in 7000 ppm of zinc in HCl 0.1 N with efficiency 90.17% (Ginting, et al, 2016). Beside as corrosion inhibitor, Schiff base also has antimicrobial properties (Amanullah et al, 2011). Aysen et al (2010) also synthesize Schiff base by using 4-benzylloxybenzaldehide with 2-aminophenol and the result has good antibacterial properties in *E. coli, B.subtilis, S. aureus* (Sirumapea et al, 2015). Wang et al (2015), synthesize Schiff base from cinnamaldehyde with some of amino acid and found that it has antibacterial properties in *Eschericia coli, Aspergillus niger, Penicillium citrinum* and *Staphylococcus aureus*. Cinnamaldehyde is a natural product kind of phenylpropionate (C6-C3) which is instead of synthesizing, it is also as the main component of cinnamon oil (Guenther, 1990). The utilization of Schiff base should be improved by changing cinnamaldehyde to its derivative. By its chemical properties, cinnamaldehyde has benzene ring, alkene, and aldehyde so it can be transformed to cinnamaldehyde derivatives (Ngawidiyana et al, 2007). Glutamic acid is an amino acid used by organism in protein biosynthesis. This kind amino acid is one of nonessential amino acid for human which mean it can be synthesized in their body (IUPAC-IUB, 2008). Glutamic acid as component of protein contain in food, but only can be tasted in

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original form. Most of glutamic acid is exist in many foods like cheese and ketchup. Glutamic acid also used as additive in food, and as flavor in its natrium salt known as monosodium glutamic (MSG). Based on the description, the researcher interest to synthesize Schiff base by using cinnamaldehyde with glutamic acid and it used as antibacterial.

2 MATERIALS AND METHODS

2.1 Materials and Equipment

The tools used in this study include: two neck flasks, reflux devices, thermometers, glassware, vacuum pumps, analytical balance sheets, chromatographic columns, chambers, UV lamps, petri dishes, osseous needles, paper discs, incubators, FT-IR spectrophotometer, UV-Vis spectrophotometer. While the materials used in this study include: Cinnamaldehyde, ethanol, glutamic acid, ethyl acetate, n-hexane, silica gel HF254, silica gel 60 are all pro-analysis made by E. Merck.

2.2 Synthesis of 2- (3- Phenyl alylidinamine) Pentanadioate Acids

About 6.6 g of cinnamaldehyde were dissolved in 25 mL of ethanol, then put in a two-volume 250 mL neck flask. Next, a drop of 5.9 g of glutamic acid was dissolved with 50 mL ethanol through a dropper funnel slowly into the mixture. Then reflux for 5 hours while stirring. Furthermore, the ethanol solvent used was evaporated with rotary evaporator. Excess Cinamaldehyde is evaporated by vacuum distillation at 100oC and a pressure of 20mmHg. The residual weight was obtained, then thin layer chromatography (TLC) analysis was performed using developer n-hexane: ethyl acetate (8: 2 V / V), kiesel 60 HF254 adsorbent and UV lamp stain, then purified using column chromatography. The results obtained were analyzed by FT-IR and UV-Vis spectroscopy followed by an antibacterial activity test.

2.3 Schiff Base Analysis Synthesis

The purity of the Schiff base was analyzed using thin layer chromatography, using several developers and mixed developers with the stationary phase of silica gel HF254. The analysis results provide a single stain. The results obtained were then carried out FTIR spectroscopic analysis with KBr and UV-Vis pellet media in ethanol solvents then followed by an antibacterial activity test.

2.4 Antibacterial Activity Test

2.4.1 Making Nutrient Agar Media

A total of 7 g was dissolved with 250 ml of aquadest in an Erlenmeyer glass and heated to dissolve and boil, then sterilized in an autoclave at a temperature of 121ºC for 15 minutes.

2.4.2 Manufacture of Oblique and Stock Media for Bacterial Culture

In a sterile test tube, 3 ml of sterile NA media are inserted, left at room temperature until it solidifies at an angle to form an angle of 30-45ºC. Bacterial culture from the main strain was taken with a sterile osseous needle and then inoculated on the sloping NA media surface by scraping, then incubated at 35ºC for 18-24 hours.

2.4.3 Making Mueller Hinton Agar Media (MHA)

As much as 19 g of Mueller Hinton Agar powder, put in an Erlenmeyer glass and then dissolved in 500 ml of aquadest and heated until all dissolve and boil. Then sterilized in an autoclave at 121ºC for 15 minutes.

2.4.4 Making Bacterium Inoculum

A total of 3.25 g of nutrient broth was dissolved in 250 ml of aquadest in an Erlenmeyer glass and heated to all dissolve and boil, then sterilized in an autoclave at 121ºC for 15 minutes and cooled. Then the microbial colonies were taken from the stock of culture using sterile osseous needles then suspended into 10 ml sterile nutrient media in a test tube and incubated at 35ºC for 3 hours, then measured the wavelength using a UV-Vis spectrophotometer wavelength 580-600 nm.

2.4.5 Determination of Antibacterial Activity

Determination of antibacterial activity was obtained by agar diffusion method where the paper disk (ǿ 6 mm) which had been immersed with Schiff Bases 3% and in direct contact with the media which had been inoculated by *E. coli* and *S. aureus*, then clear zones formed after incubation were observed for 24 hours. The clear zone shows the inhibition that is produced

from the Schiff Base on *E. coli* and *S. aureus*. The clear zone formed is measured by using the calipers (accuracy mm).

3 RESULT AND DISCUSSION

3.1 Synthesis of Bases Schiff

The Schiff base is a 2- (3- Phenylalylidinamine) Pentanadioate which is produced through condensation between cinnamaldehyde as a source of aldehyde and glutamic acid as a source of amine in ethanol solvents under reflux conditions for 5 hours. The excess of cinnamaldehyde from the reaction results was evaporated through vacuum distillation and analyzed by thin layer chromatography using developer n-hexane: ethyl acetate (8: 2 v / v), the price of product Rf still mixed was 0.11 and 0.75. From 6.6 g of cinnamaldehyde used the results were as much as 9.47 g (93.20%) yellowish brown solids. The purification is continued through column chromatography with eluent n-hexane: ethyl acetate (8: 2 v / v), where purification results are 0.53 g, so that the total yield is 49.39%. The results obtained were analyzed using thin layer chromatography using developer n-hexane: ethyl acetate (8: 2 v / v) giving a single stain at an Rf price of 0.67. The physical form of the Schiff base obtained is a solid form with a melting point 124-129^{o}C indicating that changes have been made from the solid base material namely glutamic acid with a melting point 247- 249^{o}C. The results of the Schiff base analysis produced using FT-IR spectroscopy obtained spectra with absorption vibration peaks at the wave number area 3410 cm^{-1}, 3024 cm^{-1}, 2924 cm^{-1}, 1720 cm^{-1}, 1674 cm^{-1}, 1627 cm^{-1}, 1450 cm^{-1}, 1126 cm^{-1} (Figure 1).

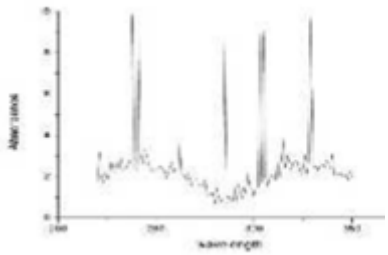

Figure 1: FT-IR Spectrum of Schiff Base.

From the results of UV-Vis spectroscopy there was an increase in wavelength of 238 nm for cinnamaldehyde (Figure 2) to 321 nm for the Schiff base (Figure 3). This shows the addition of conjugated double bonds to the products produced due to the presence of new functional groups that are bound to the synthesized part of the molecule.

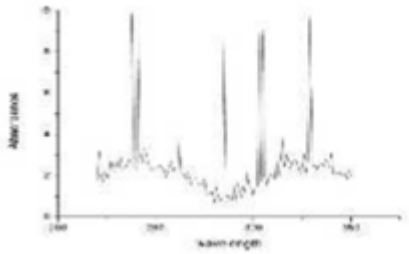

Figure 2: UV-Vis Spectrum of Cinnamaldehyde.

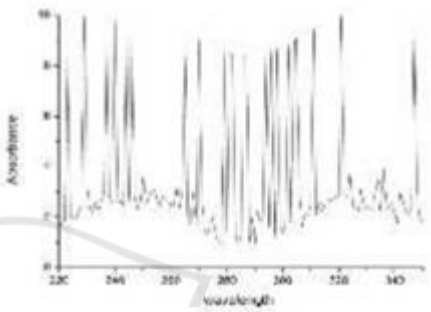

Figure 3: UV-Vis Spectrum of Schiff Base.

The Schiff base results from a condensation reaction between cinnamaldehyde and glutamic acid as evidenced by the support of the FT-IR spectrum which shows the emergence of a stretch of C = N at the absorption peak of the wave number 1627 cm^{-1} supported by stretching C-N at wave number 1126 cm^{-1}. Uptake in the wave number area 3024 cm^{-1} shows that C-H aromatic from the benzene ring supported by stretching absorption of 1674 cm^{-1} shows the vibration of C = C of aromatic compounds. This is also supported by the vibration peak in the wave number region 2924 cm^{-1} which shows the typical absorption of vibration stretching (C-H) sp^3 which is supported by bending vibration (C-H) sp^3 in the wave number region of 1450 cm^{-1}. Hypothetically the Schiff base formation reaction is shown in Figure 4.

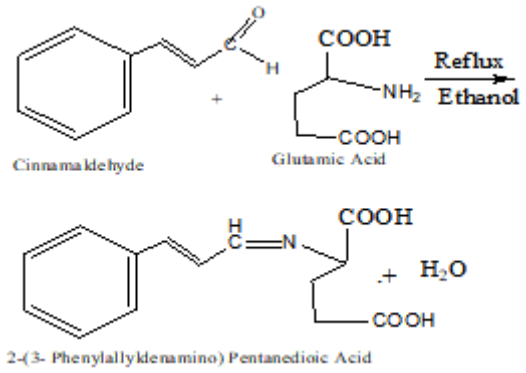

Figure 4: Schiff Base Formation Reaction.

3.2 Antibacterial Activity Test

Antibacterial tests on the Schiff base using *Escherichia coli* and *Staphylococcus aureus* can be seen in Table 1.

Table 1: Antibacterial Activity Test.

Bacteria	Inhibited Zone Diameter (mm)	Diameter Disc Paper (mm)
E. coli	6.6	6.0
S. aureus	13.3	6.0

Cluster C = N in the Schiff base can be antibacterial where the nitrogen atom has free electrons. The presence of an imine group which has a cationic charge that is able to bind the food source of the bacterium thus inhibits food nutrition into bacterial cells (Darmanto et al., 2010). Antibacterial strength is classified into 3, which is strong if it produces a diameter inhibition zone of more than 8 mm, moderate activity if it produces a 7-8 mm inhibition zone diameter, and weak activity if it has a diameter inhibition diameter of less than 7 mm, thus that the Schiff base is formed has strong antibacterial strength. The wider the inhibition zone produced shows the stronger Schiff's base ability in inhibiting bacterial growth. The antibacterial test data showed that the Schiff base had good antimicrobial activity against the *Staphylococcus aureus* bacteria which is a common bacterium outside the body. For *Escherichia coli* bacteria, the Schiff base is not very good. *Escherichia coli* bacteria are commonly found in the body.

4 CONCLUSIONS

The condensation reaction between 6.6 g of cinnamaldehyde and 5.9 g of glutamic acid produced a Schiff base of 9.47 g obtained for a total yield of 49.39%. Supported by FT-IR spectroscopic data, namely by the appearance of a vibration peak in the area of the wave number 1627 cm^{-1} which indicates the group C = N (Imina). The UV-Vis data showed a change in the wavelength of 238 nm for cinnamaldehyde to 321 nm for the Schiff base. The results of the Schiff alkaline antibacterial activity test showed strong results against the Staphylococcus aureus bacteria and were weak for Escherichia coli bacterial.

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