

Analysis Of Antioxidant Activity Of A Combination Of Turmeric Rhyme Extract (*Curcuma Domestica* Val.) And Katuk Leaves (*Sauropus Androgynus*) As Additional Therapy For Type 2 DM

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Input : May 19, 2024
Accepted : June 23, 2024

Revised : May 24, 2024
Published : June 27, 2024

ABSTRACT

*The importance of reform in the health sector will be ammunition in realizing the society 5.0 era. In Indonesia, there is currently an epidemiological transition which is causing a shift in disease patterns, namely an increase in degenerative diseases, one of which is diabetes mellitus. It is hoped that the creation of an innovative herbal drink combining turmeric rhizome and katuk leaves will be an additional therapy for people with type 2 diabetes mellitus. The aim of this research is to analyze antioxidant activity using the DPPH method. The research was carried out by analyzing antioxidant activity based on the IC₅₀ value. The samples in this study were turmeric rhizome extract (*Curcuma domestica* Val.) and katuk leaf extract (*Sauropus androgynus*). There were 3 test samples, namely turmeric rhizome extract (sample 1), katuk leaf extract (sample 2) and a combination extract of turmeric rhizome and katuk leaves (sample 3). Based on the research, IC₅₀ values were obtained from three formulations, namely sample 1 at 40 ppm, sample 2 at 40 ppm and sample 3 at 30 ppm. These results were also compared with the standard antioxidant activity of vitamin C used at 20 ppm. Based on the three samples with antioxidant activity results, sample 3 has the best antioxidant activity compared to samples 1 and 2 so that it can inhibit free radicals and can prevent insulin resistance caused by oxidative stress due to free radicals in the body.*

Keywords: Antioxidants, DPPH, Diabetes Mellitus Type 2, *Sauropus androgynus*, *Curcuma domestica* Val.

INTRODUCTION

Society 5.0 is the concept of a technology-based society that focuses on humans (human-centered), which is an era where technology will become part of humans themselves (Suherman *et al.*, 2020). Internet media is not just for sharing information but for living life. Meanwhile, in the era of society 5.0, new values and lifestyles will be created through technological developments in the hope of minimizing economic disparities in society. In the era of society 5.0, there is a goal of realizing a society where humans in it truly enjoy life and feel comfortable so that this era is present as a solution to the era of industrial revolution 4.0 which threatens to degrade humans by AI

The role of young scientists in filling and working towards the realization of the Society 5.0 era in Indonesia is one of them by developing strategies and appropriate technological innovations so that they can be implemented in society and can move the community ecosystem towards a smart, comprehensive and well-being society in



accordance with the principles of society 5.0 (Suherman *et al.*, 2020). The crucial problems faced by various countries to date is the health sector. Innovation in the health sector will be an asset for development in preparing and realizing society 5.0 era.

Currently, Indonesia is experiencing an epidemiological transition which has resulted in changes in disease patterns, namely an increase in degenerative diseases. Degenerative diseases are non-communicable diseases that are chronic due to decreased function of the body's organs as part of the aging process. Examples include heart disease, diabetes, obesity, hypertension and others (Anies, 2018). One of the diseases that is of concern in this case is diabetes mellitus, which is a degenerative disease because it changes the function of the pancreas organ and is related to the insulin hormone, causing an increase in blood sugar levels.

The number of cases of diabetes mellitus sufferers in the world always shows an increase every year. The International Diabetes Federation (IDF) estimates that in 2019 there will be at least 463 million people (aged 20-79 years) in the world suffering from diabetes. This figure is equivalent to a prevalence of 9.3% of the total population of the same age. Based on gender, IDF estimates that the prevalence of diabetes in 2019 is 9% in women and 9.65% in men. The prevalence is estimated to increase as the population ages to 111.2 million people (19.9%) aged 66-79 years. This is predicted to continue to increase, reaching 578 million in 2030 and 700 million in 2045 (Kemenkes RI, 2020).

Based on the study above, the researchers initiated a herbal drink with a millennial taste made from turmeric rhizomes (*Curcuma domestica*) and katuk leaves (*Sauropus androgynus*). It is hoped that this innovation will be an additional therapy for sufferers of type 2 diabetes mellitus by utilizing plants that have medicinal properties, namely turmeric rhizomes and katuk leaves which have antioxidant activity. It is hoped that this research can have an impact on society as a form of real implementation to realize society 5.0 in Indonesia.

The problem formulation in this research centers on analyzing the antioxidant activity of a herbal drink that combines turmeric rhizomes and katuk leaves using the DPPH method. The primary objective is to determine the antioxidant activity of this combination through the specified method.

THEORETICAL BASIS

2.1 Diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disease caused by abnormalities in insulin performance, insulin secretion or both with characteristics of hyperglycemia (Azizah and Qomariyah, 2021). DM is characterized by blood glucose (blood sugar) levels exceeding normal, instant blood sugar levels equal to or more than 200 mg/dl, and fasting blood sugar levels above or equal to 126 mg/dl (Petersmann *et al.*, 2018).

Etiologically, diabetes mellitus can be divided into type 1 DM, type 2 DM, pregnancy DM, and other types of DM. Type 1 DM is a type of diabetes caused by an absolute lack of insulin. This is due to progressive damage to pancreatic cells so that insulin cannot be synthesized by the pancreatic gland. Meanwhile, type 2 DM is a type of diabetes caused by the body's inability to utilize insulin, which leads to weight gain and decreased physical activity (Lestari *et al.*, 2021). There is also gestational diabetes or gestational diabetes which is found during pregnancy (Adli, 2020). Several factors that influence blood glucose control in type 2 DM sufferers include changes in lifestyle, knowledge, habits of consuming high-calorie foods, lack of physical activity, obesity, smoking, and sleep disorders (Abadi *et al.*, 2020).

The pathophysiology of diabetes mellitus consists of 2 general causes, specifically impaired insulin secretion due to damage to pancreatic β -cells, and impaired insulin work due to insulin resistance (Ozougwu, *et al.*, 2013).

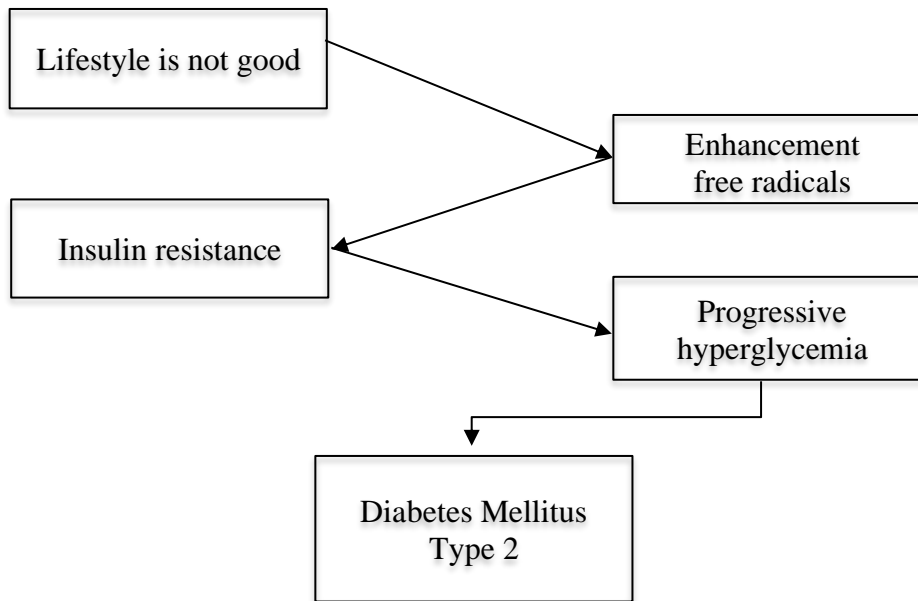


Figure 1. Pathophysiology of type 2 DM (Ozougwu *et al.*, 2013)

Unhealthy lifestyle habits such as smoking and consuming alcoholic drinks can trigger an increase in the number of free radicals in the body. Free radicals are molecules that lose one electron from their lone pair and are the result of homolytic separation of a covalent bond. This homolytic breakdown results in a molecule breaking down into free radicals (Fakriah, *et al.*, 2019). Free radicals in the body cause protein damage due to protein oxidation which leads to damage to the basic protein tissue, one example of which is insulin resistance due to damage to the working mechanism of pancreatic β -cells (Farkriah *et al.*, 2019).

Insulin resistance induced by free radicals will cause a chain reaction which causes a response in the form of increasing blood sugar levels in the body, causing diabetes. Insulin resistance is a condition when insulin fails to signal the glucose transporter (GLUT-4) to open the way for glucose to enter cells, resulting in a buildup of glucose in the blood (Yaribeygi, *et al.*, 2018).

2.2 Turmeric Plant



Figure 2. Turmeric Rhizome (*Curcuma domestica* Val.) (Pranata, 2014)

Turmeric is a herbal plant with a height of up to 100 cm. It has false stems, erect, round, forming rhizomes, and yellowish green in color. Turmeric leaves are single leaves, elongated lanceolate in shape, 3-8 leaves in number with a pointed base, flat

edges, measuring 20-40 cm x 8-12.5 cm, pinnate leaf spines pale green (Astuti, 2018). The classification of turmeric plants is as follows:

Kingdom : Plantae
Division : Spermatophyta
Sub division : Angiosperms
Class : Monocotyledonae
Order : Zingiberales
Family : Zingiberaceae
Genus : Curcuma
Species : Curcuma domestica Val

Turmeric rhizome contains 1.5-2.5% essential oil, curcumin, resin, oleoresin, demethoxy curcumin, and bisdesmethoxy curcumin. Tumeron, terpinolene carvacrol, and α -felandrene are the constituents that make up the most essential oils in several varieties of turmeric (Muadifah, *et al.*, 2019).

2.3 Katuk Plants



Figure 3. (A) Katuk leaves, (B) Whole katuk plant, (C) Katuk flowers and (D) Katuk fruit (Zhang, *et al.*, 2020).

The katuk plant (*Sauropus androgynus*) is a plant native to Southeast Asia and is usually cultivated as an ingredient in traditional medicine. Katuk plants grow in hot environments and in humid conditions. The katuk plant has a brownish white taproot, the leaves are light green to dark green with a size of 2-6 cm x 1.5-3 cm, has dark red flowers and distinctive spots, the white fruit of the katuk plant is small round in shape (Yunita, *et al.*, 2021). The classification of katuk plants is as follows:

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Malpighiales
Family : Phyllanthaceae
Genus : Sauropus
Species : androgynous
Binomial name : *Sauropus androgynus*

Katuk leaves contain flavonoids, tannins, alkaloids, triterpenes, organic acids, proteins, essential oils, amino acids, minerals and carbohydrates. The flavonol compound derived from flavonoids in katuk leaves, specifically quercetin, can improve the immune system by increasing IL-2 activity and lymphocyte proliferation (Proklikningsih *et al.*, 2019).

2.4 Antioxidant Activity

Antioxidants are compounds that donate electrons (electron donors). Judging from biological activity, antioxidants are compounds that are able to neutralize the negative impacts of oxidants in the body, such as somatic cell damage. Antioxidants can be defined as compounds that are able to fight free radicals. Antioxidants play a role in reducing the ability of free radicals to cause cell damage. There are two ways to get antioxidants, id est from outside and inside the body. Antioxidants are obtained from foods or drinks that contain vitamins A, C, E, antioxidant enzymes, and beta-carotene. Antioxidants can be categorized into enzyme antioxidants and vitamin antioxidants. Antioxidant enzymes are superoxide dismutase and glutathione peroxidase. Meanwhile, antioxidant vitamins are beta carotene (vitamin A), ascorbic acid (vitamin C) and alpha-tocopherol (vitamin E) which can be obtained from plants or animals (Suprihatin *et al.*, 2020).

2.5 DPPH Test

The free radical that is generally used as a model in research on antioxidants or free radical reducers is 1,1-diphenyl-2-picrylhydrazyl (DPPH) (Windono *et al.*, 2001). DPPH is a stable free radical (has an N atom in the middle) and can react with compounds that can donate hydrogen atoms which can be useful for testing the antioxidant activity of certain components in a sample (Dinis, *et al.*, 1994). Due to the presence of unpaired electrons, DPPH provides strong absorption at a wavelength of 517 nm. When the electrons become paired due to the presence of free radical scavengers, the absorbance decreases stoichiometrically according to the number of electrons taken. The presence of antioxidant compounds can change the color of the DPPH solution from purple to yellow (Dehpour, *et al.*, 2009). Changes in absorbance resulting from this reaction have been used widely to test the ability of several molecules to scavenge free radicals (Dinis, *et al.*, 1994). DPPH is an easy, fast and sensitive method for testing the antioxidant activity of certain compounds or plant extracts

MATERIAL AND METHOD

This research uses experimental methods which include the stages of making simplicia, extracting simplicia and testing antioxidant activity using the DPPH method. The ingredients used are turmeric rhizomes, katuk leaves, distilled water, ethanol pro-analysis, DPPH powder, and vitamin C powder. The tools used are analytical scales, beakers, measuring cups, measuring pipettes, dropper pipettes, bulbfillers, measuring flasks, and UV-vis spectrophotometers. Research carried out from April 1-14 2023. Research took place in several Pharmacy laboratories, Faculty of Mathematics and Natural Sciences, Udayana University.

A. Research Phase

1. Drying Turmeric Rhizomes (*Curcuma domestica* Val.) and Katuk Leaves (*Sauropus androgynus*)

2 kg of turmeric rhizomes were weighed and wet sorted. Then wash with running water. After washing, the turmeric was sliced lengthwise into thin slices and dried in an oven at 60°C for 3 days. After drying, turmeric rhizome simplicia is obtained, then a dry filtration process is carried out to separate unused materials, then the turmeric is ground with a blender until turmeric rhizome powder is obtained which is ready to be extracted. The procedure was repeated for katuk leaves.

2. Extraction

100 grams of turmeric rhizome powder was added to 1000 ml of 96% ethanol. Then cover with aluminum foil, leave for 24 hours. Filter to separate the residue and filtrate. Repeat for 3 days, collect the filtered filtrate, and to get a thick extract use a rotary evaporator at temperature of 60°C. The procedure was repeated for katuk leaf simplicia.

3. DPPH Test Stage

Preparation of DPPH Solution

The DPPH solution was made at a concentration of 100 ppm. Weigh 10 mg DPPH powder (BM 394.32) and add a little pro-analysis ethanol until dissolved. Then put it in a 100 mL volumetric flask and add back ethanol pro-analysis until the limit mark. The work is carried out in a dark container and protected from light.

Maximum Wavelength Measurement

Determination of the maximum wavelength measured with DPPH solution. 3 mL DPPH solution was put into a cuvette, the blanko used was ethanol pro-analysis. Screening was carried out at a wavelength between 400-600 nm, observed until the maximum absorbance value was obtained at a wavelength of 517 nm. DPPH was stable at an incubation time of 30 minutes.

Preparation of a Vitamin C Standard Curve

Weigh 10 mg of vitamin C, dissolve it in 100 ml of methanol pro analysis, and shake until a homogeneous mixture is obtained. The 100 ppm vitamin C stock solution was then made into concentrations of 10, 15, 20, 25, and 30 ppm. Pipette 1 ml of each vitamin C series into a test tube, add 2 ml DPPH, shake until homogeneous, incubate for 30 minutes at room temperature, then measure the absorbance at a wavelength of 517 nm using UV-Vis spectrophotometry. Vitamin C is used as a comparison because it is an antioxidant with very strong activity and is relatively safe and does not cause toxicity.

Sample Test Solutions

First, a main liquor is made with a concentration of 100 ppm. Weigh 10 mg of the thick extract then dissolve it in 100 mL of pro-analysis ethanol, then shake until homogeneous. Three samples were made from extracts of turmeric rhizomes and katuk leaves, id est turmeric rhizomes (Sample 1), katuk leaves (Sample 2), a combination of turmeric rhizomes and Katuk leaves 1:1 (Sample 3).

Next, extract solutions for samples 1, 2, and 3 were made with a concentration series of 10, 20, 30, 40, and 50 ppm. The series solution is made from a 100 ppm sample solution which is pipetted with 500 μ L then added ethanol pro analysis to a 5 mL volumetric flask until the limit mark is then homogenized.

Testing is carried out by pipetting series solutions of 1 mL each, then put into a test tube. 2 mL of DPPH was added then shaken until homogeneous. It was incubated at room temperature for 30 minutes and the absorbance was measured using UV-vis spectrophotometry with a wavelength of 517 nm.

B. Data Analysis

Data from experiments and literature reviews collected in this research were analyzed using qualitative and quantitative comparative descriptive analysis techniques. Each test requires an analysis technique that uses several equations. These equations are processed into tabular form and then displayed in the form of linear regression graphs to facilitate the data analysis process.

The antioxidant activity test using the DPPH method was assessed by IC₅₀ (inhibition concentration 50%). The IC₅₀ value in the DPPH method is the sample concentration that is able to capture 50% of free radicals.

$$\% \text{ Inhibition} = \frac{\text{blanko absorbance} - \text{sample absorbance}}{\text{blanko absorbance}} \times 100\%$$

After obtaining the percentage of inhibition from each concentration, then analysis is carried out using a linear regression curve (x,y), where x is the concentration (µg/ml) and y is the percentage of activity (%) from this calculation the formula $y = bx+a$ is obtained. From the equation $y = bx+a$, then input the y value as 50 because it uses 50% inhibition, then the x value will be obtained. The smaller the IC₅₀ value, the stronger the antioxidant activity.

Table 1. Classification of Antioxidant Activity based on IC₅₀ Value (Fikri *et.al*, 2020)

IC ₅₀ value	Antioxidant
< 50 ppm	Very strong
50-100 ppm	Strong
100-150 ppm	Moderate
150-200 ppm	Weak

RESULT AND DISCUSSION

Table 2. Antioxidant Activity Test Results

No	Sample	IC ₅₀
1	Sample 1	40 ppm
2	Sample 2	40 ppm
3	Sample 3	30 ppm
4	Vitamin C	20 ppm

Based on the activity test results summarized in table 2, it shows that the antioxidant activity obtained is expressed by the intermediate inhibition IC₅₀. The smaller the IC₅₀ value, the stronger the sample's antioxidant activity. Based on IC₅₀ analysis test data, the amount of antioxidant activity in sample 1 (turmeric rhizome extract) was 40 ppm, in sample 2 (katuk leaf extract) it was 40 ppm, and in sample 3 (extract of a combination of turmeric rhizome and katuk leaves) it was 30 ppm. These data show that the combination of turmeric rhizome and katuk leaf extracts in a one to one ratio provides the best antioxidant activity among other samples, because with a smaller concentration compared to other samples it is able to reduce free radicals. Overall, all samples have good antioxidant activity because they meet the IC₅₀ value requirements which can be said to be very good <50 ppm (Fikri *et al.*, 2020).

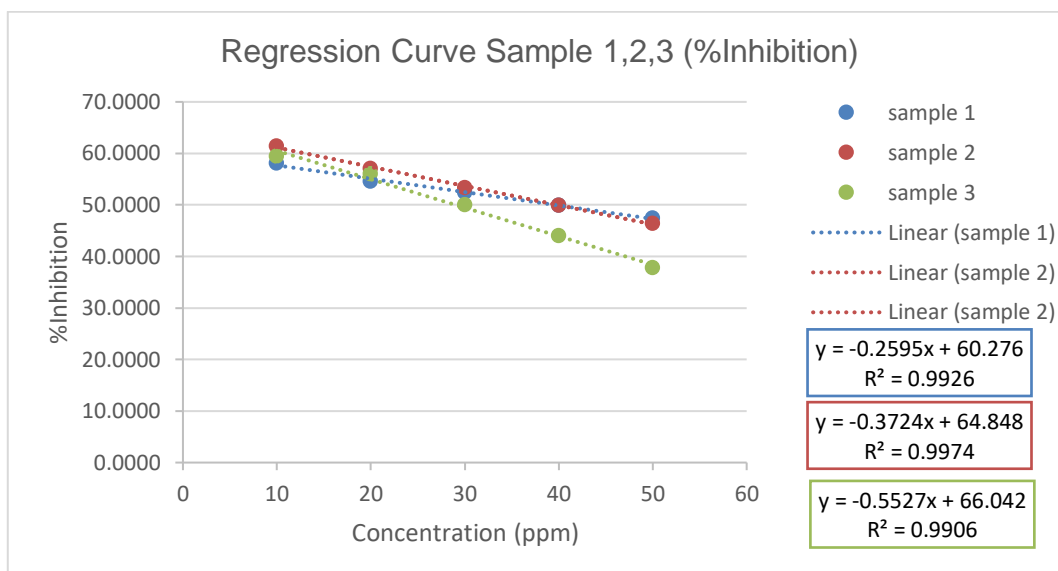


Figure 4. Linear Regression Analysis of %Inhibition on sample concentration

The IC_{50} value is obtained from the results of linear regression curve analysis linear regression calculation (x,y) in Figure 4. between sample concentration (x) ($\mu\text{g/ml}$) and % Inhibition (y) as a percentage of activity. From this calculation, the equation for sample 1 is $Y = -0.2595x + 60.276$ with $R^2 = 0.9926$. The equation for sample 2 is $Y = -0.3724x + 64.848$ with $R^2 = 0.9974$ and sample 3 is $Y = -0.5527x + 66.042$ with $R^2 = 0.9906$. Then, in this equation, 50% inhibition is used, then input $y = 50$, so that the x value will be obtained as IC_{50} as in Tables 3, 4, and 4. Apart from that, the IC_{50} value of vitamin C was also calculated as a standard for comparison.

Table 3 Antioxidant Activity and %Inhibition of Sample 1 (Turmeric Rhizome Extract)

Concentration (ppm)	DPPH Absorbance	Sample Absorbance	%Inhibition	IC_{50} (ppm)
10	0.8408	0.3522	58.11132	40
20		0.3821	54.55519	
30		0.4004	52.37869	
40		0.4205	49.98811	
50		0.4421	47.41912	

(Source: Data Analysis, 2023)

Table 4. Antioxidant Activity %Inhibition Sample 2 (Katuk Leaf Extract)

Concentration (ppm)	DPPH Absorbance	Sample Absorbance	%Inhibition	IC_{50} (ppm)
10	0.8404	0.3337	60.2927	40
20		0.3603	57.1275	
30		0.3921	53.3436	
40		0.4203	49.9881	
50		0.4502	46.4302	

(Source: Data Analysis, 2023)

Table 5. Antioxidant Activity %Inhibition Sample 3
(Combination of Turmeric Rhizome Extract and Katuk Leaf Extract)

Concentration (ppm)	DPPH Absorbance	Sample Absorbance	%Inhibition	IC ₅₀ (ppm)
10	0.8411	0.34113	59.44240	30
20		0.36991	56.02069	
30		0.42056	49.99881	
40		0.47056	44.05421	
50		0.52323	37.79218	

(Source: Data Analysis, 2023)

Table 6 Antioxidant Activity %Inhibition of Vitamin C Standard

Concentration (ppm)	DPPH Absorbance	Sample Absorbance	%Inhibition	IC ₅₀ (ppm)
10	0.8412	0.4006	52.3775	20
15		0.4103	51.2244	
20		0.4207	49.9881	
25		0.4305	48.8231	
30		0.4440	47.2111	

(Source: Data Analysis, 2023)

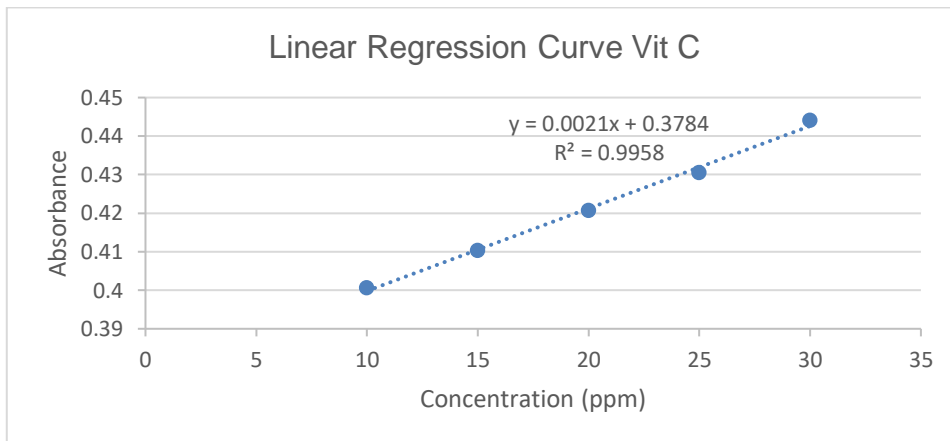


Figure 5. Linear Regression Analysis of absorbance on vitamin C concentration

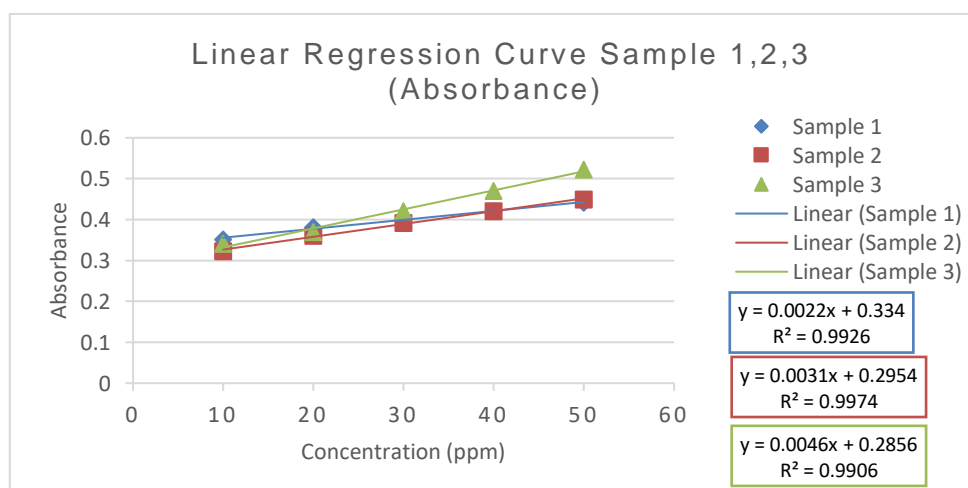


Figure 6. Linear Regression Analysis of absorbance on sample concentration

Based on the data in Table 5, the antioxidant activity results of sample 3 are within the IC₅₀ parameter is 30 ppm. The IC₅₀ parameter is a value used to determine the degree of reduction in antioxidants by 50%. Based on the data obtained, the combination of ethanol extract of turmeric rhizomes and katuk leaves at a concentration of 30 ppm was able to reduce free radicals (DPPH solution) by 50%. DPPH solution is a stable free radical and therefore can be a good comparison to determine antioxidant activity. When testing antioxidant activity, it was found that the composition of the DPPH solution used was twice that of the sample compound. Based on these results, it can be concluded that the combination of turmeric rhizome extract and katuk leaves has good antioxidant activity and is further proven to play a synergistic role in antioxidant activity.

The good antioxidant activity of the combination of turmeric rhizome extract and katuk leaves comes from the flavonoid compound (quercetin) contained therein (Zanaria *et al.*, 2019; Sandra, *et al.*, 2016). The mechanism of action of flavonoid compounds can reduce blood glucose levels with their ability as antioxidants. Flavonoids are protective against damage to β -cells which produce insulin and can increase insulin sensitivity. Antioxidants can suppress β -cell apoptosis without changing the proliferation of pancreatic β -cells. Antioxidants can bind free radicals so they can reduce insulin resistance. Antioxidants can reduce Reactive Oxygen Species (ROS). In the formation of ROS, oxygen will bond with free electrons that come out due to leaking of the electron chain. This reaction between oxygen and free electrons produces ROS in mitochondria.

The mechanism of action of flavonoid compounds is that they can reduce blood sugar levels through their ability as antioxidants. Flavonoids can prevent damage to insulin-producing β -cells and increase insulin sensitivity. Antioxidants can inhibit β -cell apoptosis without changing pancreatic β -cell proliferation. Antioxidants can bind free radicals and reduce insulin resistance. Antioxidants can reduce Reactive Oxygen Species (ROS). When ROS are formed, oxygen will bind to free electrons that come out as a result of leaking electron chains. The reaction between oxygen and free electrons will produce ROS in the mitochondria.

The antioxidants contained in flavonoids release hydrogen atoms, thereby suppressing the radical nature of free radicals. Flavonoids are oxidized and bind to free radicals, which then become more stable compounds. Another mechanism is the ability of flavonoids, especially quercetin, to inhibit GLUT-2 in the intestinal mucosa and reduce glucose absorption. Absorption of glucose and fructose from the intestine will decrease, thereby lowering blood sugar levels. GLUT-2 is the main glucose transporter in the intestine under normal conditions. Flavonoids inhibit glucose absorption, thereby reducing excess insulin production. This helps prevent hyperinsulinemia. The presence of glucose-inhibitory mechanisms in the gut may help give pancreatic β -cells time to overcome problems with insulin production.

Based on the mechanism of action, the antioxidant activity contained in the combination of turmeric rhizomes and katuk leaves is able to inhibit factors that inhibit radical reactions and can prevent insulin resistance in type 2 diabetes patients at an early stage. Simultaneously, it also gives pancreatic β -cells the opportunity to overcome insulin production problems. When insulin is produced well, it will work better in regulating the distribution of glucose entering the cells, so that glucose levels that were previously high in the blood can be distributed properly to the cells so that the cells can work.

CONCLUSION

Based on the data analysis and discussion that has been carried out, a conclusion can be drawn, namely that the results of the analysis of antioxidant activity with the IC_{50} parameter show that the antioxidant activity value of sample 1 is 40 ppm, sample 2 is 40 ppm and sample 3 is 30 ppm. All samples can be categorized as good because they are below 50 ppm. The highest antioxidant activity was found in the combination of turmeric rhizome and katuk leaf samples so that the mechanism of action of the two ingredients could work synergistically as natural antioxidants. Therefore, the herbal drink combining turmeric rhizomes and katuk leaves has the potential to be an additional therapy for type 2 diabetes mellitus because of its excellent antioxidant activity and ability to prevent free radical chain reactions that can trigger insulin resistance

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