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The effect of sucrose and yeast extract on total phenolic, flavonoid, and anthocyanin of lactic-acid-fermented mangosteen fruit peel (*Garcinia mangostana* L.)

Short Title: SYE increase TPFA in LAF

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ABSTRACT
Objective: This study aims to decide the most suitable concentration of sucrose and yeast extract (SYE) and its impact on the levels of total phenol, flavonoid, and anthocyanin (TPFA) for lactic acid fermentation (LAF) in mangosteen fruit peel.
Materials and Methods: In this study, the primary components were mangosteen fruit peel, sucrose, yeast extract, and lactic acid bacteria starter. The experimental design was conducted using the Factorial Design method. The colorimetric method was used to determine total phenol (Folin-Ciocalteu reagent) and total flavonoid ($AlCl_3$ reagent). In addition, the differential pH method was used to determine total anthocyanins using KCl and the CH_3COONa reagent.
Results: The addition of SYE during the fermentation of mangosteen fruit peel can significantly increase the concentrations of TPFA if compared to the control (*p* value of 0.0001). The high sucrose concentration and low yeast extract produced the highest TPFA levels in mangosteen rind fermentation.
Conclusion: The use of SYE affects the levels of TPFA in lactic acid-fermented mangosteen fruit peel, with the most suitable concentrations obtained by sucrose (45 g/L) and yeast extract (2.5 g/L).
Keywords: Fermentation, *Garcinia mangostana* fruit peel, sucrose, yeasts

INTRODUCTION

Herbal products are parts of plants intended for health utilization according to their properties and can be developed into medicinal products, food supplements, and cosmetics.[1,2,3] One of the plants that have the potential to be developed into herbal products is the mangosteen fruit (*Garcinia mangostana* L.) has health benefits for the body so it is dubbed the Queen of Fruits.[4] The amount of waste that is generated by the mangosteen processing industry is considerable, as approximately 60% of the mangosteen fruit is made up of inedible fruit peel.[5] Mangosteen fruit peel extract has been reported to contain much of phenolic compounds that can help overcome such health issues such as cancers, tumors, diabetes, hypertension, inflammation, and skin aging.[6,7,8]
The extraction process is one of the important steps that need to be determined by a researcher to obtain the desired bioactive compounds.[9,10] Fermentation is one of the natural extraction processes involving microorganisms and enzymatic processes that result in the degradation of plant cell walls so that the phytochemical components can be released from the matrix.[11] Lactic acid fermentation has been shown in previous studies that significantly enhance the nutrient and phytochemical profile of the substrate.[12,13,14] A different research also suggested that lactic acid fermentation on mulberry fruit substrate significantly influences the levels of total phenol, flavonoid, and anthocyanin compounds.[15,16] In addition, lactic acid fermentation also causes the fermentation environment to become acidic which correlates with the release of bioactive compounds and by-products of fermentation.[17,18] Several factors that influence the fermentation of lactic acid are the source of carbon and nitrogen, in particular their type and concentration. The carbon source used in this research is sucrose, and the nitrogen source is yeast extract.[19,20]. In another study, a sucrose concentration of 15-45 g/L was used as a carbon source, and yeast extract of 2.5-7.5 g/L was used as a nitrogen source during fermentation.[19] However, the fermentation of mangosteen peel has not been widely studied as an advanced processing step to

increase phytochemical components, so it is considered necessary to conduct further studies. In this study, Experimental Design was used using the Regular Two Factorial Design 2^2 method, which was analyzed using ANOVA integrated into the Design Expert Software.[21]

MATERIALS AND METHODS

Mangosteen fruit peel dry simplicia (*Garcinia mangostana* L.) purchased from the Center for Post-Harvest Processing of Medicinal Plants (Bali, Indonesia). Other materials provided at Unud Forensic and Criminology Laboratory such as sucrose, yeast extract, lactic acid bacteria starter, potassium chloride, sodium acetate trihydrate, hydrochloric acid, aluminum chloride, ethanol, quercetin standard, gallic acid standard, Folin-Ciocalteu, and distilled water. All of the materials used were of analytical grade.

Mangosteen Fruit Peel Fermentation

The concentration of sucrose and yeast extract used varies, sucrose with a concentration range of 15-45 g/L and yeast extract with a concentration range of 2.5-7.5 g/L designed with Design Expert Software using the Regular Two-Level 2^2 Factorial Design method. The design of the experiment is listed in Table 1 (attached).

Table 1. Mangosteen Peel Fermentation Run Using Factorial Design Method: Regular Two Level 2^2

Run	Level		Concentration	
	A: Sucrose	B: Yeast Extract	Sucrose (g/L)	Yeast Extract (g/L)
1	-1	-1	15	2.5
2	-1	+1	15	7.5
3	+1	-1	45	2.5
4	+1	+1	45	7.5

Fermentation was carried out on a total of 100 g of dried simplicia of mangosteen fruit peel, sucrose, yeast extract, lactic acid bacteria starter, and water in an Erlenmeyer flask. The fermentation runs on a shaker at 100 rpm at room temperature for 4 days, equipped with an airlock. Sampling for analysis was carried out at 96 hours of fermentation. The sample was centrifuged for 20 minutes at 5°C and 6000 rpm. In preparation for further analysis, the samples were collected and kept at a low temperature.

Total Phenolic Content (TPC) Determination

TPC was determined using the Folin-Ciocalteu reagent and NaOH in a colorimetric method. The sample was put into a vial, then 10% v/v Folin-Ciocalteu solution was added and allowed to stand for 8 minutes. 1% v/v NaOH solution was added and incubated for 1 hour. A blank solution was prepared in the same manner without the addition of the test solution. A UV-Vis spectrophotometer was used to determine the absorbance of each solution at a wavelength of 730 nm. The TPC was calculated using the linear regression equation and expressed in mg GAE/L.

Total Flavonoid Content (TFC) Determination

TFC was determined using the colorimetric technique with $AlCl_3$ and CH_3COONa reagents. The sample was put into a vial, then added ethanol, $AlCl_3$ 10%, CH_3COONa 1M, and water. Shaken and incubated at room temperature for 30 minutes. In the same way, a blank solution was prepared without using the test solution. A UV-Vis spectrophotometer was used to determine the absorbance at a wavelength of 425 nm. The TFC was calculated using the linear regression equation and expressed in mg QE/L.

Total Anthocyanin Content (TAC) Determination

The sample was initially dissolved in KCl buffer pH 1, which was used to establish the proper dilution factor for the sample. The sample was put into several different vials. While the remaining vials received a pH 4.5 buffer solution (0.4 M CH_3COONa), the other vials received a pH 1 buffer solution (0.025 M KCl). After being incubated for 15 minutes, the absorbance of all test solutions was measured at 520 nm and 700 nm. The quantity of all anthocyanins was calculated using the calculation below:

$$TAC : ((A_{520}-A_{700})_{pH1.0} - (A_{520}-A_{700})_{pH4.5})/(\varepsilon \times l) \times MW \times DF \times 1000$$

Where, TAC stands for total anthocyanin content (mg Cyanidin-3-glucoside/L), A stands for absorbance of each wavelength at a different pH, Ɛ stands for molar absorptivity coefficient (26.900 L/mol.cm), MW stands for molecular weight (449.2 g/mol), DF stands for dilution factor, l stands for pathlength in cm (1 cm), and 1000 stands for the factor of conversion from g to mg.

Data analysis

The effect of sucrose and yeast extract and its optimal levels for fermentation of mangosteen fruit peels (*Garcinia mangostana* L.) were analyzed using ANOVA integrated with design expert software. Determination of the optimum condition based on the highest response of TPC, TFC, and TAC levels during 96 hours of fermentation.

RESULTS

Total Phenolic Content (TPC) Determination

The link between the standard concentration of gallic acid and its absorbance was calculated in this study and then obtained the equation y = 0.0094x - 0.1317 as shown in Figure 1. The results of the TPC determination can be seen in Table 2.

Figure 1. Gallic acid standard calibration curve

Table 2. Results of total phenolic content determination of lactic-acid-fermented mangosteen fruit peel

Sample	Replication	TPC (mg GAE/L)	Average Value of TPC (mg GAE/L) ± SD
Non-fermented mangosteen fruit peel (control)	1	592.65	593.62 ± 0.84
	2	593.93	
	3	594.25	
Run 1	1	665.96	666.10 ± 0.16
	2	666.10	
	3	666.28	
Run 2	1	684.47	684.47 ± 0.21
	2	684.26	
	3	684.68	
Run 3	1	791.91	792.20 ± 0.33
	2	792.13	
	3	792.55	
Run 4	1	681.06	681.17 ± 0.18
	2	681.06	
	3	681.38	

Total Flavonoid Content (TFC) Determination

The link between the standard concentration of quercetin and its absorbance was calculated in this study and then obtained the equation y = 0.0077x – 0.4372 as shown in Figure 2. The results of the TFC determination can be seen in Table 3.

Figure 2. Quercetin Standard Calibration Curve

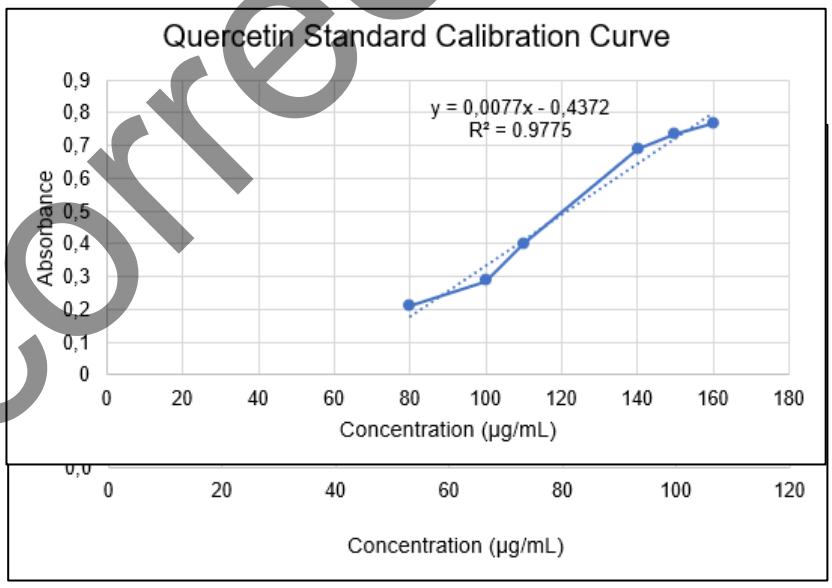


Table 3. Results of total flavonoid content determination of lactic-acid-fermented mangosteen fruit peel

Sample	Replication	TFC (mg QE/L)	Average Value of TFC (mg QE/L) ± SD
	1	200.13	200.03 ± 0.10

Non-fermented mangosteen fruit peel (control)	2	200.05	
	3	199.92	
Run 1	1	239.17	239.37 ± 0.19
	2	239.43	
	3	239.53	
Run 2	1	252.94	253.01 ± 0.33
	2	252.73	
	3	253.38	
Run 3	1	311.48	311.28 ± 0.19
	2	311.27	
	3	311.09	
Run 4	1	301.77	301.94 ± 0.96
	2	301.09	
	3	302.98	

Total Anthocyanin Content (TAC) Determination

Table 4. Results of total anthocyanin content determination of lactic-acid-fermented mangosteen fruit peel

Sample	Replication	TAC (mg C3GE/L)	Average Value of TAC (mg C3GE/L) ± SD
Non-fermented mangosteen fruit peel (control)	1	3.45	3.49 ± 0.03
	2	3.51	
	3	3.52	
Run 1	1	4.67	4.67 ± 0.04
	2	4.64	
	3	4.71	
Run 2	1	3.53	3.58 ± 0.05
	2	3.58	
	3	3.62	
Run 3	1	6.60	6.64 ± 0.21
	2	6.45	
	3	6.88	
Run 4	1	2.08	2.14 ± 0.05
	2	2.19	
	3	2.15	

Data Analysis

The data were inputted into software and analyzed using ANOVA integrated with design expert software which can be seen in Table 5.

Table 5. Data analysis

Source	**F value**	***p* value**	
Determination of Total Phenolic Content (TPC)			
Model	218642.77	<0.0001	significant
A-Sucrose	244356.76	<0.0001	
B-Yeast extract	139042.57	<0.0001	
AB	272698.57	<0.0001	
Determination of Total Flavonoid Content (TFC)			
Model	22933.01	<0.0001	significant
A-Sucrose	66446.12	<0.0001	
B-Yeast extract	109.11	<0.0001	
AB	2243.79	<0.0001	
Determination of Total Anthocyanin Content (TAC)			
Model	826.88	<0.0001	significant
A-Sucrose	16.24	0.0038	
B-Yeast extract	1796.47	<0.0001	
AB	667.93	<0.0001	

DISCUSSION

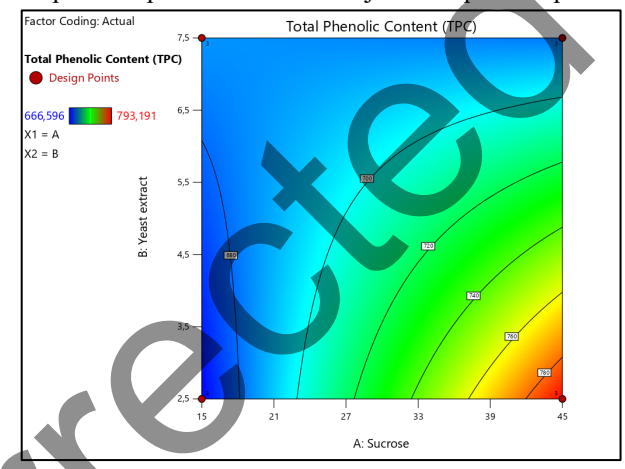
Mangosteen Fruit Peel Fermentation

Fermentation of mangosteen fruit peel was carried out using four Erlenmeyers, each filled with 100 g of mangosteen fruit peel dry simplicia, sucrose with a concentration between 15-45 g/L, yeast extract with a concentration between 2.5-7.5 g/L, lactic acid bacteria starter as much as 10 mL. The elements needed by lactic acid bacteria for growth and reproduction are carbon and nitrogen source, which can be obtained through sucrose and yeast extract.[19] Fermentation runs at room temperature, which is around 30ºC with constant stirring, where temperatures between 30 and 40ºC are ideal to promote the development of lactic acid bacteria.[22] Constant stirring during fermentation was also done on a shaker at 100 rpm. Constant stirring treatment at 100 rpm will improve lactic acid bacteria's rate of growth during fermentation.[23]

With microbes, the process of fermentation helps break down organic macromolecules into simpler ones.[9] The purpose of fermentation on mangosteen peel is to increase the phytochemical components contained in it, namely phenol group compounds, flavonoids, and anthocyanins produce fermentation by-products in the form of lactic acid which has many benefits. The production of organic acids that make the environment acidic will increase the solubility of phenolic compounds in water. The optimal pH in the extraction process of phenol compounds is in acidic conditions in the 3.0-5.3 pH range. The degradation of phenolic compounds is directly related to the pH level.[24]

In lactic acid fermentation, sucrose will undergo hydrolysis first to become the simplest sugar, namely glucose. Hexokinase, phosphogluconolactonase, and epimerase enzymes were produced by lactic acid bacteria that play a role in converting glucose through a series of chemical modifications. It also enters the phosphoketolase pathway and undergoes new chemical modifications to produce pyruvate, which can then be converted to lactic acid by the enzyme lactate dehydrogenase. The nitrogen source used in fermentation, namely yeast extract, also contains many nutrients in the form of vitamins, amino acids, and pyruvate so this will also affect the proliferation of lactic acid bacteria.[25]

The fermented mangosteen fruit peel samples will then be subjected to phase separation using a centrifuge at



6000 rpm for 20 minutes. Centrifugation is done to separate yeast extract, lactic acid bacteria, and powdered simplicia so that the fermentation process can be stopped. Sample centrifugation has a working principle, namely the application of centrifugal force and sedimentation to separate particles based on their specific gravity or density. The centrifugation results will separate two phases, namely supernatant, and pellet. The supernatant is the result of centrifugation with a lower specific gravity than pellets, while pellets are the result of centrifugation with a higher specific gravity than supernatant. The position of the pellet is located at the bottom of the centrifugation tube.[26] Water has a density of 0.99 g/mL, sucrose has a density of 1.6 g/mL, and yeast extract has a density of 1.4 g/mL. This shows that as compared to water, sucrose, and yeast extract have a larger density. So that the components of sucrose, yeast extract, and simplicia will be at the bottom of the tube.

Total Phenolic Content (TPC) Determination

The Folin-Ciocalteu and NaOH reagents were used in the spectrophotometric method of this study to measure TPC levels. The basic principle of using this method is the oxidation of phenolic-hydroxyl groups. Folin-Ciocalteu reagent will oxidize phenol and reduce heteropoly acids into a molybdenum tungsten (Mo-W) complex. When the sample is treated with the Folin-Ciocalteu reagent, a greenish-yellow hue is produced that indicates the presence of a phenolic compound. The amount of phenolic compounds present correlates exactly with the amount of blue color produced by this reaction.[27,28,29] TPC is expressed in mg gallic acid equivalents per liter (mg GAE/L).

Compared to the control group in this study, the total phenolic content of the lactic acid fermented mangosteen fruit peel was significantly higher. Lactic acid bacteria will produce several enzymes like β-glycosidase that play a role in β-glycoside hydrolysis, as well as the production of decarboxylase, esterase, hydrolase, and reductase which have a significant influence on increasing the phenolic levels in mangosteen fruit peel fermentation.[30,31,32] In addition, it is also influenced by the constant stirring carried out during fermentation. According to previous

research, constant stirring during fermentation will cause hydrolysis of the glycoside bond but will not degrade the phenolic aglycone.[33] The increase in phenolic components is also caused by the increment in extraction ability and the release of phenolic compounds from bound forms to free forms.[34] The contour plot of the relationship between sucrose and yeast extract concentration in mangosteen fruit peel fermentation to its total phenolic content can be seen in Figure 3.

Figure 3. Contour plot of the relationship between sucrose and yeast extract concentration in mangosteen fruit peel fermentation to its total phenolic content

Based on the *p* value of 0.0001, the contour plot of the TPC test results of mangosteen (*Garcinia mangostana* L.) fruit peel fermentation with different amounts of sucrose and yeast extract shows significant results. This value indicates that the mathematical model used to calculate the total phenolic content of the fermentation products can accurately capture the real conditions. The following linear equation represents the total phenol test results from the factorial design calculation.

$$Y = 6.36(A) + 16.66(B) - 0.83(A*B)$$

Where, Y= total phenolic content (TPC); A = sucrose; B = yeast extract; A*B = interaction between sucrose and yeast extract. Based on the equation obtained, it can be interpreted that an increase in sucrose and yeast extract components can increase total phenol content during fermentation. However, the interaction between the two can reduce the total phenol content. The resulting R-Squared value is 1.000 and the resulting pred R-Squared value is 1.000. This indicates that the predicted value is the same as the R-value generated through actual experiments. The resulting Adeq Precision value is 1016.4183. Adeq Precision is needed to measure the noise level of an experiment, and this value is expected to be more than 4.

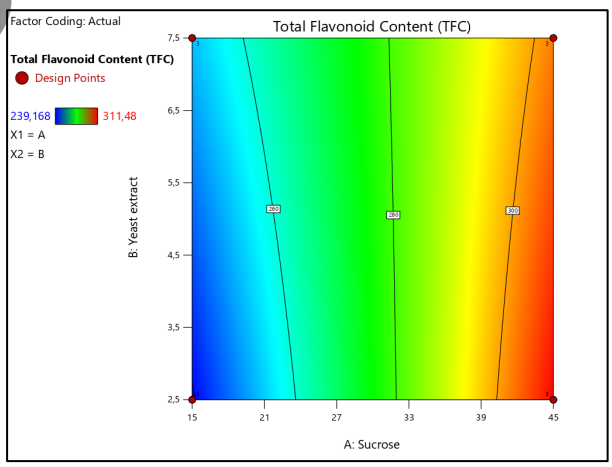
Total Flavonoid Content (TFC) Determination

The UV-Vis Spectrophotometric technique with an $AlCl_3$ and CH_3NOONa reagent was used in this work to determine the total flavonoid content. The basic principle of the use of this method is the great affinity to bind $AlCl_3$ metal ions to form Al(III)-flavonoid chelates. The addition of $AlCl_3$ will cause the OH group on C3 and C5 to form a stable complex so that the solution turns yellow. Furthermore, the addition of CH3NOONa is known to create an acidic atmosphere which will form a complex compound so that the solution turns pink where the absorbance will be measured. [35] TFC was measured at a wavelength of 425 nm using quercetin standards and $AlCl_3$ and CH_3NOONa reagents. TFC is expressed as the amount of quercetin in milligrams per liter of sample (mg QE/L) or mg quercetin.

A significant difference was found between the total flavonoid content of the lactic acid fermented mangosteen fruit peel and the control group in this study. The increase in flavonoid compounds is caused by changes in the environment, which becomes more acidic as a result of organic acid synthesis by lactic acid bacteria that triggers the release of bound flavonoid components and increases their availability in water in their free form.[36] Figure 4 shows the contour plot showing the relationship between the concentration of sucrose and yeast extract in the mangosteen fruit peel fermentation and the total amount of flavonoids present.

Figure 4. Contour plot of the relationship between sucrose and yeast extract concentration in mangosteen fruit peel fermentation to its total flavonoid content

Based on the *p* value of 0.0001, the contour plot of the TFC test results of mangosteen (*Garcinia mangostana* L.) fruit peel fermentation with different amounts of sucrose and yeast extract shows significant results. This value indicates that the mathematical model used to calculate the total flavonoid content of the fermentation results can accurately capture the real conditions. The following linear equation shows the results of the factorial design calculation for the total flavonoid assay.



$$Y = 2.768(A) + 4.957(B) - 0.148(A*B)$$

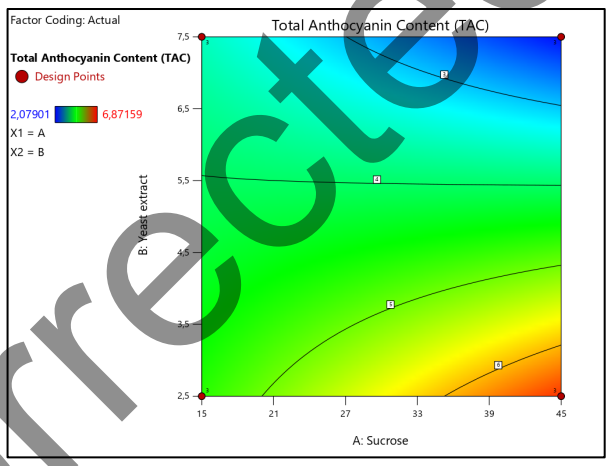
Where Y is total flavonoid content (TFC); A is sucrose; B is yeast extract; and A*B is the interaction between sucrose and yeast extract. According to the equation, an increase in the sucrose and yeast extract components can

increase the total flavonoid content during fermentation. However, the interaction between the two can decrease the total flavonoid content. The resulting R-squared value is 0.999, as is the resulting pred R-squared value. This means that the predicted value is the same as the R-value obtained from the experiments. The resulting Adeq Precision value is 434.3983. Adeq Precision is required to measure the noise level of an experiment, and this number is predicted to be greater than 4.

Total Anthocyanin Content (TAC) Determination

The difference in absorbance caused by the change in anthocyanin structure due to pH changes is what drives the differential pH technique used to measure total anthocyanin content. Anthocyanins in a strongly acidic condition at pH 1 have a colored flavylium cation (oxonium) form, while weak acidic conditions at pH 4.5 have a pseudo base carbinol (hemiketal) form that does not produce color. [37,38] At pH 4.5, the majority of anthocyanin monomers are in the hemiketal state, but there are polymerized anthocyanins and non-enzymatic browning pigments that are not reversible to pH changes and must be omitted from absorbance calculation.[37,39] As a result, the difference in absorbance values between pH 1 and 4.5 at the maximum wavelength of the anthocyanins is directly proportional to the anthocyanin content.[37]

In comparison to the control group, the mangosteen fruit peel's TAC was considerably greater. The use of sugar and yeast extract during fermentation contributes to the increase in TAC. Pyruvate from the fermentation process and yeast extract is converted to acetaldehyde during sucrose glycolysis, which acts as a terminal electron acceptor in the production of ethanol. Pyruvate and acetaldehyde are produced in the cytoplasm of yeast extracts and metabolized simultaneously, with pyruvate being decarboxylated to acetaldehyde or used to produce acetyl CoA. However, some of them will diffuse out of the cell and become reactive, allowing them to attack other molecules and facilitate the transition of anthocyanins into various derivative compounds such as proanthocyanins. The most important anthocyanin derivatives in fermentation products are proanthocyanin. Pyruvate and anthocyanins react to form proanthocyanin carboxy compounds (visitin type A), while acetaldehyde and anthocyanins react to form anthocyanin 3-O-glycoside-4-vinyl (visitin type B).[42] However, compared to the control group, run 4 has lower amounts of total anthocyanins. This is due to the degradation of anthocyanin compounds through hydrolysis by glucosidase and polyphenol oxidase enzymes, which break the



glycoside bond between the aglycone and glycone groups. The hydrolysis process converts anthocyanin molecules to the chalcone form and ultimately to aldehydes and phenolic acids. As a result, the component identified as cyanidin-3-glucoside on the spectrophotometer is lower in the test group than in the control group. Figure 5 shows a contour plot of the relationship between sugar and yeast extract concentration in mangosteen fruit peel fermentation and total anthocyanin content.

Figure 5. Contour plot of the relationship between sucrose and yeast extract concentration in mangosteen fruit peel fermentation to its total anthocyanin content

The contour plot of the TAC test results of mangosteen (*Garcinia mangostana* L.) peel fermentation with varying amounts of sucrose and yeast extract indicates significant results based on the *p* value of 0.0001. This figure shows how the equation model used can describe the actual conditions of calculating the total anthocyanin content of fermentation results. The results of the factorial design calculation for the total anthocyanin assay are shown in the linear equation below.

$$Y = 0.12(A) + 0.12(B) - 0.02(A*B)$$

Y is the total anthocyanin content (TFC), A is sucrose, B is yeast extract, and A*B is the reaction between the two. Based on the equation found, it can be deduced that during fermentation, an increase in the components of yeast extract and sucrose can lead to an increase in the total amount of anthocyanins. However, the combined anthocyanin content may decrease due to their interaction. The R-squared value obtained is 0.9968, while the pred R-squared value obtained is 0.9928. This shows that the R-value obtained from actual experiments and the

predicted value are identical. 68.2291 is the derived Adeq Precision value. To quantify the noise level of an experiment, Adeq Precision is required and this number is expected to be greater than 4.

CONCLUSION

The use of sucrose as a carbon source at a high concentration (45 g/L) and yeast extract as a nitrogen source at a low concentration (2.5 g/L) resulted in a significant increase in total phenol, flavonoid, and anthocyanin levels compared to the control group. An increase in the components of yeast extract and sucrose can lead to an increase in the concentration of total phenol, flavonoid, and anthocyanin. However, their interaction may decrease its concentration.

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