Optimization of Microwave Drying of *Aquilaria malaccensis* Leaves

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Abstract*— In this study, the operating condition of microwave drying of *Aquilaria malaccensis* leaves was optimized by Response Surface Methodology using existing data from the previous study. It is found that the extract from the *A. malaccensis* leaves have a promising potential in treating diabetic patients because of its anti-diabetic properties known as α-amylase inhibitor. In order to retain the valuable medicinal contents, the leaves were preserved using microwave drying prior to extraction process. Therefore, operating parameters of the microwave drying, such as power output and drying time, must to be optimized to obtain a better quality dried product and maximum α-amylase inhibitor activity. A face-centered Central Composite Design in the Design Expert Version 7.1.3 software program was employed to optimize the microwave drying process conditions. At the end of this study, the optimum operating conditions for the microwave drying process were obtained. The optimized operating conditions selected by the software for the microwave drying process are at power input of 150W and drying time of 9.35 minutes in which gave the desired lowest moisture content of 0.158538 kg H_2O/kg dry solids. The dried leaves obtained from these optimized conditions would result a maximum percentage of α-amylase inhibition of 96.77% with a combination of using ethanol solvent during the extraction process. The results from this study showed that a high percentage of α-amylase inhibition activity can be obtained from the extracts of *Aquiliria malaccensis* leaves that was preserved at optimized microwave drying conditions as stated here.

***Keywords*— Analysis of Variance, Central Composite Design, Microwave drying, Response Surface Methodology**

I. Introduction

According to recent estimates, the prevalence of diabetes mellitus has been increasing rapidly in global scale, every year. It has affected about 171 million people globally in the year 2000 and the number is expected to reach 366 million by 2030 [1]. Diabetes mellitus is a condition in which our body failed to metabolize the ingested sugars and starch due a deficient production of insulin by the pancreas. As a result, sugars will accumulate in the blood and urine which leads to many complications affecting the kidneys, heart, and nervous system [2].

One of the approach to treat diabetes is by increasing the insulin hormone secretion thus controls the glucose level in blood. Modern medical treatment for diabetes called insulin therapeutic treatment uses drugs such as Sulfonylureas, Metformin, and Meglinitides. However, insulin therapy still has its drawbacks. Hypoglycemia is the most common and serious side effect of insulin which could results in serious health problems and even death to the patients [3]. Therefore, finding alternative methods to control diabetes is crucial. One of the methods being studied is the inhibition of the activity of α-amylase enzyme. If the activity of α-amylase is inhibited, the glucose absorption in hyperglycemic individuals is also inhibited, thus maintaining the blood glucose level at normal level. There are many synthetic α-amylase inhibitors in the markets like Sulfonlurea, but they can cause uncomfortable side effects such as abdominal discomfort [4]. As an alternative, many researchers focused their studies in finding a more effective natural inhibitor from medicinal plants. A variety of plants has been reported to show α-amylase inhibitory activity and potential anti-diabetic properties; among them is the aqueous extract from *Aquilaria malaccensis* leaves.

A. malaccensis is a large evergreen trees occurring in the base of mountainous areas in Bangladesh, India, Malaysia, Thailand, Indonesia, and Philippines. The *Aquilaria spp.* has been traded internationally for the fungi-infected wood called ‘gaharu’ to be used as incense and perfumes [5]. The leaves, however, has a potential antidiabetic properties due to its bioactive constituents such as phytochemicals and phenolic compounds. Medicinal plants and their corresponding phytochemicals have been used to support and maintain good health for millennia. Therefore, processing and preservation of the leaves is the most important steps in order to preserve the bioactive constituents. Drying is the most common preservation method and it can be carried out using different methods at different temperatures. One of the drying techniques that stood out to be the most energy and time efficient is microwave drying. This technique outcast passive and lengthy conventional drying methods as it can give more uniform heat distribution to the materials and faster rate of drying [6]. However, adverse drying condition such as higher temperature and drying time during microwave drying of the *A. malaccensis* leaves can lead to the chemical and biological irreversible degradation which may alters the antidiabetic properties. Hence, it is crucial that drying process is performed under the optimized conditions so that the bioactive constituents can be maintained to a greater extent.

Therefore, the purpose of this research is to determine the optimum operating conditions of microwave drying of *A. malaccensis* leaves to obtain the quality dried product as well as to study the relationship between the optimised parameters and the inhibition activity of the α-amylase extracted from the dried leaves. Response surface methodology (RSM) is one of the most common optimization method used in many recent studies. RSM is useful in improvement and development of existing products properties by adopting the existing data from previous study. For this reason RSM was used to determine the optimum operating condition of microwave drying of *A. malaccensis* leaves.

II. METHODOLOGY

C. Experimental setup

All material and instrumentation set-up involved in this study were conducted in the previous research. The resulting data from the previous research was collected and used in this research as the main focus of this research is only to optimize the microwave drying of Aquilaria malaccensis leaves. Therefore, the sample preparation and analysis were described in general in this section.

Based on the previous research, the leaves of *Aquilaria malaccensis* were obtained from a habitat in Jalan Kebun, Shah Alam, Malaysia. Then, the leaves were dried in a microwave oven with different drying time and power output level. The power output level was set ranging to be at low, medium, and high for a certain amount of drying time. After that, the dried leaves were powdered and extracted before being analysed for its drying rate, total moisture content, and α-amylase inhibition activity. The extraction was conducted by ultrasonic-assisted extraction with 70% of aqueous ethanol solvent. The extracts were then subjected to the polyamide, silica gel, and Sephadex LH-20 column chromatography to track the α-amylase inhibitors presence. After that, the aqueous extracts will be concentrated on a rotary vacuum evaporator before being assayed using a substrate specifically known as p-nitrophenyl-a-D-maltopentaoside (PNPG5).

D. Optimization analysis

Based on the existing data from the previous research, the operating parameters of microwave drying were optimized by Response Surface Methodology (RSM) so that the optimum conditions for the microwave drying can be achieved. Design Expert Software (Version 10.0, Stat-Ease Inc.) was applied in this research to optimize the independent variables and also to predict the best value of responses. RSM is a collection of mathematical and statistical analysis. It is able to find a suitable approximation to the true value of responses [7].

The first step in RSM is to determine the order of polynomial. The most common form for RSM analysis is a second-order polynomial model because a first-order model suffers a lack of fit due to interaction between variables and surface curvature. Therefore, choosing second-order model can significantly improve the optimization process. A general second-order quadratic model is defined as below:

$$y = \beta_0 + \sum_{i=1}^{k} \beta_i X_i + \sum_{i<j}^{k} \beta_{i_j} X_i Y_i + \sum \beta_{i_i} X_i^2 \quad \text{Equation 1}$$

Where y = predicted response
x_i and x_j = input variables
Y = response variable
β_0 = the intercept
β_{i_j} = the interaction between x_i and x_j
β_{i_i} = quadratic effect of x_i

A central composite face-centered experimental design was chosen in this research because it is the most popular RSM design. This design contains three groups of design points known as two-level factorial design points, axial points, and center points. These points allow the estimation of curvature in the response surface contour plots and three-dimensional surface. It is also suitable for fitting a quadratic surface to optimize the variables with minimum number of experiments.

To determine the optimum operating conditions for the microwave drying process, a number of factors influencing the process were examined. For the first experimental data, the interaction between the variable X_1 (drying time: 0-20 seconds) and X_2 (power input: 50-150W) and their corresponding response Y_1 (moisture content) of each run were investigated. Meanwhile, for the second data, the interaction that was investigated is between variable X_3 (power input: 50-150W) and X_4 (solvent: water coded as -1, hexane coded as 0, ethanol coded as +1) and their corresponding response Y_2 (α-amylase inhibition). Analysis of variance (ANOVA) was applied to analyze the results and to achieve the best model of optimization.

III. RESULTS AND DISCUSSION

A. Experimental data for optimization with central composite design

The main focus of this research is to optimized the operating conditions of microwave drying of *Aquilaria malaccensis* leaves in an attempt to obtain the best conditions that will give the best response for α-amylase inhibition activity. The data to be optimized is obtained from the previous research where the leaves are dried using a microwave dryer at different drying time and power input prior to extraction process by ultrasonic-assisted extraction. The moisture content of the dried leaves after being subjected to a microwave dryer at different drying time and power input is tabulated in Table 4.1. While, the percentage of α-amylase inhibition extracted from the dried leaves using different types of solvents is tabulated in Table 4.2.

Table 4.1: Moisture content of the dried Aquilaria malaccensis leaves.

Power Input (Watt)	Types of Extraction Solvent	Percentage of α-Amylase Inhibition (%)
50	Ethanol	95.5455
	Hexane	5.87879
	Water	78.0000
100	Ethanol	96.2424
	Hexane	6.12121
	Water	78.3333
150	Ethanol	96.8485
	Hexane	6.30303
	Water	78.4242

Parameters of Microwave Drying		Moisture Content (kg H_2O/kg dry solids)
Power input (Watt)	Drying Time (minutes)	
50	0	0.609147172
	5	0.452659119
	10	0.320660489
	15	0.20565736
	20	0.137911966
100	0	0.609040932
	5	0.331953414
	10	0.236436477
	15	0.115710121
150	0	0.609022616
	5	0.203961654
	10	0.135436837
	15	0.072888295

Table 4.2: Percentage of alpha-amylase inhibition activity

According to the data tabulated in these tables, two experimental responses, which is moisture content (Response 1) and percentage of α-amylase inhibition (Response 2), were selected to be optimized by RSM with Central Composite Design

(CCD). A commonly used statistical package namely Design Expert Software (Version 10.0, Stat-Ease Inc.) was applied for optimization of these responses in attempt to find the best model for the microwave drying process. This software will also automatically design the minimum number of experiments (fully randomized) with regard to minimize the error due to the planning of the experiments.

From Table 4.1, drying time (X_1) and power input of the microwave dryer (X_2) were chosen as the major independent variables that affecting Response 1. Meanwhile, the types of solvent used (X_4) to extract the phenolic compounds from the leaves dried at different power input (X_3), form Table 4.2, were chosen as major variables that affecting Response 2. Each variables, specifically known as numeric factor, is varied over 5 levels in axial points (+ alpha, - alpha), factorial points (+1 level, -1 level) and the center point. The value for alpha is set to be equal to 1 in order to create a face-centered CCD. RSM analysis was fitted to a quadratic-order polynomial model to improve the optimization process.

The design of experiment for Response 1 and Response 2 are shown in Table 4.3 and Table 4.4 respectively. Total minimum number of experiments are 13 runs.

Table 4.3: Correlations of RSM for Response 1.

Run	Space Type	Factor 1	Factor 2	Response 1
		A: Drying time (minutes)	B: Power input (Watt)	Moisture content (kg H_2O/ kg of dry solid)
1	Unknown	15	150	0.0728883
2	Unkown	10	150	0.135437
3	Unkown	15	50	0.205657
4	Axial	0	100	0.609041
5	Unknown	5	150	0.203962
6	Factorial	0	150	0.609023
7	Unknown	5	50	0.452659
8	Unknown	20	50	0.137912
9	Axial	15	100	0.115710
10	Unknown	10	50	0.320660
11	Factorial	0	50	0.609147
12	Axial	5	100	0.331953
13	Axial	10	100	0.236436

Table 4.4: Correlations of RSM for Response 2.

Run	Space Type	Factor 1	Factor 2		Response 1
		A: Power input (Watt)	B: Solvent used	Coded as	Percentage of α-amylase inhibition (%)
1	Factorial	150	Ethanol	-1	96.8485
2	Factorial	150	Water	1	78.4242
3	Axial	100	Ethanol	-1	96.2424
4	Axial	100	Water	1	78.3333
5	Factorial	50	Ethanol	-1	95.5455
6	Axial	150	Hexane	0	6.30303
7	Center	100	Hexane	0	6.12121
8	Factorial	50	Water	1	78.0000
9	Axial	50	100		0.115710

B Analysis of variance and model adequacy checking

The results from experiments for optimization with central composite design were completely analyzed using analysis of variance (ANOVA). ANOVA is a statistical methods performed on three or more groups of numbers to test differences of means. It looks at the variation in the data and where the variation comes from. Hence, ANOVA specifically compares the amount of variation between the groups for observational and experimental studies. The results from ANOVA for the two responses (Response 1: moisture content, Response 2: percentage of α-amylase inhibition) are listed in Table 4.5. The table lists down the regression coefficients and the terms in empirical models based on Equation 1.

Table 4.5: Evaluation of regression coefficients for each response.

Types of Regression Coefficient	Response 1	Response 2
R-Squared	0.9491	1.0000
Adj. R-Squared	0.9127	1.0000
Pred. R-Squared	0.7348	0.9999
Adequate Precision	15.328	743.310
Term	**Response 1 (coefficient)**	**Response 2 (coefficient)**
Intercept	+0.16	+6.14
A	-0.24	+0.36
B	-0.075	-8.98
AB	-0.021	-0.22
A^2	+0.20	-0.066
B^2	$-1.197e^{-3}$	+81.13

From the table above, there are several types of regression coefficient namely R-Squared, Adjusted R-Squared, Predicted R-Squared and Adequate Precision. R-Squared is a squared multiple correlation coefficient or also known as Coefficient of Determination. It measures of the amount of variation around the mean explained by the model. If the calculated model has a perfect predictability, R-Squared will be equal/close to 1. While R-squared equal/close to 0 means the model has no predictive capability hence the overall variations will not fit the model (Dallal, 2012). The coefficient of R-Squared for Response 1 and Response 2 were 0.9491 and 1.0000 respectively.

Adjusted R-Squared is a measure of the amount of variation around the mean, adjusted for the number of terms in the model. Specifically, during adjustment process, adjusted R-Squared is always smaller. The coeficients for Adjusted R-Squared for Response 1 and Response 2 were 0.9127 and 1.0000 respectively.

Predicted R-Squared is a measure of the amount of variation in new data in the model. To avoid any problems with either the data or the model, the Predicted R-Suared and the Adjusted R-Squared should be within 0.20 of each other. The coefficients for the Predicted R-Squared for Response 1 and Response 2 were 0.7348 and 0.9999 respectively. This indicates that there are no problems with the data and the model as the difference between Predicted R-Squared and Adjusted R-Squared is less than 0.20 for both responses.

Adequate Precision indicates a signal to noise ratio. It generally compares the range of the predicted values at each design points to the average prediction error. The desired output for Adequate Precision is greater than 4. From Table 4.5, Adequate Precision for Response 1 and Response 2 were 15.328 and 743.310 respectively. This concludes that the model is “adequate” enough to navigate through the design space and is able to predict the response.

The regression equations obtained for the moisture content (Y_1) and percentage of α-amylase inhibition (Y_2) were as shown below:

$$Y_1 = 0.16 - 0.24X_1 - 0.075X_2 - 0.021X_1X_2 + 0.20X_1^2 - (1.197e^{-3})X_2^2 \quad \text{Equation 2}$$

$$Y_2 = 6.14 + 0.36X_3 - 8.985X_4 - 0.22X_3X_4 - 0.066X_3^2 + 81.13X_4^2 \quad \text{Equation 3}$$

The positive sign indicates that the variable gives a positive effect on the response and vice versa.

Table 4.6: Analysis of variance (ANOVA) table for response surface quadratic model.

Source (Response 1)	Sum of Squares	df	Mean Square	F value	p-value Prob>F	Rate of Significant
Model	0.45	5	0.089	26.10	0.0002	Significant
A-Drying Time	*0.054*	*1*	*0.054*	*15.64*	*0.0055*	
B-Power Input	*0.029*	*1*	*0.029*	*8.59*	*0.0220*	
AB	*8.513E-04*	*1*	*8.153E-04*	*0.25*	*0.6334*	
A^2	*0.023*	*1*	*0.023*	*6.59*	*0.0371*	
B^2	*3.855E-06*	*1*	*3.855E-06*	*1.126E-03*	*0.9742*	
Residual	0.024	7	3.425E-03			
Lack of Fit	*5.2*					
Pure Error	*0*					
Cor Total	0.47	12				
Source (Response 2)						
Model	13649.37	5	2729.87	1.213E+05	<0.0001	Significant
A-Drying Time	*0.77*	*1*	*0.77*	*34.28*	*0.0099*	
B-Power Input	*483.82*	*1*	*483.82*	*21497.23*	*<0.0001*	
AB	*0.19*	*1*	*0.19*	*8.58*	*0.0611*	
A^2	*8.622E-03*	*1*	*8.622E-03*	*0.38*	*0.5798*	
B^2	*13164.58*	*1*	*13164.58*	*5.849E+05*	*<0.0001*	
Residual	0.068	3	0.023			
Lack of Fit	*3*					
Pure Error	*0*					
Cor Total	13649.44	8				

Based on the Table 4.6, ANOVA carried out a statistical analysis to determine whether the factors were statistically significant and in reasonable agreement. The table summarizes the sum of squares, degree of freedom (*df*), mean square, F-value and p-value of each responses.

The most important statistical test in ANOVA is known as Fisher test (F-test) which is claculated by Model Mean Square divided by Residual Mean Square. It is used to determine the fitness of the proposed regression model to the data. The Mean Square value for the Model and Residual were 0.089 and 3.425e^{-3} for Response 1, while 2729.87 and 0.023 for Response 2. Dividing these values for each responses give us F-value of 26.10 for Response 1 and 1.213e^{5} for Response 2, indicating the models are highly significant. Based on the F-test, there is only 0.02% chance that the “model F-value” could occur due to noise for Response 1 and 0.01% chance of that in Response 2. The models were significant in terms of the independent variables at the 98-99% confidence level.

Prob>F value is the probability value (p-value) of seeing the observed F-value if the null hypothesis is true (there is no factor effect). If Prob>F value is less than 0.05, then the terms in the regression model in Equation 2 and 3 have a significant effect on the response. The values greater than 0.1 indicate that terms in the model not significant and hence, rejected. From Table 4.6, the p-value for Response 1 and Response 2 were 0.0002 and >0.0001 respectively. These values are well below 0.05, indicating that the null hypothesis is true and the model terms in Equation 2 and 3 are significant and correctly selected.

A large regression coefficients and a very small p-value exert a more significant effect on the respective response variables for the terms in the regression model. This is proven in this research whereby the the model terms in Equation 2 and 3 composed of a large regression coefficients of above 90% and smaller p-value of >0.0001 would result a significant effect on the respective response variables.

From the statistical analysis of ANOVA, it can be indicated that the estimated model for each responses fits the experimental data adequately. The predicted values were in reasonable agreement with the data. Furthermore, the good distribution of the data which is indicated by the F-value meaning that the choice of the operating parameters and their levels were acceptable.

C. Response surface plot of independent variable upon each responses

(a)

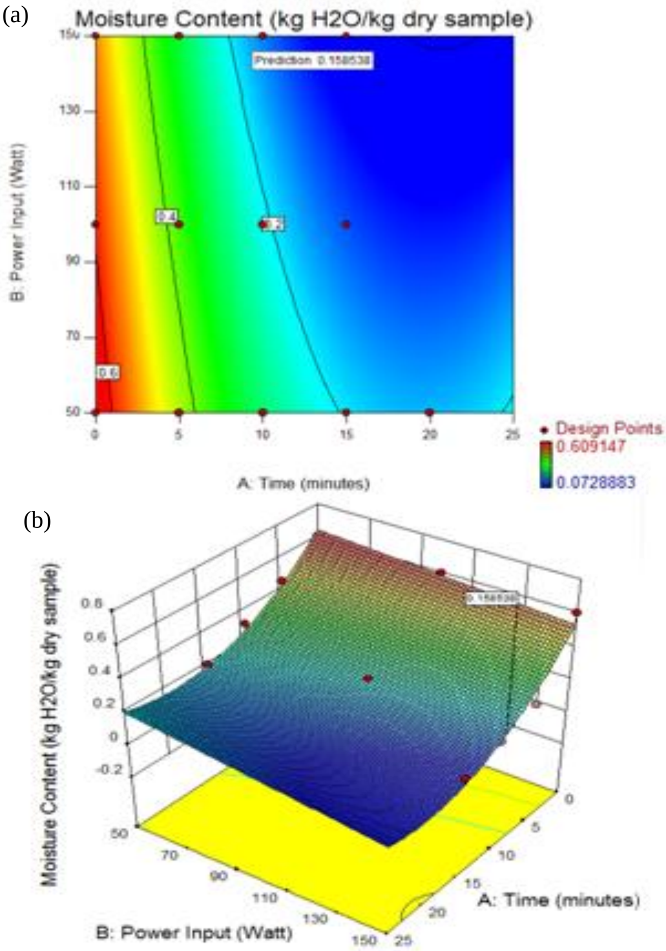

Figure 4.1: Effect of (a)response contour plot and (b)3-Dimensional surface view of drying time and power input on moisture content of dried *Aquilaria malaccensis* leaves.

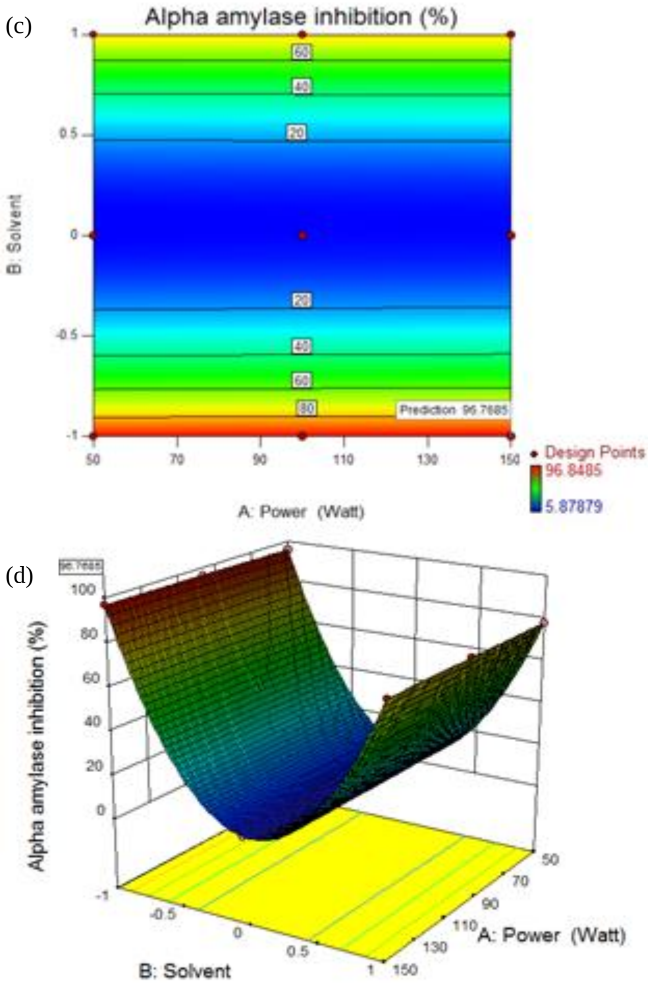

Figure 4.2: Effect of (c)response contour plot and (d)3-Dimensional surface view of power input and types of extraction solvent on the percetage alpha-amylase inhibition from Aquilaria malaccensis leaves.

After a complete statistical analysis by analysis of variance (ANOVA), the solutions to generate optimum conditions for microwave drying associated were done under Numerical Optimization. First step is to determine the goal for each independent variables and their responses. The goals can be set to be either maximized, minimized, in range, target, or equal to.

To optimize Response 1 (moisture content), the goals for drying time (X_1) and power input of the microwave dryer (X_2) were set to be 'in range' while Response 1 was set to be 'minimized'. In simpler words, we want to achieved the best drying conditions with adequate drying time and power input that removes a high moisture content from the *Aquilaria malaccensis* leaves. Doing this will optimize our process and thus save cost and energy. The effect of the Numerical Optimization was shown in Figure 4.1.

On the other hand, to optimize Response 2 (percentage of α-amylase inhibition), the same step was done but by setting the goal for the power input and the solvent type used to be 'in range' while Response 2 was set to be 'maximized'. In other words, we want to achieve the highest percentage of α-amylase inhibition activity with adequate power input and suitable solvent type. The effect from the Numerical Optimization was shown in Figure 4.2.

D.Process optimization and the relationship between the corresponding responses

From Figure 4.2, Response 1 was plotted as a function of drying time and power input where the desired optimum regions is highlighted in blue (the region where the moisture content is the lowest). 3-dimensional plot give a more accurate view of the response surface. It can be seen from the 3-dimensional plot that increasing drying time and power input will decrease the moisture content. However, from the set up goals, an adequate Response 1 could be ontained with a drying time of 9.35 minutes and the power input of 150W that would result only 0.158538 kg H_2O/kg dry *Aquilaria malaccensis* leaves. The desirability of this optimized condition was 72.5%.

From Figure 4.3, Response 2 was plotted as the function of power input and solvent type used where the desired optimum regions is highlighted in red (the region where the percentage of α-amylase inhibition activity is the highest). 3-dimensional plot of the response surface showed that the highest α-amylase inhibition activity was acquired by increasing the power input and using solvent type coded as -1. Therefore, form the set up goals, an adequate Response 2 could be obtained with power input of 150W and ethanol extraction solvent that would result 96.7685% of α-amylase inhibition activity. The desirability of this optimized condition was 99%.

Therefore, the optimized operating conditions selected by the software for the microwave drying process are as follows;

Table 4.7: Optimum values of the factors (process parameters) for the best response results.

Factor	**Optimum value**
Power input (W)	150
Drying time (minutes)	9.35
Extraction solvent	Ethanol
Responses	
Moisture content (kg H_2O/kg dry solid)	0.158538
Percentage of α-amylase inhibition activity (%)	96.7685

From the results, a relationship between microwave drying parameters and inhibition activity of alpha-amylase (α-amylase) extracted from *Aquilaria malaccensis* leaves was derived. Aquilaria malaccensis leaves that were dried at microwave dryer power of 150W for 9.35 minutes and then were extracted using ethanol solvent gave us the maximum percentage of α-amylase inhibition activity of 96.77%.

IV. CONCLUSION

The aim of this present study is to determine the optimum operating condition of microwave drying of *Aquilaria malaccensis* leaves by Response Surface Methodology (RSM) using existing data from the previous study. It is found that the extract from the leaves have a potential in treating diabetes mellitus because of its anti-diabetic medicinal content known as α-amylase inhibitior. Retaining the valuable anti-diabetic properties is crucial, thus a common preservation technique known as microwave drying is applied to preserved the leaves. Therefore, operating parameters of the microwave drying, such as power output, drying time and extraction solvent, must to be optimized to obtain a better quality dried product with highest percentage of α-amylase inhibition activity for the research.

Using a face-centered central composite design in RSM, the optimum operating conditions for the microwave drying process were obtained. The optimized operating conditions selected by the software for the microwave drying process are at power input of 150W and drying time of 9.35 minutes in which gave the desired lowest moisture content of 0.158538 kg H_2O/kg dry solids. The dried leaves obtained from these optimized conditions would result a maximum percentage of α-amylase inhibition of 96.77% with a combination of using ethanol solvent during the extraction process. A regression model in terms of a second-order quadratic equation were obtained from ANOVA analysis. ANOVA is carried out to determine whether the factors were statistically significant and in reasonable agreement. Based on the data in Table 4.5, the predicted R-squared values for Response 1 and Response 2 of were 0.9491 and 1.0000 respectively are in reasonable agreement with the adjusted R-squared values for Response 1 and Response 2 of 0.9127 and 1.0000 respectively. Meanwhile, the data in Table 4.6 showed that F-value of 26.10 for Response 1 and 1.213^{e^5} for Response 2, indicating the models are highly significant.

Based on this research, a high percentage of α-amylase inhibition activity can be obtained from the extracts of *Aquiliria malaccensis* leaves that was preserved at optimized microwave drying conditions as stated here. These valuable extracts can be used as a safer alternative for the synthethic alpha-amylase inhibitors that possess many side-effects.

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