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Optimum Parameters for Extraction of *Cinnamomum verum* Leaves Towards α-Glucosidase Inhibition

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ABSTRACT

Cinnamomum verum (kayu manis) is an herb that possesses antidiabetic properties and has been used for the treatment of diabetes traditionally. However, there is insufficient scientific data to provide optimum extraction parameters for *C. verum* leaves for antidiabetic activities. This research aims to determine the optimum extraction parameters of *C. verum* leaves towards α -glucosidase inhibition and evaluate the correlation between α -glucosidase inhibition, total phenolic content and DPPH radical scavenging activity. The *C. verum* was extracted with water through an infusion method under different temperatures (60.0°C, 77.5°C, 95.0°C) and extraction time lengths (10 minutes, 20 minutes, 30 minutes). The optimization process was designed using Design Expert software, which applied the Response Surface Method (RSM) and Central Composite Design (CCD). The analyses conducted were antidiabetic property (α -glucosidase inhibition assay), total phenolic content (TPC) (Folin-Ciocalteu colorimetric method) and antioxidant property (2,2-diphenyl-1-picrylhydrazyl, DPPH radical scavenging activity). Results showed that the obtained optimum extraction parameters for *C. verum* leaves (81.10°C, 19.54 minutes) exhibited α -glucosidase inhibition (87.30±0.67%), total phenolic content (0.12±0.00 mg GAE/g) and DPPH radical scavenging activity (51.25±0.48%). The

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Keywords: Antidiabetic, Cinnamomum verum, extraction parameter, infusion, Response Surface Method (RSM)

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INTRODUCTION

Globally, diabetes is a significant healthcare burden. According to projections made by the International Diabetes Federation (IDF), 536.6 million individuals worldwide will have diabetes in 2021 (whether diagnosed or not). By 2045, that figure will have increased by 46% to 783.2 million (Ogurtsova et al., 2022). In Malaysia, diabetes cases also showed a drastic increase (15.77 %), particularly in the prevalence of type 2 diabetes, which showed 14.39% (Akhtar et al., 2022). Three types of diabetes can be categorized: Type 1, Type 2, and gestational diabetes. Type 1 diabetes is an autoimmune disease caused by insufficient insulin production from β -cells. In contrast, the cause of type 2 diabetes is endocrine and metabolic disorders that lead to β -cell dysfunction in the pancreas and insulin resistance. For gestational diabetes, it can be caused by abnormal carbohydrate intolerance during pregnancy and eventually lead to maternal and fetal morbidity (Singab et al., 2014). There are several types of analyses for determining antidiabetic properties, and one of the methods is through α -glucosidase inhibition assay (Lee et al., 2019).

Cinnamomum verum, locally known as "kayu manis," is a Malaysian herb with antidiabetic properties (Pathak & Sharma, 2021; Singh et al., 2020). *C. verum* is an evergreen tree dispersed throughout tropical and temperate nations like Malaysia, Sri Lanka, and India. It also contributes about 70% of bark production worldwide (Fachriyah et al., 2018). *C. verum* is a traditional folk herb used in several treatments, such as antidiarrheal and anti-flatulent, and as a spice for culinary use. It also possesses antioxidant properties and phenolic content that can be used in pharmaceuticals (Tatipamula et al., 2021). *C. verum* has anti-inflammatory, antibacterial, and anticancer properties (Pathak & Sharma, 2021).

Extraction is a process of separating potential phytochemical compounds from herbal plants. The plant components will solubilize through the extraction process to obtain the crude extract that contains phytochemical contents (Nguyen et al., 2019). There are several types of extraction methods, such as infusion, decoction, maceration, and others. This study used an infusion method to extract the *C. verum* leaves. It is a process that extracts chemical compounds from plant materials in a solvent such as water, oil or alcohol by allowing the materials to remain suspended in the solvent over a certain period and is usually conducted at a temperature range of 60°C to 90°C (Katarzyna et al., 2019). A previous study reported that infusion extracts thermo-labile compounds under different extraction temperatures and extraction time lengths (Carmen et al., 2022). Both extraction parameters can affect the solubility and diffusion of *C. verum* and affect the efficiency of extraction (Nguyen et al., 2019; Singab et al., 2014).

In this study, the optimization process was crucial in evaluating the optimum parameters or conditions for a certain process, and one of the common tools in the optimization process is response surface methodology (RSM). RSM combines modeling strategies, optimization techniques, design, and analysis experiments that utilize experimental data to improve processes (Jakub & Agnieszka, 2021). This research aims to determine the optimum extraction parameters of *C. verum* leaves on α -glucosidase inhibition through Design Expert software by applying RSM and central composite design (CCD). Besides that, the correlation between α -glucosidase inhibition, total phenolic content and DPPH radical scavenging activity was also evaluated.

MATERIALS AND METHODS

Chemicals and Reagents

The chemicals used were p-nitrophenyl-D-glucopyranoside (pNPG), α -glucosidase, quercetin, Folin-Ciocalteu reagent, gallic acid monohydrate, sodium carbonate that are from Sigma-Aldrich, United States. Meanwhile, 2,2-diphenyl-1-picrylhydrazyl (DPPH) is from Calbiochem, Germany, whereas methanol is from Fisher Scientific, United States.

Preparation of Plant Materials

Cinnamomum verum leaves were collected from Nasuha Herbs & Spice Farm, Muar, Johor, Malaysia, in August 2021 and authenticated by Associate Professor Dr. Alona Cuevas Linatoc, a botanist from Universiti Tun Hussein Onn Malaysia (UTHM) with the voucher specimen number (NYM-02-20).

Sample Extraction

The *C. verum* leaves were cleaned and dried by drying oven (UN160, Memmert, Cyprus), under temperature of 60°C until the moisture content of dried leaves reached lower than 10% when tested with a moisture analyzer (MS-70, A&D Weighing, United Kingdom). It was grounded into powder form using a blender (MX-V310KSL, Panasonic, Malaysia) and stored in a desiccator at room temperature $(27^{\circ}C-30^{\circ}C)$ to retain its moisture. The dried powder was weighed at about 10 g, and it was added with 2 L of distilled water through an infusion method at different extraction temperatures (60.0°C, 77.5°C, 95.0°C) and extraction time lengths (10 minutes, 20 minutes, 30 minutes). The filter paper (Nice) with a size of 24 cm diameter was used to filter the extract, and it was stored in a chiller (4°C) for further analysis.

Experimental Design

In this study, the Design Expert software (version 6.0.4, USA) produced 11 experimental runs through Response Surface Methodology (RSM) coupled with Central Composite Design (CCD) to determine the optimum extraction parameters for achieving maximum α -glucosidase inhibition of *C. verum* leaves as shown in Table 1. The independent variables were the extraction temperature (X₁) and extraction time length (X₂), while the dependent

Table 1

variables were α -glucosidase inhibition assay (Y₁), total phenolic content (Y₂) and DPPH activity (Y₃).

Antidiabetic Property (α-Glucosidase Inhibition Assay)

The antidiabetic property of extracts was determined through α -glucosidase inhibition assay with slight modifications (Lee et al., 2019). The *C. verum* leaf extract was prepared in a concentration of 0.05 mL/mL, and quercetin was used as the positive control at different concentrations (0.01 M, 0.001 M, 0.0001 M, and 0.000001 M). The α -glucosidase enzyme

	Run	Extraction	Extraction time
	order	temperature, X ₁ (°C)	length, X_2 (min)
	1	60.0	20
	2	60.0	10
	3	77.5	10
	4	95.0	20
	5	95.0	30
	6	95.0	10
	7 ^a	77.5	20
	$8^{\rm a}$	77.5	20
	9ª	77.5	20
	10	77.5	30
	11	60.0	30
-			

Design layout for optimization process by using RSM

Notes. (a) center point

(0.01 U/mL) and *p*-nitrophenyl-D-glucopyranoside (pNPG) substrate were prepared in 1 mM phosphate buffer (pH 6.8). In each cuvette, the sample (20 μ L) was added with 20 μ L of α-glucosidase and 75 μ L of phosphate buffer; the solution was preincubated at 25.0°C for 10 minutes. After preincubation, pNPG (50 μ L) was added into the solution and re-incubated at 25°C for 5 minutes. The absorbance of the mixture was determined by using a UV-Vis-spectrophotometer (T60, PG Instruments, UK) at a wavelength of 405 nm. Sodium carbonate (0.2 M) was used to terminate the reaction. The higher inhibitory rate indicates the solution has a higher potential to inhibit the α-glucosidase, and the inhibition rate was calculated using Equation 1:

$$Inhibition (\%) = \frac{A \ control - A \ sample}{A \ control} \times \ 100$$
[1]

Where, A control: absorbance of control solution; and A sample: absorbance of sample solution.

Total Phenolic Content (TPC)

As in a previous study, the total phenolic content (TPC) was analyzed using the Folin-Ciocalteu colorimetric method with minor modifications (Ainsworth & Gillespie, 2007). The standard solutions were prepared using gallic acid monohydrate at different concentrations, which are 0 mg/mL, 20 mg/mL, 40 mg/mL, 60 mg/mL, 80 mg/mL, and 100 mg/mL through serial dilution. Then, gallic acid solution (0.5 mL) was inserted for each concentration into a test tube filled with Folin-Ciocalteu reagent (1 mL) and distilled water (9 mL). About 0.5 mL of 7.5% sodium carbonate solution was added to the mixture and was stored in a dark place for 2 hours (Ainsworth & Gillespie, 2007; Kunyanga et

al., 2012). These standard solutions were inserted into the UV-Vis-spectrophotometer to measure the absorbance at a wavelength of 725 nm, and the results were recorded using a standard calibration curve (Bisceglie et al., 2014). The *C. verum* leaf extract was treated with the same method as standard, and the TPC value of the leaf extract was calculated using Equation 2, and it was expressed as gallic acid equivalent (mg GAE/g):

$$TPC = C \times \frac{V}{m}$$
 [2]

Where, C: Concentration of gallic acid from the calibration curve; V: volume of the extract used; and m: mass of the extract used.

Antioxidant Activity (DPPH Radical Scavenging Activity)

The 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity was carried out to test the antioxidant activity of the *C. verum* leaves (Vinci et al., 2022). The concentration of *C. verum* leaf extract used was 0.05 mL/mL. Then, the sample was pipetted into 2 mL of DPPH solution (prepared by dissolving DPPH in methanol) in a test tube and wrapped with aluminum foil. The test tubes of all samples were vortexed and placed in a dark place for 30 minutes. The incubation length was 30 minutes, and the *C. verum* leaf extract's absorbance was measured using a UV-Vis-spectrophotometer at a wavelength of 517 nm (Irda, 2015). The percentage of inhibition of DPPH radical scavenging activity was calculated based on the value of absorbance through the following Equation 3:

Antioxidant Activity (%) =
$$\frac{A \text{ control} - A \text{ sample}}{A \text{ control}} \times 100$$
 [3]

Where, $A_{control}$: absorbance of control solution; and A_{sample} : absorbance of sample solution.

Statistical Analysis

Each studied analysis was done in triplicates for each run. The mean for the triplicate value of α -glucosidase inhibition, TPC and DPPH radical scavenging activity was measured and analyzed to determine the extracts that possess the highest potential in α -glucosidase inhibition. The statistical analysis and the result of analysis of variance (ANOVA) were carried out by using Design Expert 6.0.4® (State Ease, Inc) and SPSS ® (IBM, 1.0.0.1406, United Kingdom) software, and it shows a significant difference when *p*<0.05 (Giovanni et al., 2020).

RESULTS AND DISCUSSION

Model Fitting

Model fitting is important in showing the mathematical model of RSM for optimization of extraction parameters of *C. verum* leaves on different analyses studied. Table 2 shows the

polynomial equation generated through Design Expert software to fit all the independent variables and their responding dependent variables. The positive sign indicates a synergistic effect for each equation, whereas the negative sign represents an antagonistic effect (Jakub & Agnieszka, 2021; Rahim et al., 2022).

Equations
$X_1 = 86.63 + 5.25 X_1 - 1.69 X_2 - 6.54 X_1^2 - 3.36 X_2^2 - 2.72 X_1 X_2$
$X_2 = 0.10 + 0.01 X_1 + 5.03 e^{-003} X_2$
$X_3 = 50.53 + 8.02 X_1 + 7.81 X_2 - 13.48 X_1^2 - 10.53 X_2^2 - 2.58 X_1 X_2$

 Table 2

 Polynomial equations of Cinnamomum verum leaves extract

Notes. (X₁) extraction temperature (°C), (X₂) extraction time length (minutes)

Table 3 shows the ANOVA for the *p*-value and F-value for *C. verum* leaf extract for all analyses. Table 3 presented that the *p*-values for the model of all analyses were less than 0.05. Meanwhile, the F-values achieved were greater than 1 for a-glucosidase inhibition (220.94), TPC (15.42) and DPPH radical scavenging activity (1266.93). All analyses are significant as the *p*-value is less than 0.05 and the F-value is greater than 1 (Eleni, 2010). Besides that, *p*-values for the lack of fit on all analyses obtained were larger than 0.05, which indicates insignificant, and this signifies that the data was fitted to the model obtained (Duarte et al., 2021).

Table 3ANOVA for Cinnamomum verum leaf extract

Desmonaes	ANOVA					
Responses	Sum of squares	DF	Mean square	F-value	<i>p</i> -value	Lack of fit
α-Glucosidase inhibition	391.1900	5	78.2400	220.9400	< 0.0001	0.5503
TPC	0.0008	2	0.0004	15.4200	0.0018	0.0665
DPPH radical scavenging activity	1783.1300	5	356.6300	1266.9300	< 0.0001	0.5965

Notes. Degree of freedom (DF), total phenolic content (TPC)

Optimization of Extraction Parameters

Table 4 shows the results of different analyses on the influence of extraction temperature and extraction time length of *C. verum.* It shows that the percentage of α -glucosidase inhibition has a higher value in run orders 4, 6, 7, 8 and 9, which are 85.81±0.98%, 86.34±0.49%, 86.34±0.49%, 86.13±0.49% and 86.45±1.33%, respectively, with no significant difference among each other. The extraction conditions for these run orders were at 77.5°C and 95.0°C, and extraction time lengths of 20 and 30 minutes. The results

revealed that this range of extraction temperature and extraction time length show a high α -glucosidase inhibition activity, which is similar to the previous study that reported the effect of high extraction temperature (98°C) and extraction time length (20 and 30 minutes) give a high α -glucosidase inhibition of *Cinnamomum burmannii* (Ervina et al., 2019). Whereas the run orders 2 (70.86 \pm 0.32%) and 11 (72.57 \pm 0.74%) showed the lowest percentage of a-glucosidase inhibition. It may be because the phenolic compounds present in the Cinnamomum species extracts might be degraded at low extraction temperature and extraction time length in a short period, and this may contribute to a lower potential of α -glucosidase inhibition. One of the phenolic compounds contributing to the antidiabetic activity is coumarin, which exists in C. verum leaf extract (Goyal et al., 2018). It is supported by the previous study by Matsumura et al. (2000) that stated the coumarin was diffused out from leaves as the temperature of water increased and bound with α -glucosidase active site to inhibit α -glucosidase in the process of glucose production and eventually reduce blood glucose level. However, as the duration of extraction time length increased, it shows the α -glucosidase inhibition percentage reduced, which may be influenced by the presence of phenolic compounds in C. verum leaves extract has been denatured as the extracts immersed in high temperature of water for a long period (Antony & Farid, 2022).

Extraction parameters Analyses Sample Antidiabetic Antioxidant activity Extraction Extraction / Run temperature, time length, TPC, Y_2 (mg DPPH radical scavenging α-Glucosidase order $X_1 (^{\circ}C)$ X₂ (minutes) inhibition, Y_1 (%) GAE/g) activity, Y₃ (%) 1 60.0°C 20 74.39±2.42^{dc} $0.0912{\pm}0.00^{\rm f}$ 29.33±0.36^{gh} 2 60.0°C 10 70.86±0.32° 0.0910 ± 0.00^{f} 7.98 ± 0.46^{i} 3 77.5°C 10 84.63 ± 1.78^{ab} $0.0914{\pm}0.00^{\circ}$ 31.99 ± 0.13^{f} 4 95.0°C 20 85.81±0.98^a 0.0950±0.00^a 44.46±0.16^d 5 95.0°C 30 77.16±0.49° 0.1061 ± 0.00^{a} 40.05±0.20° 6 95.0°C 10 86.34±0.49^a $0.1083{\pm}0.00^{\rm d}$ 29.62 ± 0.28^{g} 7 77.5°C 51.25±0.48^a 20 86.13±0.49^a 0.1101±0.00^{cd} 8 77.5°C 20 86.45±1.33ª 0.1151±0.00^{cb} 50.51±0.29^{ab} 9 77.5°C 20 87.30±0.67ª 0.1054±0.00b 50.14±0.19^b 10 77.5°C 30 $81.96{\pm}0.81^{b}$ $0.1149{\pm}0.00^{a}$ 47.69±0.11° 72.57±0.74de 11 60.0°C 30 0.1156±0.00f 28.72 ± 0.06^{h}

Table 4The effect of extraction temperature and extraction time length for all analyses

Notes. a-h Means different letters at each column indicate significant differences (p < 0.05), value is presented as mean \pm SD (n=3), total phenolic content (TPC)

In addition, it shows that the TPC values for run orders 4, 5 and 10 are similar, which are $0.0950\pm0.00 \text{ mg GAE/g}$, $0.106\pm0.00 \text{ mg GAE/g}$ and $0.1149\pm0.00 \text{ mg GAE/g}$, respectively, as there are no significant different (p < 0.05). The high TPC values can be obtained at

temperatures of 77.5°C and 95.0°C with an extraction time of 30 minutes. It indicates that the TPC values increased as the temperature increased. A previous study has shown a similar result with the extract of Matricaria chamomilla that was prepared by infusion method at extraction temperatures of 80.0°C and 100.0°C for 10 minutes displayed an increase of TPC values as the extraction temperature increased (Sotiropoulou et al., 2020). The extraction time length in this previous study is only 10 minutes, which may be due to the extraction temperature being slightly higher than in this study, which could degrade the compounds present in the plants when the duration of extraction is longer (Romero et al., 2020). Whereas run orders 1, 2 and 11 showed the lowest phenolic content with no significant difference (p>0.05) at the condition of 60.0°C, 10 min; 60.0°C, 20 min, and 60.0° C, 30 min, respectively because at medium temperature (60.0° C), the cell wall of plants broke down in slower rate to allow the diffusion of phenolic compounds into the surrounding solution. However, the phenolic compound was increased with extraction time length because this provides sufficient time for the phenolic compound to diffuse out from the leaves (Nguyen et al., 2019). High TPC indicates a high potential for antidiabetic, as proven in the previous study where the phenolic compounds of Origanum majorana leaves can show significant hypoglycemic effect and α -glucosidase inhibitory activity in rat intestines (Tatipamula et al., 2021).

Moreover, the antioxidant of *C. verum* leaf extracts is determined by DPPH radical scavenging activity. Run orders 7 and 8 have a high antioxidant ability, with the percentage of inhibition obtained at $51.25\pm0.48\%$ and $50.51\pm0.29\%$ with no significant difference (p> 0.05). It might be because of the presence of polyphenols in the extract of these run orders that could contribute to inhibiting the DPPH radicals by providing hydrogen atoms and turning them into colorless compounds (Alaraa et al., 2018; Kodagoda et al., 2023). Based on a previous study shows that the extract of *Garcinia forbesii* can reduce serum glucose levels, and it also possesses a strong radical scavenging activity; this indicates that the remedy with stronger antioxidation activity may also come along with high antidiabetic potential (Wairata et al., 2021).

Mixture Proportion Optimization

Figures 1, 2, and 3 show the response surface plot of *C. verum* for the interaction effect between the extraction temperature and extraction time length on different analyses. Figure 1 shows the response surface plot on the percentage inhibition of α -glucosidase assay. It shows that when the water temperature was at 95.0°C and the extraction time length was 10 minutes, it exhibited a high value of α -glucosidase inhibition, between 88.30% and 83.84%. Whereas, when the *C. verum* leaves were soaked in the water at 60.0°C and extraction time length of 10 minutes, they showed a lower value of α -glucosidase inhibition, which is 70.45%. It displays a trend that the percentage of α -glucosidase inhibition will increase as the temperature increases. However, the high temperature will also reduce the α -glucosidase inhibition activity due to the loss of phenolic compounds (Matsumura et al., 2000). Doctor et al. (2020) supported this by showing that the phenolic compounds might partially degrade after being heated to 200.0°C for 60 minutes.

Figure 2 shows the response surface plot on the total phenolic content (TPC) assay. It shows a high value of TPC was achieved when the extraction condition was at 95.0°C of extraction temperature and 30 minutes of extraction length, which is 0.12 mg GAE/g. It is comparable to the previous study, where the TPC increased because the cell wall

can be easily broken down under high temperatures, and prolonged extraction time length can provide sufficient time to break down cellulose to release phenolic compounds (Kunyanga et al., 2012).

Figure 3 shows the response surface plot on DPPH radical scavenging activity. The result showed that a high percentage of DPPH radical scavenging activity (52.00%) can be obtained at 95°C with an extraction time of 30 minutes. This result showed that the DPPH radical scavenging activity could be increased as the temperature increases but decreased when extracted at a longer extraction time. The longer extraction time



Figure 2. Response surface plot of *C. verum* leaves extract showing the effect of extraction temperature and extraction time length on total phenolic content



Figure 1. Response surface plot of C. verum leaves extract showing the effect of extraction temperature and extraction time length on α -glucosidase inhibition percentage



Figure 3. Response surface plot of *C. verum* leaves extract showing the effect of extraction temperature and extraction time length on DPPH radical scavenging activity

length might cause polyphenol degradation and, indeed, affect the antioxidant ability of the *C. verum* leaves (Antony & Farid, 2022). Phenolic compounds have redox characteristics that provide antioxidant activity as the hydroxyl group in plant extracts facilitates the scavenging of free radicals by the plant (Aryal et al., 2019). Hence, it can be concluded that TPC and DPPH radical scavenging activity are responsible for assessing antioxidant activity. Besides, DPPH radical scavenging activity has been widely used as it demonstrates a shorter time for analysis globally (Baliyan et al., 2022).

Validation of the Model

Table 5 shows the validation values at an optimum *C. verum* leaves extract extraction condition. By using statistical software, the optimum extraction condition was found by maximizing the desirability responses, which are near to 1. The optimum extraction condition obtained was at an extraction temperature of 81.10°C with an extraction time of 19.5 minutes. At this condition, the a-glucosidase inhibition was 83.51%, TPC values achieved was 0.12 mg GAE/g, and DPPH radical scavenging activity was 49.21%. The model's validity was evaluated by the percentage of error achieved from the experimental and predicted values generated from Design Expert software. The error percentage should be below 5% to be considered valid and reliable as it showed a high confidence level (95%) with the true value of coverage probability (Liu et al., 2018). Table 5 shows that the validation value of all conducted analyses is below 5%, indicating a low percentage of error, and the results are reliable.

Responses	Predicted value	Experimental value	Percentage of error (%)
α-Glucosidase inhibition (%)	87.30	83.51	4.34
TPC (mg GAE/g)	0.11	0.12	2.00
DPPH radical scavenging activity (%)	51.27	49.21	4.01

Experimental data of validation values at optimum extraction condition of Cinnamomum verum leaves extract

Notes. Total phenolic content (TPC)

Correlation Analysis

Table 5

The correlation analysis was conducted among different analyses: α -glucosidase inhibition activity, total phenolic content (TPC) and DPPH activity, as presented in Table 6. It showed that α -glucosidase inhibition positively correlates with the TPC (0.63) and DPPH radical scavenging activity (0.76). It has been proven in previous studies that phenolic compounds possess high antioxidant activity along with high antidiabetic potential (Dias et al., 2020; Tatipamula et al., 2021). It indicates that a-glucosidase inhibition increases as TPC and DPPH activity increases. Similar outcomes have appeared for the correlation of TPC and DPPH activity with other analyses. It is portrayed in Table 4 for run orders

A	analyses	Pearson correlation	Significant different (p-value)	
α-Glucosidase inhibition	TPC	0.63	0.0438	
α-Glucosidase inhibition	DPPH radical scavenging activity	0.74	0.0481	
TPC	DPPH radical scavenging activity	0.76	0.0189	

Table 6 Correlation analysis between analyses

Notes. Total phenolic content (TPC)

7 and 8 for the TPC and antioxidant activity, whereas the antioxidant activity increases with increased extraction temperature and time.

CONCLUSION

In a nutshell, we can deduce that the optimum extraction condition obtained was at an extraction temperature of 81.10°C with an extraction time length of 19.5 minutes exhibiting α -glucosidase inhibition, 87.30%, TPC, 0.11 mg GAE/g and DPPH radical scavenging activity, 51.27%. Besides that, the correlation analysis showed that the α -glucosidase inhibition positively correlates with the TPC and DPPH radical scavenging activity. Therefore, these findings can benefit the herbal industry as the optimum extraction parameters achieved can be a guideline for developing herbal products, particularly on products involving *C. verum* leaf extract.

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REFERENCES

- Alaraa, O., Hamid, N., & Azharic, N. (2018). Vernonia cinerea leaves as the source of phenolic compounds, antioxidants, and anti-diabetic activity using microwave-assisted extraction technique. Industrial Crops & Products, 122(1), 533–544. https://doi.org/10.1016/j.indcrop.2018.06.034
- Akhtar, S., Nasir, J. A., Ali, A., Asghar, M., Majeed, R., & Sarwar, A. (2022). Prevalence of type-2 diabetes and prediabetes in Malaysia: A systematic review and meta-analysis. *PloS One*, 17(1), Article e0263139. https://doi.org/10.1371/journal.pone.0263139
- Ainsworth, E. A., & Gillespie, K. M. (2007). Estimation of total phenolic content and other oxidation substrates in plant tissues using Folin-Ciocalteu reagent. *Journal of Nature Protocols*, 2(4), 875–877. https://doi. org/10.1038/nprot.2007.102

- Antony, A., & Farid, M. (2022). Effect of temperatures on polyphenols during extraction. *Applied Sciences*, 12(4), Article 2107. https://doi.org/10.3390/app12042107
- Aryal, S., Baniya, M. K., Danekhu, K., Kunwar, P., Gurung, R., & Koirala, N. (2019). Total phenolic content, flavonoid content and antioxidant potential of wild vegetables from Western Nepal. Plants, 8(4), Article 96. https://doi.org/10.3390/plants8040096.
- Baliyan, S., Mukherjee, R., Priyadarshini, A., Vibhuti, A., Gupta, A., Pandey, R. P., & Chang, C. M. (2022). Determination of antioxidants by DPPH radical scavenging activity and quantitative phytochemical analysis of *Ficus religiosa*. *Molecules*, 27(4), Article 1326. https://doi.org/10.3390/molecules27041326
- Bisceglie, F., Pinelli, S., & Goldoni, M. (2014). Cinnamaldehyde and cumin aldehyde thiosemicarbazones and their copper and nickel complexes: a study to understand their biological activity. *Inorganic Biochemistry*, 140(1), 111–125. https://doi.org/10.1016/i.jinorgbio.2014.07.014
- Carmen, S. M., Benjamin, F. A., Vicente, S. S., Julissa, S. B., Lisette A. F., Alejandra, A. D., & Maria, E. Z. (2022). Antioxidant and antimicrobial capacity of *Maytenus boaria* leaves recovery by infusion and solvent extraction. *Electronic Journal of Biotechnology*, 56, 47–53. https://doi.org/10.1016/j.ejbt.2022.02.002
- Duarte, A. W., Bonugli-Santos, R. S. Duarte, A. L., & Gomes, E. (2021). Statistical experimental design applied to extracellular lipase production by the marine Antarctic yeast *Leucosporidium*. *Biocatalysis* and Agriculture Biotechnology, 32, 102-110. https://doi.org/10.1016/j.bcab.2021.101954
- Doctor, N., Parker, G., Vang. K, Smith, M., Berkant, K., & Yang, Y. (2020). Stability and extraction of vanillin and coumarin under subcritical water conditions. *Molecules*, 25(5), Article 1061. https://doi.org/10.3390/ molecules25051061
- Dias, C., Fonseca, A. M., Amaro, A. L., Boas, A., Oliveira, A., & Santos, S. A. (2020). Natural-based antioxidant extracts as potential mitigators of fruit browning. *Antioxidants*, 9(8), Article 715. https://doi.org/10.3390/ antiox9080715
- Ervina, M., Lie, H. S., Diva, J., Caroline, Tewfik, S., & Tewfik, I. (2019). Optimization of water extract of *Cinnamomum burmannii* bark to ascertain its in vitro antidiabetic and antioxidant activities. *Biocatalysis* and Agricultural Biotechnology, 19, Article 101152. https://doi.org/10.1016/j.bcab.2019.101152
- Fachriyah, E., Ariestiani. B., & Khikmah, L. (2018). Antidiabetic activity from cinnamaldehyde encapsulated by nanochitosan. *Conference on Materials Science and Engineering*, 349(1), 25–31. https://doi. org/10.1088/1757-899X/349/1/012048
- Goyal, M., Kaur, H., Bhandari, M., Rizvanov, A. A., Khaiboullina, S. F., & Baranwal, M. (2018). Antioxidant and immune effects of water soluble polysaccharides isolated from *Cinnamomum verum* bark. *Bio Nano Science*, 8(3), 935–940. https://doi.org/10.1007/s12668-018-0542-3
- Jakub, R., & Agnieszka, D. (2021). Application of response surface methodology (RSM) for the optimization of chromium (III) synergistic extraction by supported liquid membrane. *Membranes*, 11(11), Article 854. https://doi.org/10.3390/membranes11110854
- Kunyanga, C. N., Imungi J. K., & Okoth, M. W. (2012). Total phenolic content, antioxidant and antidiabetic properties of methanolic extract of raw and traditionally processed Kenyan indigenous food ingredients. *Journal of Food Science and Technology*, 45(2), 269–276. https://doi.org/10.1016/j.lwt.2011.08.006

- Katarzyna, J., Karolina, J., Patrycja, K., Mateysz, B., & Izabela, G. (2019). Mineral composition and antioxidant potential in the common poppy (*Papaver rhoeas*) petal infusions. *Biological Trace Element Research*, 199, 371–381. https://doi.org/10.1007/s12011-020-02134-7
- Kodagoda, Y. K., Jayasinghe, C. V., & Dharmadasa, R. M. (2023). In vitro antioxidant and antidiabetic potential of five spiral ginger (*Costus specious* (J. Koeing sm) populations available in Sri Lanka. *Journal of Agriculture and Food Research*, 12, Article 100553. https://doi.org/10.1016/j.jafr.2023.100553
- Lee, Y. R., Lee, S. H., Jang, G. Y., Lee, Y. J., Kim, M. Y., Kim, Y. B., Lee, J., & Jeong, H. S. (2019). Antioxidative and antidiabetic effects of germinated rough rice extract in 3T3-L1 adipocytes and C57BLKS/J-db/db mice. *Food & Nutrition Research*, 63, 1-10. https://doi.org/10.29219/fnr.v63.3603
- Liu, L., Zhao, Y., Chang, D., Xie, J., Ma, Z., Sun, Q., & Yin, H. (2018). Prediction of short-term pv power output and uncertainty analysis. *Applied Energy*, 228, 700–711. https://doi.org/10.1016/j.apenergy.2018.06.112
- Matsumura, T., Kasai, M., & Hayashi, T. (2000). a-glucosidase inhibitors from Paraguayan natural medicine Nangapiry, the leaves of *Eugenia uniflora*. Journal of Pharmaceutical Biology, 38(4), 302–307. https:// doi.org/10.1076/1388-0209(200009)3841-AFT302
- Nguyen, Q. V., Tran, T. H., Pham, T. N., Thuoc, D. V., Cao, V. D., & Boo, K. H. (2019). Inhibitory effects of *Bidens pilosa* plant extracts on the growth of the bloom-forming alga *Microcystis aeruginosa*. *Water, Air* & *Soil Pollution, 230*(24), 1-16. https://doi.org/10.1007/s11270-019-4077-1
- Ogurtsova, K., Guariguata, L., Barengo, N. C., Ruiz, P. L. D., Sacre, J. W., Karuranga, S., & Magliano, D. J. (2022). IDF diabetes Atlas: Global estimates of undiagnosed diabetes in adults for 2021. *Diabetes Research* and Clinical Practice, 183, Article 109118. https://doi.org/10.1016/j.diabres.2021.109118
- Pathak, R., & Sharma, H. (2021). A review on medicinal uses of *Cinnamomum verum* (Cinnamon). Journal of Drug Delivery and Therapeutics, 11(6-S), 161–166. https://doi.org/10.22270/jddt.v11i6-S.5145
- Rahim, N. F. A, Muhammad, N., & Abdullah, N. (2022). Optimum extraction condition of *Anacardium occidentale* on antiurolithiatic activities (*in-vitro*). Sains Malaysiana, 51(4), 1099–1109. http://doi.org/10.17576/jsm-2022-5104-12
- Romero, E. F., Chavez-Quintana, S. G., & Siche, R. (2020). The kinetics of total phenolic content and monomeric flavan-3-ols during the roasting process of *Criollo cocoa*. *Antioxidants*, 9(2), Article 146. https://doi.org/10.3390/antiox9020146
- Singab, A. N., Youssef, F. S., & Ashour, M. L. (2014). Medicinal plants with potential antidiabetic activity and their assessment. *Medicinal and Aromatic Plants*, 3(151), 2167–0412. http://dx.doi.org/10.4172/2167-0412.1000151
- Singh, N., Rao, A. S., Nandal, A., Kumar, S., Yadav, S. S., Ganaie, S. A., & Narasimhan, B. (2020). Phytochemical and pharmacological review of *Cinnamomum verum* J. persl-a versatile spice used in food and nutrition. *Food Chemistry*, 338, Article 127773. https://doi.org/10.1016/j.foodchem.2020.127773
- Sotiropoulou, N. S., Megremi, S. F., & Tarantilis, P. (2020). Evaluation of antioxidant activity, toxicity, and phenolic profile of aqueous extracts of chamomile (*Matricaria chamomilla* L.) and sage (*Salvia officinalis* L.) prepared at different temperatures. *Applied Sciences*, 10(7), Article 2270. https://doi.org/10.3390/app10072270

- Tatipamula, V. B., & Kukavica, B. (2021). Phenolic compounds as antidiabetic, anti-inflammatory, and anticancer agents and improvement of their bioavailability by liposomes. *Cell Biochemistry & Function*, 39(8), 926–944. https://doi.org/10.1002/cbf.3667
- Vinci, G., D'Ascenzo, F., Maddaloni, L., Antonia, S., & Tiradritti, M. (2022). The influence of green and black tea infusion parameters on total polyphenol content and antioxidant activity by ABTS and DPPH assays. *Beverages*, 8(2), Article 18. https://doi.org/10.3390/beverages8020018
- Wairata, J., Fadlan, A., Purnomo, A. S., Taher, M., & Ersam, T. (2022). Total phenolic and flavonoid contents, antioxidant, antidiabetic and antiplasmodial activities of *Garcinia forbesii* king: A correlation study. *Arabian Journal of Chemistry*, 15(2), Article 103541. https://doi.org/10.1016/j.arabjc.2021.103541