Hybrid drying of *Murraya koenigii* leaves: anti-diabetic and anti-ageing activities

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Abstract

This study aims to compare the anti-diabetic and anti-ageing effect of the *Murraya koenigii* leaves by using the drying method of convective hot-air drying (40, 50 and 60 °C) and two hybrid drying methods through microwave vacuum-drying (6, 9 and 12 W/g) and convective hot-air pre-drying followed by microwave vacuum finishing-drying (50 °C followed by 9 W/g), in addition to the freeze-drying, which was used as a control method. The anti-diabetic activity was evaluated by using α -amylase and α -glucosidase inhibition method, while the anti-ageing activity was measured by using acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibition effect. The results indicated that the dried leaves of *M. koenigii* were more selective towards α -glucosidase inhibition with the percentage ranging from 7.92 to 23.57% at the concentration of 62.52 ± 22.18 to 20.39 ± 2.01 mg dried leaves/mL. Concerning the anti-ageing activity, the inhibition effect of AChE was significantly weaker compared to BChE inhibition, revealing that the dried *M. koenigii* leaves were more selective towards BChE inhibition with the percentage ranged from 79.47 to 87.07%. Furthermore, the Page model and diffusion models showed a good fitting of the model to the empirical data of drying kinetics with the highest coefficient of determination (0.9996; 0.9995) and the lowest values of root-mean-square error (0.0102; 0.0090) and Chi-square coefficients (0.0010; 0.0008). Overall, microwave vacuum-drying is the recommended drying method to be used for *M. koenigii* leaves due to its promising result obtained for the inhibition of α -glucosidase and BChE.

Keywords Acetylcholinesterase (AChE) · Butyrylcholinesterase (BChE) · α -amylase · α -glucosidase · Convective hot-air drying · Microwave vacuum-drying (MVD)

1 Introduction

Good health and well-being are one of the global goals to ensure healthy lives and promote well-being for all at all ages. Diabetes is on the rise across the globe. Referring to the World Health Organization (WHO), an estimated 422 million people were diagnosed with diabetes in 2014, and these numbers are expected to further increase to 9.9% by the year 2045 [1]. Diabetes mellitus is an increasingly prevalent medical condition which characterised by oxidative stress. Previous findings have reported oxidative stress

is the primary source of diabetes as it has increased the generation of free radicals [2]. Ageing is also one of the factors that increase the rate of diabetes patients. Ageing is a biological process of oxidative damage caused by free radicals. Due to the unpaired electrons of the free radicals, they cause danger to cell membranes, lipids, proteins and DNA as the free radicals are the reactive molecules [3].

The α -amylase enzyme is an endoglycosidase that presents in the intestinal lumen as a constituent of pancreatic juices and catalyses the hydrolysis of complex starches to oligosaccharides. On the other hand, α -glucosidase is a

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membrane-bound enzyme located in the epithelium of the small intestine and its function is to catalyse the hydrolysis of oligosaccharides to glucose and other monosaccharides [4, 5]. Inhibition of both enzymes could delay the digestion of complex starches, as a result reducing the rate of glucose absorption to control the sugar level of the human body [6].

There are two types of enzymes that hydrolyse acetylcholine. Acetylcholinesterase (AChE) is membrane-bound which can be found at neuronal synapses in the nervous system as well as at the neuromuscular junctions. It functions as an inhibitor to terminate the action of acetylcholine by cleaving the neurotransmitter to choline and acetate [7, 8]. Another type of enzyme is butyrylcholinesterase (BChE), which hydrolyses acetylcholine and other ester choline such as succinylcholine and benzoylcholine. However, its physiological function is still unknown [7, 9].

Currently, there are several commercialised synthetic drugs to control ageing and diabetes mellitus. However, these drugs show several side effects, such as abdominal tension, bloating, flatulence and diarrhoea [5, 6]. Hence, natural sources from herbal plants play a significant role in treating ageing and diabetes with fewer side effects [3]. *Murraya koenigii*, commonly known as curry leaf, belongs to the *Rutaceae* family. Curry leaf can be found in Malaysia, India and South Asian countries, and it is frequently adopted as spices because of its aromatic scent and pharmacological properties [10, 11]. Besides, it was reported to possess several pharmacological properties such as anti-diabetic activity, anti-ageing activity and antioxidant activity [12].

It is challenging to properly preserve the bioactive compounds through the drying process of medicinal plants. Drying is considered one of the vital processes in the medicinal natural product processing industries. In the food processing industries, drying is commonly used to remove the moisture content from the medicinal plants to minimise the growth of microbiological activity as well as increase the shelf life of the materials [13, 14]. The traditional way to dehydrate foods and medicinal plants are sun-drying and air-drying. These drying methods operate at a low cost. However, foods will be contaminated with dust and microbial as both of these drying methods are considered as open-air drying methods [15]. Convective hot-air drying (CD) is widely used in current food processing industries. Two types of moisture diffusions are involved in CD which is external diffusion and internal diffusion. External diffusion occurs in the initial period and a constant period where the moisture content will be removed from the surface of the materials to the ambient air. On the other hand, external diffusion occurs in the falling period where the internal moisture content diffuses out from the inner material to the drying surface [16].

Long drying duration is one of the significant drawbacks found in CD due to the internal diffusion process. Therefore, microwave-assisted drying (MD) has been introduced to overcome the limitations of CD. The microwave-drying (MD) method has been reported to offer a significant increase in the drying rate as compared to traditional drying methods [16]. Microwave-drying uses microwave energy, which able to penetrate through the materials and generates heat to push out moisture content from the interior to the surface of the materials [17]. Besides, due to its permeability of microwave energy, MD has been reported to shorten drying duration and increase the drying rate in the falling period [16, 17]. However, the limitation of microwave-drying is the non-uniform temperature distribution in microwave-drying, which leads to scorching. Thus, it is usually combined with other drying techniques such as vacuum-drying and intermittent drying to enhance the performance of microwave-drying [16].

Microwave vacuum-drying (MVD) is a hybrid drying method that is combining microwave-assisted drying and vacuum-assisted drying into one drying system. The mechanism is similar to microwave-assisted drying; however, MVD allows to lower the boiling point of internal moisture content and reduces the formation of an over-burnt spot of the materials [18]. However, one of the disadvantages of MVD is that the intensive water evaporation from the leaves may exceed the capacity of the vacuum pump; thus, this requires a reduction in raw materials or increases the size of the vacuum pump [19]. This matter can be overcome by introducing convective hot-air as a pre-drying method (CPD) to reduce the loading capacity of the vacuum system in MVD. Convective hot-air pre-drying followed by microwave vacuum finishing-drying (CPD-MVFD) allows to reduce the total cost of the drying process as well as improves the quality of products. CPD-MVFD was applied in several plants such as *Phyllanthus nodiflorus*, *Strobilanthes crispus*, *Zuzuphus jujube*, and garlic slices, which resulted in effectively reduced the drying time as well as providing an excellent quality of dried products [19–23]. Thus, CPD-MVFD could also comply with one of the global goals of sustainable cities and communities.

In the previous study of *M. koenigii* [24], the authors focused on the specific energy consumption of *M. koenigii* dried using CD, MVD and CPD-MVFD. Besides, few quality studies were also included, such as antioxidant activity, profiling of volatile compounds, colour and water analysis. However, the concern of diabetics and ageing are slowly rising across the globe. Therefore, this present study focused on the effect of CD and two hybrid drying techniques such as MVD and CPD-MVFD on the *M. koenigii* leaves to evaluate the quality of *M. koenigii* leaves through anti-diabetic activity (α -amylase inhibition and α -glucosidase inhibition) and anti-ageing activity (AChE

and BChE) as an alternative natural source as well as determining a suitable drying method for both activities. Besides, the kinetic modelling of the drying process was also modelled with three other thin-layer models to compare with the previous models as well as study the transport mechanism and to simulate or scale up the whole drying process for further optimisation.

2 Material and methods

2.1 Chemical reagents

Sodium phosphate buffer, α -amylase solution, starch solution, dinitrosalicylic acid colour reagent, α -glucosidase enzyme solution, intestinal acetone powder, saline, potassium phosphate buffer, *p*-nitrophenyl- α -D-glucopyranoside solution, sodium carbonate, phosphate buffer, 5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB), acetylthiocholine iodide (ATChI), Ellman solution, acetylcholinesterase solution (AChE) and butyrylthiocholinesterase (BChE) were purchased from Sigma-Aldrich (Steinheim, Germany).

2.2 Sample preparation

5 kg of fresh leaves of *M. Koenigii* was purchased from Ukay Nursery (Kuala Lumpur, Malaysia) and identified at the Forest Research Institute Malaysia (FRIM) with the voucher number of 031/18. The dirt of the leaves was cleaned off using distilled water. The bone drying weight of *M. Koenigii* leaves was obtained using an oven dryer dried at 105 °C for 24 h, according to the ASTM standard (D1348-94) [17].

2.3 Drying of fresh *Murraya koenigii* leaves

Fresh *M. koenigii* whole leaves were dried using four drying methods such as a convective hot-air drying (CD), a single-stage hybrid drying microwave vacuum-drying (MVD), a two-stage hybrid convective hot-air pre-drying followed by vacuum microwave finishing-drying (CPD-MVFD) and freeze-drying (FD) [19, 25, 26]. Freeze-dried samples were used as the control samples. For weight loss measurement of CD, the weight loss was collected at 5-min interval for the first hour, 30-min interval for the next four hours and an hour interval until the mass loss difference was 0.05 g or less using an analytical balance (Radwag, PS600/C/2, Poland). In the case of MVD, the weight loss of the leaves was recorded for every 4-, 3- and 2-min interval for 6, 9 and 12 W/g, respectively, until the difference in the mass loss was 0.05 g or less using an analytical balance (Radwag, PS600/C/2, Poland).

2.3.1 Convective hot-air drying (CD)

Approximately 40 g of fresh *M. koenigii* whole leaves was dried using a convective hot-air dryer at 40, 50 and 60 °C. The leaves were placed on a wire mesh tray and spread evenly.

2.3.2 Microwave vacuum-drying (MVD)

40 g of fresh *M. koenigii* leaves were dried using a microwave vacuum dryer (Plazmatronika, Wrocław, Poland) using 6, 9 and 12 W/g microwave power. The leaves were first placed in an organic glass container which was attached to a vacuum system with a constant rotating speed of 6 rpm throughout the drying process to prevent local overheating of leaves. The temperature of the leaves was measured immediately after the samples were taken out of the dryer.

2.3.3 Convective pre-drying followed by vacuum microwave finishing-drying (CPD-MVFD)

Fresh *M. koenigii* leaves were partially dried using CPD in a convective hot-air dryer at 50 °C for 2 h until the moisture ratio reached 0.4727, which the surface moisture was mostly evaporated. Then, the samples were completely dried using a microwave vacuum dryer (Plazmatronika, Wrocław, Poland) at 9 W/g. The convective hot-air temperature at 50 °C and microwave wattage at 9 W/g were used in CPD-MVFD to ensure the better quality of the dried product [20, 27].

2.3.4 Freeze-drying (FD)

The *M. Koenigii* whole leaves were dehydrated using a freeze dryer (OE-950, Hungary) at a vacuum pressure of 65 Pa. The freezing temperature was – 60 °C, while the heating plate was set to 30 °C for the sublimation process.

2.4 Modelling of drying kinetics

The mathematical modelling of drying kinetics of *M. koenigii* leaves dried using CD, MVD and CPD-MVFD at all drying conditions was determined based on the mass loss throughout the drying process. The drying kinetics were plotted as a function of moisture ratio (M_R) against time. M_R is determined using Eq. (1) [28].

$$M_R = \frac{M_i - M_e}{M_o - M_e} \quad (1)$$

where M_t is the moisture content at the respective time (g water/g dw), M_e is the equilibrium moisture content (g water/g dw) and M_o is the initial moisture content (g water/g dw).

The drying rate (D_R) is calculated using Eq. (2) [28]:

$$D_R = \frac{M_t - M_{t+\Delta t}}{\Delta t} \quad (2)$$

Thin-layer models were frequently used to model the drying behaviours of dried leaves [28]. Three thin-layer models which are often used to describe the drying kinetics of leaves, namely diffusion approach [Eq. (3)], Page [Eq. (4)] and Wang and Singh [Eq. (5)], were adopted to model the drying kinetics of dried *M. koenigii* leaves [29–32] in this research.

$$M_R = a \exp(-kt) + (1 - a) \exp(-kbt) \quad (3)$$

$$M_R = \exp(-kt^n) \quad (4)$$

$$M_R = 1 + at + bt^2 \quad (5)$$

where (M_R) denotes as moisture ratio, a , b denotes as model constants, k denotes as drying constant, n is the dimensionless empirical constant and t is the drying time.

The goodness of fitting was evaluated and compared using the statistical measures such as coefficient of determination (R^2), root-mean-square error (RMSE) and Chi-square coefficient (χ^2). The goodness of fit was identified based on the highest (R^2) value and the lowest RMSE and χ^2 .

2.5 Extraction of dried *Murraya koenigii* Leaves for anti-diabetic and anti-ageing activities

The standard extraction of dried leaves of *M. Koenigii* was conducted using the procedure described by Chua et al. [21] with some modification. 0.5 g of powdered samples was extracted with 9 mL of 80% methanol acidified with 1% of hydrochloride acid. The extraction was performed in an ultrasonic bath (Sonic 6D; Polsonic, Warsaw, Poland) for 15 min with the frequency of 50 Hz under the room temperature. The extract solution was kept at 4 °C overnight and sonicated again at the same extraction conditions. Then, the extracts will be centrifuged at 10,000 rpm for 5 min using a centrifuge (MPW, MPW-350R). Lastly, the supernatant was collected through filtration using hydrophilic PTFE 0.20 µm membrane (Millex Simplicity Filter, Merck) and subjected to anti-diabetic and anti-ageing activity analysis.

2.6 Anti-diabetic activity and anti-ageing activity of dried *Murraya koenigii* leaves

Considering different aspects of the reactivity compound(s) towards anti-diabetic and anti-ageing activities, two in vitro inhibition assays were performed for each activity's analysis. Two anti-diabetic activity assays were conducted, namely α -amylase inhibition, which targeted the hydrolysis of complex starches to oligosaccharides and α -glucosidase inhibition, which targeted on the hydrolysis of oligosaccharides to glucose and other monosaccharides [5, 33]. Besides, two anti-ageing activity assays were conducted, namely acetylcholinesterase (AChE) inhibition, which targeted the termination action of acetylcholine at the postsynaptic membrane in the neuromuscular junction and butyryl-cholinesterase (BChE) inhibition which targeted on the termination action of other choline esters [3, 8].

2.6.1 α -amylase inhibition

The α -amylase inhibitory activity was performed using the method described by Gonzalez-Munoz et al. [34]. 0.5 mL of leave extract was mixed with 0.5 mL of 0.02 M sodium phosphate buffer and adjusted to pH 6.9 using 0.006 M of NaCl to give 0.5 mg/mL of α -amylase solution. The mixture was incubated at room temperature for 10 min. Then, 0.5 mL of 1% starch solution in 0.02 M of sodium phosphate buffer was added into the mixture and incubated for 10 min. Then, 1 mL of dinitrosalicylic acid colour reagent was added into the mixture, and the mixture was incubated for a duration of 10 min in a water bath which was heated to 100 °C and allowed to cool to room temperature. Lastly, the mixture was diluted by adding 15 mL of water, and the absorbance value was measured at 540 nm using a UV-2401 PC spectrophotometer (Shimadzu, Kyoto, Japan). All samples were performed in duplicate, and the result was expressed as inhibitor % and IC_{50} .

2.6.2 α -glucosidase inhibition

The α -glucosidase inhibitory activity was conducted with slight modification based on previous works [4]. The α -glucosidase enzyme solution was prepared by dissolving 0.5 g of intestinal acetone powder in 10 mL of saline (0.9% w/v) and sonicated 12 times at 30-s intervals in an ice bath. Thereafter, the mixture was centrifuged at 3000 rpm for 30 min at 4 °C, and the supernatant was diluted as the enzyme solution two times with 0.1 M potassium phosphate buffer (pH 6.9). For the α -glucosidase inhibition, 50 µL of leave extract was mixed with 50 µL of enzyme solution and incubated at room temperature for 10 min. The enzyme reaction was initiated by adding 50 µL of 5 mM

p-nitrophenyl- α -D-glucopyranoside solution into the mixture and incubated at 37 °C for 20 min. Lastly, 100 μ L of 0.1 M sodium carbonate solution was added into the mixture, and the absorbance value was measured at 405 nm using a UV-2401PC spectrophotometer (Shimadzu, Kyoto, Japan). All samples were done in duplicate, and the result was expressed in inhibitor % and IC_{50} .

2.6.3 AChE and BChE inhibition

The AChE and BuChE inhibition were performed using the methods described by G. Hasbal et al. [35]. The Ellman solution consisted of phosphate buffer (pH 7.5) with 318 μ M DTNB and 955 μ M of ATChI. 20 μ L of the sample solution and 220 μ L of Ellman solution were mixed, and the absorbance value was measured using a UV-2401PC spectrophotometer (Shimadzu, Kyoto, Japan) at 412 nm for the duration of 10 min. Then, 10 μ L of acetylcholinesterase (AChE) solution (0.5 U/mL) was added into the mixture, and the absorbance value of the samples was measured at 412 nm for 10 min using UV-2401PC spectrophotometer (Shimadzu, Kyoto, Japan). The percentage of inhibition can be calculated using Eq. (1). The BuChE inhibition was performed similarly by replacing 10 μ L of AChE solution to butyrylthiocholine (BChE) solution (0.5 U/mL). 20 μ L of sample solution was replaced with distilled water as a control. All samples were done duplicated, and the results were expressed in % inhibition.

$$\text{AChE/BChE inhibition activity(\%)} = \left(1 - \frac{\text{Absorbance value of the sample}}{\text{Absorbance value of control}} \right) \times 100\% \quad (6)$$

2.7 Statistical analysis

Results were expressed as mean $\pm$ standard deviation, and the error bars in the figures indicate the standard deviation. The differences between means were analysed using one-way ANOVA test through SPSS 23 (IBM, USA). Significant differences ($p \leq 0.05$) between means were determined using Tukey's test. The thin-layer modelling of the CD, MVD and CPD-MVFD was modelled using Table Curve 2D windows version 2.03 (Jandel Scientific Software, San Jose, CA, USA), and the fit of goodness was evaluated using the coefficient of determination (R^2), root-mean-square error (RMSE) and Chi-square coefficient (χ^2) [19].

3 Results and discussion

3.1 Modelling of drying kinetics for dried *Murraya koenigii* leaves

The statistical parameters, model constants and drying time describing the drying kinetics of *M. koenigii* leaves using CD, MVD and CPD-MVFD are shown in Table 1. Three thin-layer models, namely Page, diffusion and Wang and Singh models, were used to model the drying kinetics of *M. koenigii* leaves. The models for CD, MVD and CPD-MVFD at all conditions were evaluated through the highest value of the coefficient of determination (R^2) and the lowest value of root-mean-square error (RMSE) and Chi-square coefficient (χ^2). As a result, the Page model and diffusion model showed a good fitting of the model to the empirical data which R^2 ranged from 0.9660 to 0.9996 and 0.9657 to 0.9995, RMSE ranged from 0.2331 to 0.0102 and 0.2330 to 0.0090 and χ^2 ranged from 0.3802 to 0.0010 and 0.3802 to 0.0008, respectively. The parameters b , k and n were describing the drying rate; the greater the values, the faster the drying process. This statement agreed quite well with the results obtained in this study. As the drying time of MVD increased from 18 to 44 min, all parameters of the Page model describing the drying kinetics of *M. koenigii* leaves were decreased from 1.8593 to 0.8505 for parameter n and 0.0876 to 0.0400 for parameter k . The same trend was also obtained on CD.

Figure 1a, b presents the plot of experimental and predicted moisture ratio to illustrate the best performance of Page model for CD, CPD-MVFD and MVD. The figures showed an excellent fitting of the Page model, which is overall in line with the experimental results. As compared to the previous finding [24], the diffusion model in the current study demonstrated an excellent fitting to the experimental data of CD at all conditions, whereas Page model and Modified Page model in the previous finding demonstrated a good fitting to the experimental data of MVD and CPD-MVFD.

3.1.1 Anti-diabetic activity of dried *Murraya koenigii* leaves

The anti-diabetic activity of dried *M. koenigii* leaves using CD, MVD, CPD-MVFD and FD on α -amylase and α -glucosidase was determined in this study, and the results are shown in Fig. 2. In the case of α -amylase, the highest inhibition was obtained on CD at 40 °C, and the

Table 1 Statistical parameters and model constants describing the drying kinetics of *M. koenigii* leaves

Drying method	Models	R^2	RMSE	χ^2	a	b	k	n	t
CD40	Page	0.9976	0.0159	0.0068			0.0082	0.8505	1020
	Diffusion	0.9978	0.0150	0.0061	0.1338	0.11948	0.0247		
	Wang and Singh	0.9744	0.0698	0.1316	−0.0025	0.00000			
CD50	Page	0.9969	0.0219	0.0105			0.0064	1.0197	570
	Diffusion	0.9973	0.0208	0.0095	0.0176	0.00357	1.9238		
	Wang and Singh	0.9929	0.0450	0.0446	−0.0048	0.00001			
CD60	Page	0.9977	0.0192	0.0055			0.0090	1.1179	270
	Diffusion	0.9982	0.0170	0.0043	−63.0888	0.99237	0.0229		
	Wang and Singh	0.9949	0.0361	0.0195	−0.0100	0.00002			
MVD 6 W/g	Page	0.9994	0.0108	0.0014			0.0400	1.5961	44
	Diffusion	0.9995	0.0081	0.0008	−1.4640	0.52517	0.4624		
	Wang and Singh	0.9171	0.1007	0.1217	−0.0739	0.00123			
MVD 9 W/g	Page	0.9996	0.0113	0.0013			0.0625	1.7681	27
	Diffusion	0.9995	0.0090	0.0008	−1.6359	0.46829	0.8775		
	Wang and Singh	0.9235	0.0981	0.0962	−0.1194	0.00323			
MVD 12 W/g	Page	0.9996	0.0102	0.0010			0.0876	1.8593	18
	Diffusion	0.9995	0.0084	0.0007	−77.7443	0.98189	0.7127		
	Wang and Singh	0.9481	0.0793	0.0629	−0.1711	0.00674			
CPD50-MVFD360	Page	0.9660	0.2331	0.3802			1.0349	0.6605	138
	Diffusion	0.9657	0.2330	0.3802	0.9169	0.23863	0.8429		
	Wang and Singh	0.8973	0.2911	0.5931	−0.1936	0.00810			

R^2 determination coefficient, RMSE root-mean-square error, χ^2 Chi-square coefficient, a , b , k , n model constants, t total drying time (min), CD convective hot-air drying, MVD microwave vacuum-drying, CPD convective hot-air pre-drying, MVFD microwave vacuum finishing-drying

lowest inhibition was obtained on MVD at 12 W/g with the inhibition percentage of 30.61% and 0.95%, respectively. As the drying intensity of CD increased from 40 to 60 °C, the inhibition percentage decreased from 30.61 to 21.06%. This decreasing trend might be due to the long exposure time to a high degradative temperature, which caused the corresponding bioactive compound to degrade [36]. Concerning FD, MVD and CPD-MVFD, the inhibition of α -amylase was not promising compared to CD at all drying temperatures. This phenomenon might be due to the vacuum system that loses the corresponding bioactive compounds during the drying process. However, this occurrence could be overcome by increasing the pressure slightly in the chamber to reduce the loss of those corresponding bioactive compounds [26].

On the other hand, dried leaves of *M. koenigii* leaves showed higher inhibition of the α -glucosidase. The highest inhibition on α -glucosidase falls on CD at 60 °C, and the lowest was obtained on CD at 50 °C, having an inhibition percentage of 23.57% and 7.92%, respectively. With the combination of MVFD at 9 W/g as a finishing-drying, which shortened the drying duration of CPD at 50 °C from 570 to 138 min and resulted in an increment in α -glucosidase inhibition from 7.92 to 20.64%. This occurrence happened might be due to CPD-MVFD helped to shorten the

exposure duration to the oxidative condition during the drying process and prevented the corresponding bioactive compound from degrading [36]. In the case of MVD, increasing the microwave wattage from 6 W/g to 12 W/g resulted in the decrease in the inhibition of α -glucosidase from 22.94 to 18.87%. However, increasing drying temperature from 40 to 60 °C resulted in growing α -glucosidase inhibition from 18.79 to 23.57%. Hence, this can be concluded as the rapid drying of MVD caused by microwave energy tends to increase the heat generation inside the material, which leads to the degradation of α -glucosidase properties [20].

The inhibitory activity (IC_{50} ; mg dried leaves/mL) of α -amylase and α -glucosidase of dried *M. koenigii* leaves is shown in Table 2. The inhibitory activity was correlated with the α -amylase and α -glucosidase inhibitions as higher inhibition percentage required less concentration of extracts samples to achieve 50% inhibition activity. Overall, *M. koenigii* leaves dried using CD, MVD, CPD-MVFD and FD had high inhibitory activity against α -amylase, especially the samples dried with MVD; however, they possessed a low inhibitory activity against α -glucosidase. The lowest IC_{50} was obtained on MVD at 6 W/g, which required 20.39 mg dried leaves/mL to achieve 50% of inhibition of α -glucosidase. The highest IC_{50} occurred on CD at 50 °C,

Fig. 1 Experimental and predicted moisture ratio by Page model as a function of time for **a** CD at 40, 50 and 60 °C and CPD-MVFD; **b** MVD at 6, 9 and 12 W/g; CD convective hot-air drying, MVD microwave vacuum-drying, CPD convective hot-air pre-drying, MVFD microwave vacuum finishing-drying

Fig. 2 α -Amylase and α -glucosidase inhibition of dried *M. koenigii* leaves using CD, MVD, CPD-MVFD and FD; CD convective hot-air drying, MVD microwave vacuum-drying, CPD convective hot-air pre-drying, MVFD microwave vacuum finishing-drying, FD freeze-drying; the same letters within the bars indicate no significant differences in mean values at the level of 5%

Table 2 Inhibitory activity (IC_{50}) of *M. koenigii* leaves dried using CD, MVD, CPD-MVFD and FD

Drying methods	α -Amylase IC_{50} (mg dried leaves/ mL)	α -Glucosidase IC_{50} (mg dried leaves/ mL)
FD	214.58 $\pm$ 0.00a	34.08 $\pm$ 0.00b
CD40	60.74 $\pm$ 0.00a	25.13 $\pm$ 4.55b
CD50	110.88 $\pm$ 0.83a	62.52 $\pm$ 22.18a
CD60	88.50 $\pm$ 1.54a	20.89 $\pm$ 6.84b
MVD 6 W/g	2172.67 $\pm$ 1643.61a	20.39 $\pm$ 2.01b
MVD 9 W/g	1202.44 $\pm$ 403.98a	30.98 $\pm$ 18.21b
MVD 12 W/g	2029.86 $\pm$ 498.39a	25.93 $\pm$ 7.85b
CPD-MVFD	571.21 $\pm$ 53.12a	22.69 $\pm$ 2.79b

IC_{50} inhibitory activity, CD convective hot-air drying, MVD microwave vacuum-drying, CPD convective hot-air pre-drying, MVFD microwave vacuum finishing-drying, FD freeze-drying; all value was expressed in mean $\pm$ standard deviation

which resulted in 62.52 mg/ml to reach 50% of inhibition of α -glucosidase. About CPD-MVFD, it lowers down the required concentration of CD at 50 °C from 62.52 mg dried leaves/mL to 22.69 mg dried leaves/mL to achieve 50% of inhibition activity.

In conclusion, the dried *M. koenigii* leaves produced a significant weak α -amylase enzyme inhibition when compared to α -glucosidase inhibition. Hence, the dried leaves of *M. koenigii* were favoured on treating type 2 diabetes mellitus which helped to delay the hydrolysis of oligosaccharides to glucose and other monosaccharides in the small intestine and hence reduce the rate of digestion of carbohydrate which led to decrease in the high blood glucose levels [33, 37]. Overall, MVD showed promising inhibition of α -glucosidase, especially at the condition of 6 W/g. Besides, with the combination of CPD-MVFD, it improved the inhibition percentage of CD at 50 °C by 12.72% and

increased from 7.92 to 20.64%. The possible compounds that could contribute to the α -glucosidase inhibition were the total polyphenolic content (TPC) and essential oils of *M. koenigii* leaves, namely β -phellandrene, α -pinene and sabinene, which were identified as the major volatile compounds in the previous study [24]. However, the further affirmation should be conducted in future work.

3.2 Anti-ageing activity of dried *Murraya koenigii* leaves

The inhibition percentage of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) of dried *M. koenigii* leaves is shown in Fig. 3. With regard to AChE inhibition, the inhibition was low in all drying methods for all drying conditions. This phenomenon occurred can be concluded as the dried leaves of *M. koenigii* leave at all conditions did not respond to AChE inhibition; instead, they responded promisingly on the BChE activity.

In the case of BChE inhibition, the highest inhibition obtained with FD with an inhibition percentage of 87.07%, whereas CD at 50 °C showed the lowest BChE inhibition with a value of 79.47%. The result indicated that a low microwave wattage of 6 W/g for MVD and a higher temperature of 60 °C for CD were beneficial in the inhibition of BChE. The intensity of drying treatment also affected in inhibiting the BChE. The drying temperature increased from 40 to 60 °C, and the drying duration was shortened from 1020 to 270 min, which increased the inhibition of BChE. These results showed that the increase in drying temperature during CD is effective in improving the drying rate, thus shortening the exposure time to the highly oxygenated condition [20]. The above statement also proved in CPD-MVFD, as the drying duration of CD at 50 °C reduced from 570 to 138 min, and the inhibition of BChE increased from 79.47 to 83.19%. In the case of MVD, as

Fig. 3 AChE and BChE inhibition of dried *M. koenigii* leaves using CD, MVD, CPD-MVFD and FD; CD convective hot-air drying, MVD microwave vacuum-drying, CPD convective hot-air pre-drying, MVFD microwave vacuum finishing-drying, FD freeze-drying, AChE acetylcholinesterase BChE butyrylthiocholinesterase; the same letters within the bars indicate no significant differences in mean values at the level of 5%

Table 3 Inhibitory activity (IC_{50}) of *M. koenigii* leaves dried using CD, MVD, CPD-MVFD and FD

Drying methods	AChE	BChE
	IC_{50} (mg dried leaves/mL)	IC_{50} (mg dried leaves/mL)
FD	532.14 ± 0.00a	21.27 ± 0.00c
CD40	nd	22.30 ± 0.20abc
CD50	nd	23.37 ± 0.09a
CD60	nd	21.95 ± 0.63bc
MVD 6 W/g	193.54 ± 7.18bc	21.98 ± 0.10bc
MVD 9 W/g	266.98 ± 128.15b	22.22 ± 0.46abc
MVD 12 W/g	216.37 ± 24.02b	22.62 ± 0.15ab
CPD-MVFD	253.84 ± 81.16b	22.35 ± 0.45abc

nd not detected, CD convective hot-air drying, MVD microwave vacuum-drying, CPD convective hot-air pre-drying, MVFD microwave vacuum finishing-drying, FD freeze-drying, AChE acetylcholinesterase, BChE butyrylthiocholinesterase; all value was expressed in mean ± standard deviation; mean values with the same letters within the same column are not significantly different at level of 5%

the microwave wattage increased from 6 W/g to 12 W/g, however, it showed a decreasing trend in inhibiting the BChE from 86.21 to 82.79%. This decreasing trend occurred might be due to the enormous amount of heat generated inside the leaves caused by the microwave energy and hence reduced the inhibition of BChE [20].

The relationship between the inhibitory activity and the inhibition percentage is that the concentration of extracts samples required to achieve 50% inhibition. Table 3 shows the inhibitory activity (IC_{50} ; mg dried leaves/mL) of AChE and BChE inhibitions of dried *M. koenigii* leaves [8]. The result for AChE shows that CD was not detected at all conditions, and the concentration of sample extracts required was relatively high for all the drying treatment; this can be concluded that the dried samples of *M. koenigii* leaves did not respond to the inhibition of AChE. In the case of BChE, the inhibitory activity was ranged from 21.27 mg dried leaves/mL to 23.37 mg dried leaves/mL, where the lowest IC_{50} was obtained with FD (21.27 mg dried leaves/mL), followed by MVD at 6 W/g (21.59 mg dried leaves/mL), and the highest IC_{50} was showed with CD at 50 °C. With the implementation of CPD-MVFD, the IC_{50} of CD at 50 °C reduced from 23.37 mg dried leaves/mL to 22.35 mg dried leaves/mL to achieve 50% of the inhibition of BChE.

Overall, the dried leaves of *M. koenigii* leaves resulted in the least response to the inhibition of AChE; instead, they responded significantly with BChE inhibition compared to AChE inhibition. Therefore, the dried *M. koenigii* leaves have shown promising potential on hydrolysing many different types of choline-based esters [38, 39]. Besides, MVD at 6 W/g showed a notable inhibition on BChE with an inhibition percentage of 86.21% and required only 21.59 mg

dried leaves/mL of dose concentration to reach 50% of inhibition. With the CPD and MVFD, the performance of inhibition of BChE increased by approximately 3.7% (from 79.47 to 83.19%), and the IC_{50} requirement was reduced by 4% (from 23.37 to 22.35 mg dried leaves/mL) for CD at 50 °C. Besides, total polyphenolic content (TPC) could contribute to the inhibition of BChE; however, further confirmation should be conducted to identify the exact polyphenolic compounds that contribute to the BChE inhibition.

4 Conclusion

In conclusion, the dried *M. koenigii* leaves using CD, MVD, CPD-MVFD and FD showed a reasonable inhibition of the α -glucosidase, which had the highest inhibition of 30.61% with MVD at 12 W/g. Besides, the dried leaves also showed significant inhibition towards BChE with the highest inhibition percentage of 86.21% (21.59 mg dried leaves/mL). In terms of the drying kinetic modelling, Page model and diffusion model showed a good fitting of the model to the empirical data which R^2 ranged from 0.9660 to 0.9996 and 0.9657 to 0.9995, RMSE ranged from 0.2331 to 0.0102 and 0.2330 to 0.0090 and χ^2 ranged from 0.3802 to 0.0010 and 0.3802 to 0.0008, respectively. Overall, CPD-MVFD has successfully improved the performance of CD at 50 °C in terms of drying time, anti-diabetic and anti-ageing activity. Besides, *M. koenigii* leaves dried with MVD at all conditions showed a promising result in α -glucosidase and BChE inhibitions, which is recommended to dry *M. koenigii* leaves and *M. koenigii* leaves could be an alternative source to treat diabetic and ageing. However, further investigation should be done by comparing the inhibition of anti-diabetic and anti-ageing of *M. koenigii* leaves with the commercialised drugs.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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