



Polysaccharides and polyphenol in dried *Morinda citrifolia* fruit tea after different processing conditions: Optimization analysis using response surface methodology

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ABSTRACT

The increasing popularity of *Morinda citrifolia* has many medical and health benefits because of its rich polysaccharides (PSC) and polyphenols (PPN). It has become popular to brew the dry *M. citrifolia* fruit slice as tea in some regions of China. In this study, optimize the extraction parameters of *M. citrifolia* fruit tea polysaccharides and polyphenols using response surface methodology. The results indicated the highest PSC yield of 17% at 46 °C for 11 min and the ratio of water/*M. citrifolia* fruit powder was 78 mL/g. The optimum extraction of PPN was at 95 °C for 10 min and the ratio of water/*M. citrifolia* fruit powder 90 mL/g, with 8.93% yield. Using dry *M. citrifolia* fruit slices as a tea is reported for the first time. Based on the results, the maximum level of PSC can be obtained under condition by infusing about four dried *M. citrifolia* fruit slice with average thickness and size in warm boiled water for 11 min, taking a 300 mL cup (300 mL of water) for example. The maximum level of PPN can be obtained by adding three slices of dried *M. citrifolia* fruit slice to boiled water for 10 min. Considering the powder used in our study, the further pulverization of cutting into powder is more conducive to material precipitation. This study provides a scientific basis for obtaining PSC and PPN from dry *M. citrifolia* fruit slice tea by brewing.

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INTRODUCTION

Morinda citrifolia L. (Rubiaceae) was commonly referred to as noni in Hawaii, mengkudu in Malaysia, cheese fruit in Australia, Indian mulberry in India and also noni in China, and famous for its extensive therapeutic effects (*Chan-Blanco et al., 2006; Jia, Lan & Wu, 2020; Motshakeri & Ghazali, 2015; Rajaei-Sharifabadi et al., 2017*). As a traditional folk medical plant, especially the fruit is the most attractive part containing the most valuable chemical compounds (*Assi et al., 2017; Lin et al., 2013; Mukti et al., 2019; Prasad, Visagaperumal Zonoubia & Chandy, 2019*). Many studies have shown that noni has many functions such as anti-oxidation, anti-virus, anti-inflammatory, anti-cancer, anti-tumor, anti-injury,

anti-bacterial, and scavenging free radicals. These effects continued believed to be related to polysaccharides and polyphenols (Nayak & Mengi, 2010; Santos & De Aquino Santana, 2019; Sasmito et al., 2015; Sousa et al., 2018).

Plant polysaccharides are one of the functional components in the *M. citrifolia* fruit (Sousa et al., 2018). It not only participates in energy metabolism, but also has a variety of biological activities, such as antiviral, antioxidant, anti-tumor, anticoagulant, etc., showing good commercial development prospects functional foods and medicine (Chen et al., 2011). Polysaccharide from lotus plumule can be used to treat type I diabetes and inflammation (Liao, Guo & Lin, 2011; Liao & Lin, 2011). The polysaccharides contained in lotus leaf and Pouteria campechiana seeds have a strong ability to scavenge free radicals, which may be a potential natural antioxidant resource (Zhang et al., 2015; Ma et al., 2019). Plant polyphenols are a kind of secondary metabolites, which had antibacterial, anti-inflammatory and antioxidant activities (Cai et al., 2004; Scalbert, Johnson & Saltmarsh, 2005; Darvesh et al., 2010), and were the main antioxidant in *M. citrifolia* (Srinivasahan & Durairaj, 2014). Grape is one of the fruits with the highest content of polyphenols. It is beneficial to health to absorb phenolic compounds from grape (Iglesias-Carres et al., 2018). Extracts of *D. Morbifera* leaf are rich in polyphenols, which have antioxidant, anti-inflammatory, anti-obesity, anticancer activities and immunomodulatory functions ((Hyun et al., 2013; Hyun et al., 2015; Birhanu et al., 2018; Kang et al., 2018)). Studies have found that polyphenols are abundant in plants such as tea, thyme, rosemary and other plants (Favre et al., 2018; Favreau-Farhadi, Pecukonis & Barrett, 2015; Lunceford & Gugliucci, 2005). Plant extracts rich in polyphenols have the advantage of being a natural ingredient and are more acceptable than synthetic compounds (Peng et al., 2008). The naturally fermented *M. citrifolia* juice contains polyphenolic and polysaccharide, which is the main bioactive ingredient in *M. citrifolia* fruit (Motshakeri & Ghazali, 2015; Chang et al., 2013). The polysaccharides in *M. citrifolia* fruit can regulate the immune response, thereby significantly inhibiting tumor growth in human cancer patients (Sharma et al., 2015; Dussossoy et al., 2011). The potential use of *M. citrifolia* fruit as a health promoter caught the attention of food industry and the pharmaceutical sector made it as a part of various products. Currently, several methods have been used to reduce the unpleasant taste and smell of ripe *M. citrifolia* fruit, such as *M. citrifolia* juice, fermented juice, *M. citrifolia* syrup, *M. citrifolia* puree, *M. citrifolia* powder and *M. citrifolia* extract for medicines and chemical reagents (Almeida, De Oliveira & Hotza, 2019; Assi et al., 2017).

Tea is a time-honored and very acclaimed beverage that originated in China. It is made by young leaves and/or young stems of *Camellia sinensis* plant in a narrow sense (Kröppel et al., 2012; Taylor, Hamilton-Miller & Stapleton, 2005), and by leaves, flowers and fruit from any plant in a broad sense (Pekal, Biesaga & Pyrzynska, 2013). *Chrysanthemum morifolium* flowers (Guzelmeric, Vovk & Yesilada, 2015), flowers or flower buds of *Lonicerae Japonicae* Flos (Cai et al., 2020), the flower buds of *Rosa* (Chang et al., 2019) and the leaf of *Lycium barbarum* L. (Zhao et al., 2020) have been widely used as tea. Now there is a various unique tea in different places such as Teng Cha (China), Apple tea (Turkey), Chamomile tea (Russia and Germany), Mate tea (Argentina), Rooibos tea (South Africa) (Jin et al., 2016; Raal et al., 2012). Tea is a source of beneficial compounds that can supply nutrients for

people (Cavuldak et al., 2019). Hot water could dissolve or extract vitamins, polyphenols, polysaccharides, and other plant bioactive compounds. For example, drinking magnolia tea could improve sleep quality and adjunct to postpartum depression (Xue et al., 2020). Mate tea containing numerous active compounds was benefited to the cardiovascular system (Heck & De Mejia, 2007). Moreover, chamomile tea had many potential health benefits because of its phenolic compounds, which have antioxidant and antibacterial effects (Mckay & Blumberg, 2006). Green tea could also prevent cancer, cardiovascular disease and other diseases consequent on its high content of phenolic compounds (Lorenzo & Munekata, 2016; (Sinija & Mishra, 2008)). The *M. citrifolia* fruit is universally used by fermenting, but it is more expensive and tastes average. Under the global enthusiasm for tea drinking, making *M. citrifolia* fruit tea with dried slices or powder is a fabulous option, and also a cheap, effective and convenient way, providing its active ingredients as polysaccharides and polyphenols for people. Because *M. citrifolia* fruit has a special smell when it is ripe, people generally do not eat fresh *M. citrifolia* fruit directly, but would further process it into *M. citrifolia* enzyme, *M. citrifolia* juice, *M. citrifolia* fruit wine, etc. The processing process of these products is complicated and the cost is high. In this study, *M. citrifolia* fruit slices were used to make tea, which not only saves cost but also is convenient to eat. This was the first time that the dried *M. citrifolia* fruit was used as a tea product, but how to infuse it to get more polysaccharides and polyphenols is still unclear. For instance, the water temperature, soaking time, and the ratio of water to dried *M. citrifolia* slices are unknown. Fruit tea's resulting positive health effects would differ based on water temperature and infuse of the water-tea ratio (Şahin, 2013).

Response surface methodology (RSM) is an effective statistical method, which can predict the influence of the interaction between multiple independent variables on the dependent variables and find the optimal extraction conditions for experiments, thus significantly reducing the number of experiments, reducing the cost of experiments, and saving time (Zou et al., 2013; Silva, Rogez & Larondelle, 2007; Prasad et al., 2011). Box-Behnken design (BBD) and central composite design (CCD) are the most commonly used effective RSM techniques to optimize extraction conditions in complex extraction (Bezerra et al., 2008; Gardin et al., 2001; Han et al., 2001; Ding et al., 2016; Zhang et al., 2017; Cho & Zoh, 2007). Compared with CCD, the BBD program does not include extreme factor value combination (the highest or lowest level), which can avoid experiments under extreme factor value conditions and avoid possibly produce unsatisfactory results (Li et al., 2019). In addition, the BBD method is the most economical and efficient design, this design requires a small number of runs, thus avoiding time-consuming experiments (Bezerra et al., 2008; Ferreira et al., 2007). Successfully optimized the extraction conditions of polysaccharides and polyphenols in a variety of plants using BBD-RSM, for instance, *Camellia sinensis* (Zheng et al., 2019), *Pistacia lentiscus* L. Leaves (Detti et al., 2020), olive leaves (Wang, Yang & Yang, 2020), *Actinidia chinensis* Planch. (Han et al., 2019), *Ziziphus jujuba* cv. (He et al., 2019). Therefore, based on single-factor experiments, RSM was used to carry out measurements and compare the contents of polysaccharides (PSC) and polyphenol (PPN) in dried *M. citrifolia* fruit slice tea with a dried slice under different process conditions including temperature, time and ratio of water/*M. citrifolia* fruit powder.

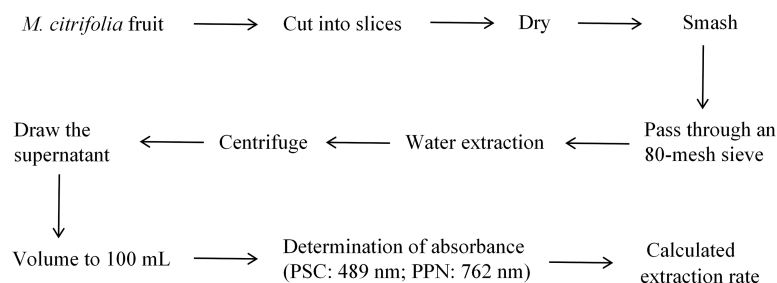


Figure 1 Schematic overview of the experimental program.

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MATERIALS AND METHODS

Overview of experimental program

Wash the collected *M. citrifolia* fruit with distilled water, slice and dry them, grind them into powder, extract with water, and determine the content of PSC and PPN with an ultraviolet spectrophotometer. [Figure 1](#) describes the experimented program.

Collection of fruit samples

The *M. citrifolia* fruit was collected from plantations located Yuanjiang, Yunnan Province, China (25° 3' 41.92" N, 102° 45' 20.39" E). *M. citrifolia* was introduced by the research team from Hawaii in the United States in 2007 and planted in Yuanjiang plantations. *M. citrifolia* is a tropical plant, and its optimal growth temperature range is 20 to 30 °C ([Gupta et al., 2020](#)). Yuanjiang has a typical dry and hot valley climate, with an average annual temperature of 24.3 °C ([Fei et al., 2017](#); [Zhao et al., 2014](#)). Collect *M. citrifolia* fruit in the white maturity stage and select fruit with the same maturity and size. Immediately after harvesting, immediately wash it carefully with distilled water to remove dust and other contaminants. Wipe off the residual moisture on the surface with absorbent paper for later use.

Chemical and solvents

The chemicals used in this study, such as Folin-Ciocalteu reagent, gallic acid and glucose standard, were purchased in Sigma-Aldrich. All other solvents such as sulfuric acid, phenol and sodium carbonate were of analytical grade.

Sample preparation and extraction

The *M. citrifolia* fruit was slice up of 0.5–0.8 mm and dried at 60 °C until the weight was constant, and grind it into a powder, pass through an 80-mesh sieve. The powder samples were put into a sealed bag and placed in a dryer at 60 °C for the later use. 0.5 g of *M. citrifolia* fruit powder was weighed, and explore the effect of different ratio of water/*M. citrifolia* fruit powder (70, 80 and 90 mL/g), extraction temperature (PSC: 40, 45 and 50 °C; PPN: 85, 90 and 95 °C) and extraction time (5, 10 and 15 min) on the extraction yield of PSC and PPN. The extraction solution was centrifuged at 3880 g for 10 min. The supernatant was used for the determination of PSC and PPN.

Table 1 The levels of parameters of BBD for extraction experimental.

Parameters		Codes	Levels		
			−1	0	1
PSC	Ratio of water/ <i>M. citrifolia</i> fruit powder (mL/g)	X ₁	70	80	90
	Extraction temperature (°C)	X ₂	40	45	50
	Extraction time (min)	X ₃	5	10	15
PPN	Ratio of water/ <i>M. citrifolia</i> fruit powder (mL/g)	X' ₁	70	80	90
	Extraction temperature (°C)	X' ₂	85	90	95
	Extraction time (min)	X' ₃	5	10	15

Determination of PSC contents

The total PSC content of *M. citrifolia* extract was determined according to the phenol–sulfuric acid method (Qu et al., 2016) with modification using glucose as the standard. Each 0.1 mL sample added 0.9 mL distilled water and one mL of 5% phenol after mixed with 3.5 mL concentrated sulfuric acid rapidly. The maximal absorption was at 489 nm and the absorbance was measured after standing for 15 min.

The yield of PSC (%) was calculated in the same way as that of Qu et al. (2016).

Determination of PPN contents

The total PPN content in the *M. citrifolia* extract was determined by using Folin–Ciocalteu method (Ab Rahman et al., 2019) with modification using gallic acid as the standard. Each 0.5 mL sample added 0.5 mL distilled water and one mL of Folin–Ciocalteu reagent, stood for 5 min. Then two mL of 10% sodium carbonate solution was added and stood about 1 h at room temperature in darkness. Finally, the maximal absorption at 762 nm was monitored.

The yield of PPN (%) was calculated in the same way as that of (Qu et al., 2016).

Experimental design and data analysis

To determine the optimized aqueous extraction parameters of PSC and PPN, a Box–Behnken design (BBD) with three levels (−1, 0 and 1) was applied. Based on the single-factor results, the main scope of extraction parameters was identified. Table 1 showed the range and center points of the three operational parameters.

All data in this study were calculated as the average of experiments in triplicate. Response surface methodology (RSM) carried out the model and the experimental design and data analysis were implemented using Design-Expert software 8.0.6. To assess the statistical significance and the reliability of the model, response surface analysis and variance analysis (ANOVA) were performed. The statistically regarded was as significant if $P < 0.05$.

RESULTS

Model fitting analysis

The optimization of aqueous extraction parameter for high PSC extracts and PPN content from dried *M. citrifolia* fruit slice tea was conducted using RSM. The yield of PSC and PPN was considered a dependent variable for BBD. The experimental conditions of 15 runs

Table 2 Design and results of RSM experiment for extraction yield of PSC and PPN.

No.	Coded parameter levels of PSC			Coded parameter levels of PPN			Observer		Predicted	
	X ₁ (mL/g)	X ₂ (°C)	X ₃ (min)	X' ₁ (mL/g)	X' ₂ (°C)	X' ₃ (min)	Yield of PSC (%)	Yield of PPN (%)	Yield of PSC (%)	Yield of PPN (%)
1	0	1	-1	0	1	-1	14.46	7.8	14.40	7.80
2	-1	-1	0	-1	-1	0	15.05	7.4	14.89	7.49
3	1	-1	0	1	-1	0	15.19	8.4	15.19	8.39
4	0	0	0	0	0	0	16.92	8.6	16.93	8.53
5	-1	1	0	-1	1	0	16.10	8.0	16.10	8.01
6	0	0	0	0	0	0	16.84	8.6	16.93	8.53
7	1	0	1	1	0	1	15.56	8.9	15.51	8.91
8	-1	0	-1	-1	0	-1	15.50	7.8	15.56	7.79
9	1	1	0	1	1	0	15.19	8.3	15.35	8.21
10	0	1	1	0	1	1	15.81	8.5	15.71	8.58
11	1	0	-1	1	0	-1	15.59	8.3	15.49	8.39
12	0	0	0	0	0	0	17.02	8.4	16.93	8.53
13	-1	0	1	-1	0	1	15.80	8.5	15.90	8.41
14	0	-1	-1	0	-1	-1	14.74	7.9	14.84	7.83
15	0	-1	1	0	-1	1	13.84	8.2	13.90	8.20

were done respectively, with predicted results from PSC change interval of 13.84–17.02% and PPN change interval of 7.4–8.9% (Table 2). The regression equation of the predicted response Y for PSC and PPN yield was obtained as follows:

$$Y_{\text{PSC}}(\%) = -89.52375 + 0.63058X_1 + 3.49650X_2 + 0.45367X_3 - 0.00165X_1X_2 - 0.00525X_1X_3 + 0.0225X_2X_3 - 0.0032208_3X_1^2 - 0.039683X_2^2 - 0.048883X_3^2 \quad (1)$$

$$Y_{\text{PPN}}(\%) = -24.35 + 0.29417X'_1 + 0.35750X'_2 + 0.25083X'_3 - 0.0005X'_1X'_2 - 0.0035X'_1X'_3 + 0.004X'_2X'_3 - 0.00116667X_1'^2 - 0.00166667X_2'^2 - 0.015667X_3'^2 \quad (2)$$

The ANOVA results determined the reliability of the model of PSC and PPN in predicting the optimum conditions and exactly displaying the real interrelationship between the selected parameters (Table 3).

The regression coefficients were showed in Table 3. For PSC, X₃, X₁², X₂², X₃², X₁X₃, X₂X₃ were significant (*P* < 0.001). For PPN, X'₁, X'₂, X'₁X'₃, X'₃² was extremely significant (*P* < 0.001). In all the significant terms, the most significant effect on PSC and PPN were X₃² and X'₂, respectively.

Response surface analysis of PSC

The relationship between the response of PSC extraction condition was directly reflected by Fig. 2. At 40~45 °C, PSC yield with the increase of extraction temperature, while the further addition of extraction temperature caused to decrease in the PSC yield (Fig. 2A).

Table 3 Variance analysis for fitting quadratic model of extraction yield of PSC and PPN.

Source	Sum of square	Degree of freedom	Mean square	F-value	P-value
Extraction of PSC					
Model	11.29	9	1.25	52.45	0.0002**
X ₁	0.11	1	0.11	4.42	0.0894
X ₂	0.065	1	0.065	2.71	0.1607
X ₃	0.94	1	0.94	39.24	0.0015*
X ₁ X ₂	0.027	1	0.027	1.14	0.3348
X ₁ X ₃	0.28	1	0.28	11.53	0.0194*
X ₂ X ₃	1.27	1	1.27	52.93	0.0008**
X ₁ ²	0.38	1	0.38	16.02	0.0103*
X ₂ ²	3.63	1	3.63	151.97	<0.0001**
X ₃ ²	5.51	1	5.51	230.6	<0.0001**
Residual	0.12	5	0.024		
Lack of fit	0.1	3	0.034	4.23	0.197
Pure error	0.016	2	0.008133		
Correlation Total	11.41	14			
R ²	0.9895	Adj R ²	0.9707		
C.V.%	0.99	Pred R ²	0.8519		
PRESS	1.69	Adeq Precision	23.991		
Extraction of PPN					
Model	2.09	9	0.23	16.76	0.0032*
X' ₁	0.6	1	0.6	43.73	0.0012*
X' ₂	0.66	1	0.66	47.8	0.001**
X' ₃	0.061	1	0.061	4.43	0.0893
X' ₁ X' ₂	0.0025	1	0.0025	0.18	0.6884
X' ₁ X' ₃	0.12	1	0.12	8.86	0.0309*
X' ₂ X' ₃	0.04	1	0.04	2.89	0.1498
X' ₁ ²	0.05	1	0.05	3.63	0.115
X' ₂ ²	0.00641	1	0.00641	0.46	0.5263
X' ₃ ²	0.57	1	0.57	40.95	0.0014*
Residual	0.069	5	0.014		
Lack of fit	0.043	3	0.014	1.06	0.5183
Pure error	0.027	2	0.013		
Correlation Total	2.16	14			
R ²	0.9679	Adj R ²	0.9102		
C.V.%	1.43	Pred R ²	0.6568		
PRESS	0.74	Adeq Precision	14.839		

Notes.*Means significant at $P < 0.05$.**Means significant at $P < 0.001$.

Moreover, under the extraction temperature of 45 °C and the ratio of water/*M. citrifolia* fruit powder of 80 mL/g, the extraction value could reach 17.02%. PSC yield was gradually increased by extension of extraction time but reduced at higher from 11 min extraction times. Moreover, up to 16.84% of PSC yield was obtained at an extraction time of 10 min

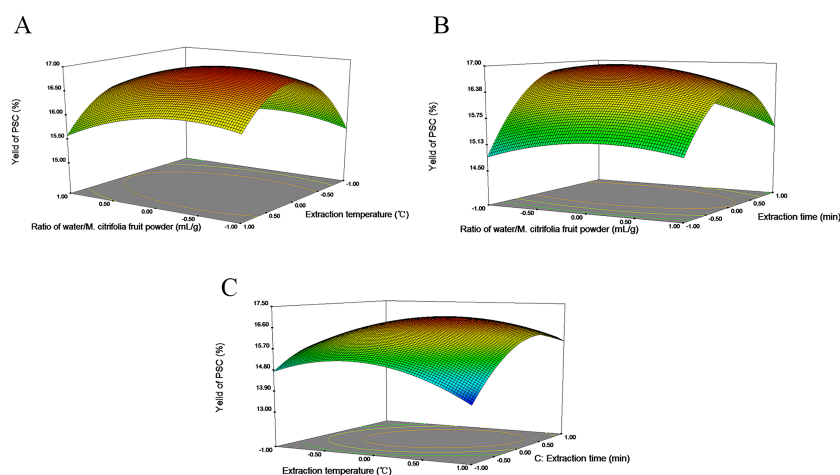


Figure 2 The 3D response surface plot and contour plot of PSC extraction yield. (A) Interaction between ratio of water/*M. citrifolia* fruit powder and temperature, while time was constant at 10 min; (B) interaction between ratio of water/*M. citrifolia* fruit powder and time, while the temperature was constant at 45 °C; (C) interaction between temperature and time, while ratio of water/*M. citrifolia* fruit powder was constant at 80 mL/g).

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and the ratio of water/*M. citrifolia* fruit powder of 80 mL/g (Fig. 2B). The extraction yield of PSC increases first and then decreases with the increase of extraction time and temperature (Fig. 2C). When the extraction time and temperature was 10 min and 45 °C, respectively, the maximum PSN yield was achieved.

Response surface analysis of PPN

The extraction yield of PPN increased with the extraction temperature and the ratio of water/*M. citrifolia* fruit powder (Fig. 3A). The optimal region was supposed to be in the ratio of water/*M. citrifolia* fruit powder above 80 mL/g, a temperature higher than 92 °C which could lead to the extraction yield of PPN over 8.8%. Furthermore, Fig. 3B illustrated that the ratio of water/*M. citrifolia* fruit powder was positively correlated with the extraction yield of PPN. An increase in the ratio of water/*M. citrifolia* fruit powder tend to enhanced the PPN yield. Moreover, the extraction time showed quadratic effects on the PPN extraction response. From 5 to 10 min, PPN yield showed an upward trend, and decline slightly over 10 min. Overall, the PPN showed the maximum yield when the ratio of water/*M. citrifolia* fruit powder was 90 mL/g for 10 min. The optimal region temperature and time of PPN extraction were about 91–95 °C and 8–15 min, respectively, and peaked at PPN yield when 95 °C and 11 min (Fig. 3C).

Optimization conditions and model effectiveness

The optimal conditions for the PSC and PPN extraction were selected based on the constructed RSM models. The predicted yield of 16.98% could be obtained under the ratio of water/*M. citrifolia* fruit powder of 77.27 mL/g, the temperature of 45.56 °C and time of 10.98 min for PSC. The predicted yield of 8.91% could be obtained under the ratio of water/*M. citrifolia* fruit powder of 90 mL/g, the temperature of 95 °C and time of 10.09

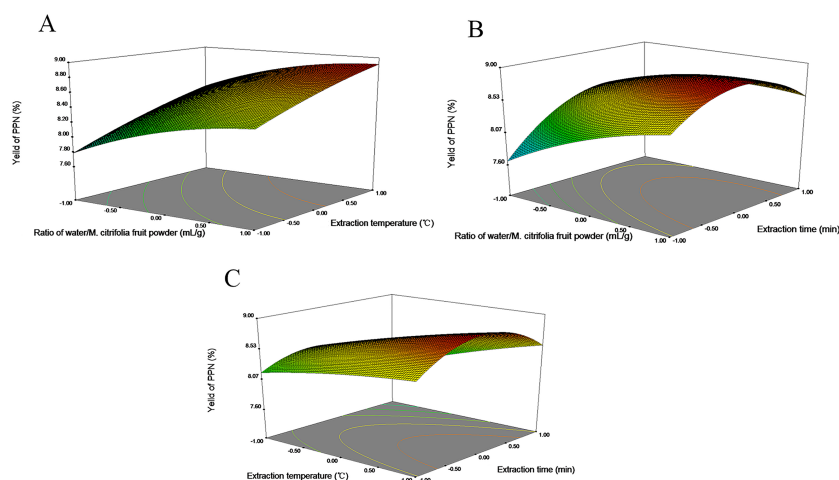


Figure 3 The 3D response surface plot and contour plot of PPN extraction yield. (A) Interaction between ratio of water/*M. citrifolia* fruit powder and temperature, while time was constant at 10 min; (B) interaction between ratio of water/*M. citrifolia* fruit powder and time, while the temperature was constant at 90 °C; (C) interaction between temperature and time, while ratio of water/*M. citrifolia* fruit powder was constant at 80 mL/g).

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Table 4 Results of experimental verification.

Response value	Optimal condition			Predicted value (%)	Experimental value (%)
	Ratio of water/ <i>M. citrifolia</i> fruit powder (mL/g)	Extraction temperature (°C)	Extraction time (min)		
Yield of PSC	78	46	11	16.98	17.00 ± 0.08
Yield of PPN	90	95	10	8.91	8.93 ± 0.04

min for PPN. To verify the effectiveness of models in predicting the yields of PSC and PPN, the conditions were modified based on the actual operation situation and experimental verification on optimized conditions. In the adjusted conditions, the practical yield of PSC and PPN was 17.00 ± 0.08 mg/g and 8.93 ± 0.04 mg/g, respectively (Table 4), which were approximately the predicted results, confirming that the response models were sufficient and precise for the prediction of PSC and PPN extraction.

DISCUSSION

P-values described the significance of the model and coefficients, and the adequacy and fitness of the model were checked into by the determination coefficient (R^2) and the adjusted determination coefficient (Adj R^2) (Zeng et al., 2020). The RSM mathematical model was significant ($P < 0.05$) for PSC and PPN did not reveal lack of fit ($P > 0.05$) (Table 3), which confirmed the model accuracy (Liu et al., 2019). According to with Adj R^2 0.9707 and 0.9102 for PSC and PPN, respectively, these models could sufficiently explain 97.07% and 91.02% response values and only about the change in 2.93%, 8.98% data could

not be explained with these model. Moreover, exceptionally high values of R^2 for PSC and PPN (0.9895 and 0.9679, respectively) and low values of the coefficient of variation (CV) showed that the model was good (Hosseini et al., 2018). In the model, the term with a large F-value and a small P-value was taken as response variables, significantly impacting the extraction yield (Akhbari et al., 2018). To sum up, the experiment design is reasonable, which indicated that the RSM analysis method was feasible to optimize the extraction of PSC and PPN from dried *M. citrifolia* fruit slice tea.

The interactive effects of temperature on PSC yield were more substantial than the ratio of water/*M. citrifolia* fruit powder (Fig. 2A). This might result from the higher temperatures that could increase cell wall structure rupture, causing more PSC to dissolve in water. However, the macromolecules started to decomposition when the sensitive temperature to extract the PSC exceeded, resulting in less available PSC (Romdhane et al., 2017). On the other hand, the extraction time also showed a stronger effect on PPN yield in comparison to the ratio of water/noni fruit powder (Fig. 2B). This might happen probably because of PSC properties during hydrolysis (Skenderidis et al., 2017; Yang et al., 2013). Therefore, the extraction temperature and time showed a more substantial effect on the PSC yield than the ratio of water/*M. citrifolia* fruit powder.

Figure 2C implied that the extraction time and temperature both had a strong effect on PSC yield and presented quadratic effects on the PSC extraction response, which verified that temperature and time (X_2X_3) in Table 3 were extremely significant. Generally, active substances' solubility could be promoted by increasing extraction time and temperature to obtain a better extraction yield. Whereas, degradation of the active substances was also facilitated by prolonged extraction time and temperature, correspondingly leading to less yield (Garlock et al., 2011; Papoutsis et al., 2016). Ji et al. (2018) reported the similar findings that excessive temperature and time had a negative effect on the extraction yield, because the chemical structure and activity of PSC dissolved in water was influenced. Moreover, the semblable phenomenons were reported in studies by Lin et al. (2017), Shang et al. (2018) and Wang et al. (2014). The influence order of the interaction between response variables on the PSC yield is as follows: interaction of temperature and time (X_2X_3) > interaction of ratio of water/*M. citrifolia* fruit powder and time (X_1X_3) > interaction of ratio of water/*M. citrifolia* fruit powder and temperature (X_1X_2). This is consistent with the results of ANOVA (Table 3).

The extraction yield of PPN increased with the increase ratio of water/*M. citrifolia* fruit powder (Fig. 3A). The mass transfer principle might be considered, with the increase of ratio of water/*M. citrifolia* fruit powder, the concentration gradient in the solution raised, which meant that the driving force to dissolve the PPN in the water improved and the diffusion rate in the solution also enhanced (Al-Farsi & Lee, 2008; Goldsmith et al., 2014). The research showed that with the increase of liquid–solid ratio, the extraction rate of phenolic substances in citrus increased (Hayat et al., 2009). Our study showed that the high extraction temperature and high ratio of water/*M. citrifolia* fruit powder were favorable for the extraction of PPN when keeping time at the optimal values (Fig. 3A). The high temperature may promote the extraction yield by increasing the solubility and mass transfer rate of phenolic compounds (Dai & Mumper, 2010). Besides, the energetic

conditions were higher when there was the higher temperature, leading to changes in solvent physical property and plant cell–matrix and an increase in the solubility and diffusion rate of PPN in water, which could be conducive to the extraction of PPN (Dos Santos Nascimento et al., 2018; Rajha et al., 2014; Zeković et al., 2014). The results of this experiments were similar to other studies on the optimization of water extraction of phenolics from lemon pomace, in which the extraction with the highest temperature was 95 °C and the highest sample-to-solvent ratio of 100 mL/g was the best yield of phenolics when compared with the yield obtained at the lower temperature and sample-to-solvent ratio (Papoutsis et al., 2016), and so did the study by Goldsmith et al. (2014). The influence order of the interaction between extraction conditions on the PPN yield is as follows: interaction of ratio of water/*M. citrifolia* fruit powder and time ($X'_1X'_3$) > interaction of temperature and time ($X'_2X'_3$) > interaction of ratio of water/*M. citrifolia* fruit powder and temperature ($X'_1X'_2$). This is consistent with the results of ANOVA (Table 3).

CONCLUSIONS

To study how to drink dried *M. citrifolia* fruit slice tea to get more PSC and PPN. This research used RSM for obtaining the optimal conditions of the aqueous extraction process of PSC and PPN from *M. citrifolia* fruit, and the models were confirmed to be effective and feasible for optimization extraction. The optimal experimental conditions for extraction of PSC and PPN in dried *M. citrifolia* fruit slice tea were: the highest yield of PSC was 17.00% at ratio of water/*M. citrifolia* fruit powder 78 mL/g, 46 °C, and 11 min, and the highest yield of PPN was 8.93% at ratio of water/*M. citrifolia* fruit powder 90 mL/g, 95 °C, and 10 min. Thus, using a 300 ml cup (300 mL of water) as an example, people can soak four average-sized dried *M. citrifolia* fruit slices in boiled water for 11 min to obtained the maximum level of PSC. To get a PPN, people can place three slices in boiling water for 10 min. The design of this study was based on the respective optimizations of PSC and PPN. If people would like to obtain more PSC and PPN at the same time, the further experimental research is needed. The use of dried *M. citrifolia* fruit powder when conditions are permitted is more conducive to the precipitation of active substances than the dried slice. *M. citrifolia* fruit contains polysaccharides, polyphenols, alkaloids, amino acids and other compounds. It has antibacterial, anti-cancer, anti-oxidant, anti-inflammatory, analgesic, cardiovascular protection, etc. *M. citrifolia* fruit containing other active ingredients The optimal processing conditions for tea also needs to be further studied. The obtained findings promoted the development and utilization of *M. citrifolia* fruit products. It laid the foundation for further research on the functions of dried *M. citrifolia* fruit sliced tea.

ADDITIONAL INFORMATION AND DECLARATIONS

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Competing Interests

The authors declare there are no competing interests.

Author Contributions

- Qingfen Wang conceived and designed the experiments, performed the experiments, analyzed the data, authored or reviewed drafts of the paper, and approved the final draft.
- Fei Yang and Dandan Jia performed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.
- Tian Wu conceived and designed the experiments, authored or reviewed drafts of the paper, and approved the final draft.

Data Availability

The following information was supplied regarding data availability:

The raw data are available in the [Supplementary File](#).

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REFERENCES

- Ab Rahman Z, Zaidan MWAM, Othman AN, Ahmad MA, Simoh S, Ismail MAH.** 2019. Optimizing extraction of phenolics and flavonoids from *Solanum ferox* Fruit. *Natural Science* **11**:99–105 DOI [10.4236/ns.2019.114011](https://doi.org/10.4236/ns.2019.114011).
- Akhbari M, Masoum S, Aghababaei F, Hamedi S.** 2018. Optimization of microwave assisted extraction of essential oils from Iranian *Rosmarinus officinalis* L. using RSM. *Journal of Food Science and Technology* **55**:2197–2207 DOI [10.1007/s13197-018-3137-7](https://doi.org/10.1007/s13197-018-3137-7).
- Al-Farsi MA, Lee CY.** 2008. Optimization of phenolics and dietary fibre extraction from date seeds. *Food Chemistry* **108**:977–985 DOI [10.1016/j.foodchem.2007.12.009](https://doi.org/10.1016/j.foodchem.2007.12.009).
- Almeida ÉS, De Oliveira D, Hotza D.** 2019. Properties and applications of *Morinda citrifolia* (Noni): a review. *Comprehensive Reviews in Food Science and Food Safety* **18**:883–909 DOI [10.1111/1541-4337.12456](https://doi.org/10.1111/1541-4337.12456).
- Assi R, Darwis Y, Abdulbaqi IM, Khan AA, Vuanghao L, Laghari MH.** 2017. *Morinda citrifolia* (Noni): a comprehensive review on its industrial uses, pharmacological activities, and clinical trials. *Arabian Journal of Chemistry* **10**:691–707 DOI [10.1016/j.arabjc.2015.06.018](https://doi.org/10.1016/j.arabjc.2015.06.018).

- Bezerra MA, Santelli RE, Oliveira EP, Villar LS, Escaleira LA. 2008.** Response surface methodology (RSM) as a tool for optimization in analytical chemistry. *Talanta* 76:965–977 DOI [10.1016/j.talanta.2008.05.019](https://doi.org/10.1016/j.talanta.2008.05.019).
- Birhanu BT, Kim JY, Hossain MA, Choi JW, Lee SP, Park SC. 2018.** An in vivo immunomodulatory and anti-inflammatory study of fermented *Dendropanax morbifera* Léveillé leaf extract. *BMC Complementary and Alternative Medicine* 18:222 DOI [10.1186/s12906-018-2282-x](https://doi.org/10.1186/s12906-018-2282-x).
- Cai Z, Chen H, Chen J, Yang R, Zou L, Wang C, Chen J, Tan M, Mei Y, Wei L, Yin S, Liu X. 2020.** Metabolomics characterizes the metabolic changes of *Lonicerae Japonicae* Flos under different salt stresses. *PLOS ONE* 15:e0243111 DOI [10.1371/journal.pone.0243111](https://doi.org/10.1371/journal.pone.0243111).
- Cai Y, Luo Q, Sun M, Corke H. 2004.** Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. *Life Sciences* 74:2157–2184 DOI [10.1016/j.lfs.2003.09.047](https://doi.org/10.1016/j.lfs.2003.09.047).
- Cavuldak A, Vural N, Akay MA, Anlı RE. 2019.** Optimization of ultrasound-assisted water extraction conditions for the extraction of phenolic compounds from black mulberry leaves (*Morus nigra* L.). *Journal of Food Process Engineering* 42:e13132 DOI [10.1111/jfpe.13132](https://doi.org/10.1111/jfpe.13132).
- Chan-Blanco Y, Vaillant F, Perez AM, Reynes M, Brillouet JM. 2006.** The noni fruit (*Morinda citrifolia* L.): a review of agricultural research, nutritional and therapeutic properties. *Journal of Food Composition and Analysis* 19:645–654 DOI [10.1016/j.jfca.2005.10.001](https://doi.org/10.1016/j.jfca.2005.10.001).
- Chang SW, Du YE, Qi Y, Lee JS, Goo N, Koo BK, Bae HJ, Ryu JH, Jang DS. 2019.** New depsides and neuroactive phenolic glucosides from the flower buds of rugosa rose (*Rosa rugosa*). *Journal of Agricultural and Food Chemistry* 67:7289–7296 DOI [10.1021/acs.jafc.9b01228](https://doi.org/10.1021/acs.jafc.9b01228).
- Chang YY, Lin YL, Yang DJ, Liu CW, Hsu CL, Tzang BS, Chen YC. 2013.** Hepato-protection of noni juice against chronic alcohol consumption: lipid homeostasis, antioxidation, alcohol clearance, and anti-inflammation. *Journal of Agricultural and Food Chemistry* 61:11016–11024 DOI [10.1021/jf4038419](https://doi.org/10.1021/jf4038419).
- Chen R, Liu Z, Zhao J, Chen R, Meng F, Zhang M, Ge W. 2011.** Antioxidant and immunobiological activity of water-soluble polysaccharide fractions purified from *Acanthopanax senticosu*. *Food Chemistry* 127:434–440.
- Cho IH, Zoh KD. 2007.** Photocatalytic degradation of azo dye (Reactive Red 120) in TiO₂/UV system: optimization and modeling using a response surface methodology (RSM) based on the central composite design. *Dyes and Pigments* 75:533–543 DOI [10.1016/j.dyepig.2006.06.041](https://doi.org/10.1016/j.dyepig.2006.06.041).
- Dai J, Mumper RJ. 2010.** Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. *Molecules* 15:7313–7352.
- Darvesh AS, Carroll RT, Bishayee A, Geldenhuys WJ, Van der Schyf CJ. 2010.** Oxidative stress and Alzheimer's disease: dietary polyphenols as potential therapeutic agents. *Expert Review of Neurotherapeutics* 10:729–745 DOI [10.1586/ern.10.42](https://doi.org/10.1586/ern.10.42).

- Deti C, Dos Santos Nascimento LB, Brunetti C, Ferrini F, Gori A. 2020.** Optimization of a green ultrasound-assisted extraction of different polyphenols from *Pistacia lentiscus* L. leaves using a response surface methodology. *Plants* **9**:1482 DOI [10.3390/plants9111482](https://doi.org/10.3390/plants9111482).
- Ding Y, Zheng J, Xia X, Ren T, Kan J. 2016.** Box–Behnken design for the optimization of nanoscale retrograded starch formation by high-power ultrasonication. *LWT-Food Science and Technology* **67**:206–213 DOI [10.1016/j.lwt.2015.11.022](https://doi.org/10.1016/j.lwt.2015.11.022).
- Dos Santos Nascimento LB, De Aguiar PF, Leal-Costa MV, Coutinho MAS, Borsodi MPG, Rossi-Bergmann B, Tavares ES, Costa SS. 2018.** Optimization of aqueous extraction from *Kalanchoe pinnata* leaves to obtain the highest content of an anti-inflammatory flavonoid using a response surface model. *Phytochemical Analysis* **29**:308–315 DOI [10.1002/pca.2744](https://doi.org/10.1002/pca.2744).
- Dussosoy E, Brat P, Bony E, Boudard F, Poucheret P, Mertz C, Giaimis J, Michel A. 2011.** Characterization, anti-oxidative and anti-inflammatory effects of Costa Rican noni juice (*Morinda citrifolia* L.). *Journal of ethnopharmacology* **133**:108–115 DOI [10.1016/j.jep.2010.08.063](https://doi.org/10.1016/j.jep.2010.08.063).
- Favre LC, Santos CDos, López-Fernández MP, Mazzobre MF, Buera MDP. 2018.** Optimization of β -cyclodextrin-based extraction of antioxidant and anti-browning activities from thyme leaves by response surface methodology. *Food Chemistry* **265**:86–95 DOI [10.1016/j.foodchem.2018.05.078](https://doi.org/10.1016/j.foodchem.2018.05.078).
- Favreau-Farhadi N, Pecukonis L, Barrett A. 2015.** The inhibition of Maillard Browning by different concentrations of rosmarinic acid and epigallocatechin-3-gallate in model, bakery, and fruit systems. *Journal of Food Science* **80**:C2140–C2146 DOI [10.1111/1750-3841.13014](https://doi.org/10.1111/1750-3841.13014).
- Fei X, Song Q, Zhang Y, Liu Y, Sha L, Yu G, Zhang L, Duan C, Deng Y, Wu C, Lu Z, Luo K, Chen A, Xu K, Liu W, Huang H, Jin Y, Zhou R, Li J, Lin Y, Zhou L, Fu Y, Bai X, Tang X, Gao J, Zhou W, Grace J. 2017.** Carbon exchanges and their responses to temperature and precipitation in forest ecosystems in Yunnan, Southwest China. *Science of the Total Environment* **616**:824–840 DOI [10.1016/j.scitotenv.2017.10.239](https://doi.org/10.1016/j.scitotenv.2017.10.239).
- Ferreira SL, Bruns RE, Ferreira HS, Matos GD, David JM, Brandão GC, Silva EGda, Portugal LA, Reis PSdos, Souza AS, dos Santos WN. 2007.** Box-Behnken design: an alternative for the optimization of analytical methods. *Analytica Chimica Acta* **597**:179–186 DOI [10.1016/j.aca.2007.07.011](https://doi.org/10.1016/j.aca.2007.07.011).
- Gardin F, Martuscelli M, Caruso MC, Galgano F, Crudele MA, Favati F, Guersoni ME, Suzzi G. 2001.** Effects of pH, temperature and NaCl concentration on the growth kinetics, proteolytic activity and biogenic amine production of *Enterococcus faecalis*. *International Journal of Food Microbiology* **64**:105–117 DOI [10.1016/s0168-1605\(00\)00445-1](https://doi.org/10.1016/s0168-1605(00)00445-1).
- Garlock RJ, Balan V, Dale BE, Pallapolu VR, Lee YY, Kim Y, Mosier NS, Ladisch MR, Holtzapple MT, Falls M, Sierra-Ramirez R, Shi J, Ebrik MA, Redmond T, Yang B, Wyman CE, Donohoe BS, Vinzant TB, Elander RT, Hames B, Thomas**

- S, Warner RE. 2011.** Comparative material balances around pretreatment technologies for the conversion of switchgrass to soluble sugars. *Bioresource Technology* **102**:11063–11071 DOI [10.1016/j.biortech.2011.04.002](https://doi.org/10.1016/j.biortech.2011.04.002).
- Goldsmith CD, Vuong QV, Stathopoulos CE, Roach PD, Scarlett CJ. 2014.** Optimization of the aqueous extraction of phenolic compounds from olive leaves. *Antioxidants* **3**:700–712 DOI [10.3390/antiox3040700](https://doi.org/10.3390/antiox3040700).
- Gupta R, Sharma RD, Rao YR, Siddiqui ZH, Verma A, Ansari MW, Rakwal R, Tuteja N. 2020.** Acclimation potential of Noni (*Morinda citrifolia* L.) plant to temperature stress is mediated through photosynthetic electron transport rate. *Plant Signaling and Behavior* **16**:1865687 DOI [10.1080/15592324.2020.1865687](https://doi.org/10.1080/15592324.2020.1865687).
- Guzelmeric E, Vovk I, Yesilada E. 2015.** Development and validation of an HPTLC method for apigenin 7-O-glucoside in chamomileflowers and its application for fingerprint discrimination of chamomile-like materials. *Journal of Pharmaceutical and Biomedical Analysis* **107**:108–118 DOI [10.1016/j.jpba.2014.12.021](https://doi.org/10.1016/j.jpba.2014.12.021).
- Han Y, Floros JD, Linton RH, Nielsen SS, Nelson PE. 2001.** Response surface modeling for the inactivation of *Escherichia coli* O157:H7 on green peppers (*Capsicum annuum* L.) by chlorine dioxide gas treatments. *Journal of Food Protection* **64**:1128–1133 DOI [10.4315/0362-028x-64.8.1128](https://doi.org/10.4315/0362-028x-64.8.1128).
- Han QH, Liu W, Li HY, He JL, Guo H, Lin S, Zhao L, Chen H, Liu YW, Wu DT, Li SQ, Qin W. 2019.** Extraction optimization, physicochemical characteristics, and antioxidant activities of polysaccharides from kiwifruit (*Actinidia chinensis* Planch). *Molecules* **24**:461 DOI [10.3390/molecules24030461](https://doi.org/10.3390/molecules24030461).
- Hayat K, Hussain S, Abbas S, Farooq U, Ding BM, Xia SQ, Jia CS, Zhang XM, Xia WS. 2009.** Optimized microwaveassisted extraction of phenolic acids from citrus mandarin peels and evaluation of antioxidant activity in vitro. *Separation and Purification Technology* **70**:63–70.
- He Z, Zhu Y, Bao X, Zhang L, Li N, Jiang G, Peng Q. 2019.** Optimization of alkali extraction and properties of polysaccharides from *Ziziphus jujuba* cv. Residue. *Molecules* **24**:2221 DOI [10.3390/molecules24122221](https://doi.org/10.3390/molecules24122221).
- Heck CI, De Mejia EG. 2007.** Yerba Mate Tea (*Ilex paraguariensis*): a comprehensive review on chemistry, health implications, and technological considerations. *Journal of Food Science* **72**:138–151 DOI [10.1111/j.1750-3841.2007.00535.x](https://doi.org/10.1111/j.1750-3841.2007.00535.x).
- Hosseini H, Bolourian S, Yaghoubi Hamgini E, Ghanuni Mahababadi E. 2018.** Optimization of heat-and ultrasound-assisted extraction of polyphenols from dried rosemary leaves using response surface methodology. *Journal of Food Processing and Preservation* **42**:e13778 DOI [10.1111/jfpp.13778](https://doi.org/10.1111/jfpp.13778).
- Hyun TK, Kim MO, Lee H, Kim Y, Kim E, Kim JS. 2013.** Evaluation of anti-oxidant and anti-cancer properties of *Dendropanax morbifera* Léveillé. *Food Chemistry* **141**:1947–1955 DOI [10.1016/j.foodchem.2013.05.021](https://doi.org/10.1016/j.foodchem.2013.05.021).
- Hyun TK, Ko YJ, Kim EH, Chung IM, Kim JS. 2015.** Anti-inflammatory activity and phenolic composition of *Dendropanax morbifera* leaf extracts. *Industrial Crops and Products* **74**:263–270 DOI [10.1016/j.indcrop.2015.05.002](https://doi.org/10.1016/j.indcrop.2015.05.002).

- Iglesias-Carres L, Mas-Capdevila A, Sancho-Pardo L, Bravo FI, Mulero M, Muguerza B, Arola-Arnal A. 2018. Optimized extraction by response surface methodology used for the characterization and quantification of phenolic compounds in whole red grapes (*Vitis vinifera*). *Nutrients* **10**:1931 DOI [10.3390/nu10121931](https://doi.org/10.3390/nu10121931).
- Ji XL, Peng Q, Yuan YP, Liu F, Wang M. 2018. Extraction and physicochemical properties of polysaccharides from *Ziziphus Jujuba* cv. Muzao by ultrasound-assisted aqueous two-phase extraction. *International Journal of Biological Macromolecules* **108**:541–549 DOI [10.1016/j.ijbiomac.2017.12.042](https://doi.org/10.1016/j.ijbiomac.2017.12.042).
- Jia DD, Lan ZQ, Wu T. 2020. Ethylene is the key signal in the accumulation process of scopoletin in noni (*Morinda citrifolia*). *Scientia Horticulturae* **261**:108980 DOI [10.1016/j.scienta.2019.108980](https://doi.org/10.1016/j.scienta.2019.108980).
- Jin L, Li XB, Tian DQ, Fang XP, Yu YM, Zhu HQ, Ge YY, Ma GY, Wang WY, Li M. 2016. Antioxidant properties and color parameters of herbal teas in China. *Industrial Crops and Products* **87**:198–209 DOI [10.1016/j.indcrop.2016.04.044](https://doi.org/10.1016/j.indcrop.2016.04.044).
- Kang MJ, Kwon EB, Ryu HW, Lee S, Lee JW, Kim DY, Lee MK, Oh SR, Lee HS, Lee SU, Kim MO. 2018. Polyacetylene from *Dendropanax morbifera* alleviates diet-induced Obesity and hepatic steatosis by activating AMPK signaling pathway. *Frontiers in Pharmacology* **1**:382–386.
- Kröppel M, Zeiner M, Cindrić IJ, Stingeder G. 2012. Differences in aluminium content of various tea powders (black, green, herbal, fruit) and tea infusions. *Eur. Chem. Bull.* **1**:382–386 DOI [10.17628/ECB.2012.1.382](https://doi.org/10.17628/ECB.2012.1.382).
- Li H, Van den Driesche S, Bunge F, Yang B, Vellekoop MJ. 2019. Optimization of on-chip bacterial culture conditions using the Box-Behnken design response surface methodology for faster drug susceptibility screening. *Talanta* **194**:627–633 DOI [10.1016/j.talanta.2018.10.048](https://doi.org/10.1016/j.talanta.2018.10.048).
- Liao CH, Guo SJ, Lin JY. 2011. Characterisation of the chemical composition and in vitro anti-inflammation assessment of a novel lotus (*Nelumbo nucifera Gaertn*) plumule polysaccharide. *Food Chemistry* **125**:930–935 DOI [10.1016/j.foodchem.2010.09.082](https://doi.org/10.1016/j.foodchem.2010.09.082).
- Liao CH, Lin JY. 2011. Lotus (*Nelumbo nucifera Gaertn*) plumule polysaccharide protects the spleen and liver from spontaneous inflammation in non-obese diabetic mice by modulating pro-/anti-inflammatory cytokine gene expression. *Food Chemistry* **129**:245–252 DOI [10.1016/j.foodchem.2011.03.103](https://doi.org/10.1016/j.foodchem.2011.03.103).
- Lin YL, Chang YY, Yang DJ, Tzang BS, Chen YC. 2013. Beneficial effects of noni (*Morinda citrifolia* L.) juice on livers of high-fat dietary hamsters. *Food Chemistry* **140**:31–38 DOI [10.1016/j.foodchem.2013.02.035](https://doi.org/10.1016/j.foodchem.2013.02.035).
- Lin LH, Xie JH, Liu SC, Shen MY, Tang W, Xie MY. 2017. Polysaccharide from *Mesona chinensis*: extraction optimization, physicochemical characterizations and antioxidant activities. *International Journal of Biological Macromolecules* **99**:665–673 DOI [10.1016/j.ijbiomac.2017.03.040](https://doi.org/10.1016/j.ijbiomac.2017.03.040).
- Liu J, Mu TH, Sun HN, Fauconnier ML. 2019. Optimization of ultrasonic-microwave synergistic extraction of flavonoids from sweet potato leaves by response surface methodology. *Journal of Food Processing and Preservation* **43**:e13928 DOI [10.1111/jfpp.13928](https://doi.org/10.1111/jfpp.13928).

- Lorenzo JM, Munekata PES. 2016.** Phenolic compounds of green tea: health benefits and technological application in food. *Asian Pacific Journal of Tropical Biomedicine* **6**:709–719 DOI [10.1016/j.apjtb.2016.06.010](https://doi.org/10.1016/j.apjtb.2016.06.010).
- Lunceford N, Gugliucci A. 2005.** Ilex paraguariensis extracts inhibit AGE formation more efficiently than green tea. *Fitoterapia* **76**:419–427 DOI [10.1016/j.fitote.2005.03.021](https://doi.org/10.1016/j.fitote.2005.03.021).
- Ma JS, Liu H, Han CR, Zeng SJ, Xu XJ, Lu DJ, He HJ. 2019.** Extraction, characterization and antioxidant activity of polysaccharide from *Pouteria campechiana* seed. *Carbohydrate Polymers* **229**:115409 DOI [10.1016/j.carbpol.2019.115409](https://doi.org/10.1016/j.carbpol.2019.115409).
- Mckay DL, Blumberg JB. 2006.** A review of the bioactivity and potential health benefits of chamomile tea (*Matricaria recutita* L.). *Phytotherapy Research* **20**:519–530 DOI [10.1002/ptr.1900](https://doi.org/10.1002/ptr.1900).
- Motshakeri M, Ghazali HM. 2015.** Nutritional, phytochemical and commercial quality of Noni fruit: a multi-beneficial gift from nature. *Trends in Food Science and Technology* **45**:118–129 DOI [10.1016/j.tifs.2015.06.004](https://doi.org/10.1016/j.tifs.2015.06.004).
- Mukti AT, Dewi E, Satyantini WH, Sulmartiwi L, Hassan M. 2019.** The effect of noni *Morinda citrifolia* L. fruit extracts on the gill histopathological changes of Nile tilapia *Oreochromis niloticus*. *IOP Conference Series: Earth and Environmental Science* **236**:012093 DOI [10.1088/1755-1315/236/1/012093](https://doi.org/10.1088/1755-1315/236/1/012093).
- Nayak S, Mengi S. 2010.** Immunostimulant activity of noni (*Morinda citrifolia*) on T and B lymphocytes. *Pharmaceutical Biology* **48**:724–731 DOI [10.3109/13880200903264434](https://doi.org/10.3109/13880200903264434).
- Papoutsis K, Pristijono P, Golding JB, Stathopoulos CE, Bowyer MC, Scarlett CJ, Vuong QV. 2016.** Optimisation of aqueous extraction conditions for the recovery of phenolic compounds and antioxidants from lemon pomace. *International Journal of Food Science & Technology* **51**:2009–2018 DOI [10.1111/ijfs.13168](https://doi.org/10.1111/ijfs.13168).
- Peng X, Zheng Z, Cheng KW, Shan F, Ren GX, Chen F, Wang M. 2008.** Inhibitory effect of mung bean extract and its constituents vitexin and isovitexin on the formation of advanced glycation endproducts. *Food Chemistry* **106**:475–481 DOI [10.1016/j.foodchem.2007.06.016](https://doi.org/10.1016/j.foodchem.2007.06.016).
- Pękal A, Biesaga M, Pyrzynska K. 2013.** Trace metals and flavonoids in different types of tea. *Food Science and Biotechnology* **22**:925–930 DOI [10.1007/s10068-013-0165-y](https://doi.org/10.1007/s10068-013-0165-y).
- Prasad KN, Hassan FA, Yang B, Kong KW, Ramanan RN, Azlan A, Ismail A. 2011.** Response surface optimisation for the extraction of phenolic compounds and antioxidant capacities of underutilised *Mangifera pajang* Kosterm, peels. *Food Chemistry* **128**:1121–1127 DOI [10.1016/j.foodchem.2011.03.105](https://doi.org/10.1016/j.foodchem.2011.03.105).
- Prasad P, Visagaperumal Zonoubia A, Chandy V. 2019.** Review: fruit of *Morinda citrifolia*. *International Journal of Pharmaceutical Science and Health* **2**:9–20 DOI [10.26808/rs.ph.i9v2.02](https://doi.org/10.26808/rs.ph.i9v2.02).
- Qu Y, Li CX, Zhang C, Zeng R, Fu CM. 2016.** Optimization of infrared-assisted extraction of *Bletilla striata* polysaccharides based on response surface methodology and their antioxidant activities. *Carbohydrate Polymers* **148**:345–353 DOI [10.1016/j.carbpol.2016.04.081](https://doi.org/10.1016/j.carbpol.2016.04.081).

- Raal A, Orav A, Püssa T, Valner C, Malmiste B, Arak E. 2012. Content of essential oil, terpenoids and polyphenols in commercial chamomile (*Chamomilla recutita* L. Rauschert) teas from different countries. *Food Chemistry* **131**:632–638 DOI [10.1016/j.foodchem.2011.09.042](https://doi.org/10.1016/j.foodchem.2011.09.042).
- Rajaei-Sharifabadi H, Ellestad L, Porter T, Donoghue A, Bottje WG, Dridi S. 2017. Noni (*Morinda citrifolia*) modulates the hypothalamic expression of stress-and metabolic-related genes in broilers exposed to acute heat stress. *Frontiers in Genetics* **8**:192 DOI [10.3389/fgene.2017.00192](https://doi.org/10.3389/fgene.2017.00192).
- Rajha HN, Louka N, Darra NE, Hobaika Z, Boussetta N, Vorobiev E, Maroun RG. 2014. Multiple response optimization of high temperature, low time aqueous extraction process of phenolic compounds from grape byproducts. *Food and Nutrition Sciences* **5**:351–360 DOI [10.4236/fns.2014.54042](https://doi.org/10.4236/fns.2014.54042).
- Romdhane MB, Haddar A, Ghazala I, Jeddou KB, Helbert CB, Ellouz-Chaabouni S. 2017. Optimization of polysaccharides extraction from watermelon rinds: structure, functional and biological activities. *Food Chemistry* **216**:355–364 DOI [10.1016/j.foodchem.2016.08.056](https://doi.org/10.1016/j.foodchem.2016.08.056).
- Şahin S. 2013. Evaluation of antioxidant properties and phenolic composition of fruit tea infusions. *Antioxidants* **2**:206–215 DOI [10.3390/antiox2040206](https://doi.org/10.3390/antiox2040206).
- Santos TRJ, De Aquino Santana LCL. 2019. Antimicrobial potential of exotic fruits residues. *South African Journal of Botany* **124**:338–344 DOI [10.1016/j.sajb.2019.05.031](https://doi.org/10.1016/j.sajb.2019.05.031).
- Sasmito E, Hertiani T, Kartika S, Putri FM, Narastika L. 2015. Optimization of polysaccharide-rich fraction ation from *Morinda citrifolia* L. fruit based on immunostimulatory effect in vitro. *Indonesian Journal of Pharmacy* **26**:78–85 DOI [10.14499/indonesianjpharm26iss2pp76](https://doi.org/10.14499/indonesianjpharm26iss2pp76).
- Scalbert A, Johnson IT, Saltmarsh M. 2005. Polyphenols: antioxidants and beyond. *American Journal of Clinical Nutrition*.
- Shang HM, Zhou HZ, Duan MY, Li R, Wu HX, Lou YJ. 2018. Extraction condition optimization and effects of drying methods on physicochemical properties and antioxidant activities of polysaccharides from comfrey (*Symphytum officinale* L.) root. *International Journal of Biological Macromolecules* **112**:889–899 DOI [10.1016/j.ijbiomac.2018.01.198](https://doi.org/10.1016/j.ijbiomac.2018.01.198).
- Sharma K, Pachauri SD, Khandelwal K, Ahmad H, Arya A, Biala P, Agrawal S, Pandey RR, Srivastava A, Srivastav A, Saxena JK, Dwivedi AK. 2015. Anticancer effects of extracts from the fruit of *Morinda Citrifolia* (Noni) in breast cancer cell lines. *Drug Research* **66**:141–147 DOI [10.1055/s-0035-1555804](https://doi.org/10.1055/s-0035-1555804).
- Silva EM, Rogez H, Larondelle Y. 2007. Optimization of extraction of phenolics from *Inga edulis* leaves using response surface methodology. *Separation and Purification Technology* **55**:381–387 DOI [10.1016/j.seppur.2007.01.008](https://doi.org/10.1016/j.seppur.2007.01.008).
- Sinija VR, Mishra HN. 2008. Green tea: health benefits. *Journal of Nutritional & Environmental Medicine* **17**:232–242.
- Skenderidis P, Petrotos K, Giavasis I, Hadjichristodoulou C, Tsakalof A. 2017. Optimization of ultrasound assisted extraction of of goji berry (*Lycium barbarum*)

- fruits and evaluation of extracts' bioactivity. *Journal of Food Process Engineering* 40:e12522 DOI 10.1111/jfpe.12522.
- Sousa SG, Oliveira LA, De Aguiar Magalhães D, De Brito TV, Batista JA, Pereira CMC, De Souza Costa M, Mazulo JCR, De Carvalho Filgueiras M, Vasconcelos DFP, Da Silva DA, Barros FCN, Sombra VG, Freitas ALP, De Paula RCM, De Andrade Feitosa JP, Barbosa ALDR. 2018. Chemical structure and anti-inflammatory effect of polysaccharide extracted from *Morinda citrifolia* Linn (Noni). *Carbohydrate Polymers* 197:515–523 DOI 10.1016/j.carbpol.2018.06.042.
- Srinivasahan V, Durairaj B. 2014. Antioxidant and free radical scavenging effect of *Morinda citrifolia* fruit extract. *International Journal of Pharmacy & Pharmaceutical Sciences* 6:55–59.
- Taylor PW, Hamilton-Miller JM, Stapleton PD. 2005. Antimicrobial properties of green tea catechins. *Food Science and Technology Bulletin* 2:71–81 DOI 10.1616/1476-2137.14184.
- Wang W, Yang J, Yang J. 2020. Optimization of ultrasound-assisted aqueous two phase extraction of polyphenols from olive leaves. *Preparative Biochemistry and Biotechnology* 21:1–11 DOI 10.1080/10826068.2020.1861012.
- Wang YF, Wang J, Wu J, Xu P, Wang YQ, Gao JJ, Hochstetter D. 2014. In vitro antioxidant activity and potential inhibitory action against α -glucosidase of polysaccharides from fruit peel of tea (*Camellia sinensis* L.). *Journal of Zhejiang University Science B* 15:173–180 DOI 10.1631/jzus.B1300186.
- Xue LL, Zhang J, Shen HX, Ai L, Wu RR. 2020. A randomized controlled pilot study of the effectiveness of magnolia tea on alleviating depression in postnatal women. *Food Science & Nutrition* 8:1554–1561 DOI 10.1002/fsn3.1442.
- Yang LQ, Qu HY, Mao GH, Zhao T, Li F, Zhu B, Zhang BT, Wu XY. 2013. Optimization of subcritical water extraction of polysaccharides from *Grifola frondosa* using response surface methodology. *Pharmacognosy Magazine* 9:120 DOI 10.4103/0973-1296.111262.
- Zeković Z, Vidović S, Vladić J, Radosavljević R, Cvejic A, Elgndi MA, Pavlić B. 2014. Optimization of subcritical water extraction of antioxidants from *Coriandrum sativum* seeds by response surface methodology. *The Journal of Supercritical Fluids* 95:560–566 DOI 10.1016/j.supflu.2014.09.004.
- Zeng WM, Li F, Wu CC, Ge YM, Yu RL, Wu XL, Shen L, Liu YD, Li JK. 2020. Optimization of ultrasound-assisted aqueous extraction of polyphenols from *Psidium guajava* leaves using response surface methodology. *Separation Science and Technology* 55:728–738 DOI 10.1080/01496395.2019.1574830.
- Zhang L, Tu ZC, Wang H, Kou Y, Wen QH, Fu ZF, Chang HX. 2015. Response surface optimization and physicochemical properties of polysaccharides from *Nelumbo nucifera* leaves. *International Journal of Biological Macromolecules* 74:103–110 DOI 10.1016/j.ijbiomac.2014.11.020.
- Zhang J, Wei Y, Li H, Zeng EY, You J. 2017. Application of Box-Behnken design to optimize multi-sorbent solid phase extraction for trace neonicotinoids

in water containing high level of matrix substances. *Talanta* **170**:392–398

[DOI 10.1016/j.talanta.2017.04.031](https://doi.org/10.1016/j.talanta.2017.04.031).

Zhao GJ, Ge L, Ma HC, Yang JJ, Huang D, Ping P. 2014. Kapok capsule formation and fiber development process in Yuanjiang dry-hot valley. *Chinese Journal of Applied Ecology* **25**:3443–3450 [DOI 10.13287/j.1001-9332.201411111.001](https://doi.org/10.13287/j.1001-9332.201411111.001).

Zhao XQ, Guo S, Lu YY, Hua Y, Zhang F, Yan H, Shang EX, Wang HQ, Zhang WH, Duan JA. 2020. *Lycium barbarum* L. leaves ameliorate type 2 diabetes in rats by modulating metabolic profiles and gut microbiota composition. *Biomedicine and Pharmacotherapy* **121**:109559–1 [DOI 10.1016/j.biopha.2019.109559](https://doi.org/10.1016/j.biopha.2019.109559).

Zheng Q, Li W, Zhang H, Gao X, Tan S. 2019. Optimizing synchronous extraction and antioxidant activity evaluation of polyphenols and polysaccharides from Ya'an Tibetan tea (*Camellia sinensis*). *Food Science and Nutrition* **8**:489–499 [DOI 10.1002/fsn3.1331](https://doi.org/10.1002/fsn3.1331).

Zou TB, Jia Q, Li HW, Wang CX, Wu HF. 2013. Response surface methodology for ultrasound-assisted extraction of astaxanthin from *Haematococcus pluvialis*. *Marine Drugs* **11**:1644–1655 [DOI 10.3390/md11051644](https://doi.org/10.3390/md11051644).