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Microwave-assisted extraction of curcuminoids from organic *Curcuma longa* L. in different oil types for cosmetic purpose: An optimization approach

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Abstract

Curcuma longa L. is a well-known plant that contains bioactive compounds that are used as cosmetic ingredients. The green microwave-assisted extraction (MAE) technique has recently been applied to extract *C. longa* bioactive compounds. The MAE parameters of organic *C. longa* were investigated to maximize curcuminoid content. The Box-Behnken design was applied to control three factors including solid amount, duration time, and number of irradiation cycles, while five responses as production yield, bisdemethoxycurcumin (BDMC) content, demethoxycurcumin (DMC) content, curcumin (CUR) content, and total curcuminoid content were monitored. Coconut oil was used as an extraction solvent. Results showed that production yield was high for low solid amount, long duration time, and high number of irradiation cycles, while high BDMC, DMC, CUR, and total curcuminoid contents were obtained at high solid amount, long duration time, and high number of irradiation cycles. The optimum condition giving the maximum total curcuminoid content was solid amount 6 g per 20 mL of coconut oil, duration time 1.5 min, and 3 irradiation cycles. This condition gave production yield of 66.10 ± 1.80%, BDMC content of 4.37 ± 0.08 mg/g, DMC content of 2.97 ± 0.05 mg/g, CUR content of 8.03 ± 0.16 mg/g, and total curcuminoid content of 15.37 ± 0.28 mg/g. The prediction by computer software was accurate with low percentage error. Optimum condition for curcuminoid extraction was investigated using ten different oil samples as almond oil, castor oil, two olive oils (A and B), peanut oil, rice bran oil, two sesame oils (A and B), and two sunflower oils (A and B). All oil samples gave comparable production yield to coconut oil, except for almond oil and sesame oil A that produced significantly higher production yield. Castor oil extracted the highest individual and total curcuminoid contents, comparable to coconut oil. Stability data indicated that castor oil gave the most stable curcuminoids when stored at 30°C and 40°C for three months. Optimization of microwave-assisted extraction of organic *C. longa* was successfully achieved. Results can be used as a guide for the selection of oil type to prepare ready-to-use curcuminoid-oil mixtures as ingredients in cosmetic formulations.

Keywords**:** *Box-Behnken design; cosmetic purpose; curcuminoid; microwave-assisted extraction; oil; optimization; turmeric.*

1. Introduction

Curcuma longa L. is included in the Thai Herbal Pharmacopoeia as a medicinal plant in the categories stomachic, carminative, coloring agent, and astringent. The three major yellow coloring matters comprise curcumin (CUR), demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC), collectively called curcuminoids (Department of Medical Sciences, 2019; Monton, Charoenchai, Suksaeree, & Sueree, 2016). Traditional uses of turmeric in the Thai National List of Essential Medicine

include the treatment of flatulence (Monton, Luprasong, & Charoenchai, 2019a; National Drug System Development Committee, 2018). Curcuminoids exhibit good anti-inflammatory properties (Daily, Yang, & Park, 2016; Hewlings & Kalman, 2017; Perkins, Sahy, & Beckett, 2017). Currently, a turmeric extract with high curcuminoid content has been launched in the market as a modern medicine for the treatment of osteoarthritis. Curcuminoids are used in cosmetics as ingredients in skincare products due to their antioxidant, anti-inflammatory, and anti-aging activities (Arct, Ratz-Łyko, Mieloch, & Witulska, 2014). Several studies assessed the roles of turmeric extracts and turmeric compounds as active ingredients in cosmetic formulations such as anti-inflammatory cream (Gonçalves et al., 2014), antiseptic cream (Lobo, Prabhu, Shirwaikar, Shirwaikar, & Ballal, 2011), excessive sebum secretion regulation cream (Zaman & Akhtar, 2013), anti-inflammatory gel (Patel, Patel, & Patel, 2009), liposomes (Kongkaneramit, Aiemsum-ang, & Kewsuwan, 2016), liposomes/ethosomes/transfersomes-loaded cream for photoprotection (Kaur & Saraf, 2011), soap for wound treatment (Ungphaiboon et al., 2005), solid lipid nanoparticle-loaded gel for anti-inflammation (Zamarioli, Martins, Carvalho, & Freitas, 2015), and transfersome-loaded antiwrinkle cream (Saraf, Jeswani, Kaur, & Saraf, 2011).

Extraction techniques affect the content of plant bioactive compounds, therefore, optimization of extraction conditions and procedures is important. Plant extraction is an essential step in chemical analysis and biological and pharmacological activity assay. The most appropriate extraction conditions and procedures give the highest content and prevent the degradation of desired labile bioactive compounds (Sasidharan, Chen, Saravanan, Sundram, & Yoga Latha, 2010). Conventional extraction methods for curcuminoids as maceration using ethyl acetate (Binello et al., 2020), ethanol (Binello et al., 2020) or acetone (Mandal, Dewanjee, Sahu, & Mandal, 2009) or Soxhlet extraction using acetone (Mandal et al., 2009; Valizadeh Kiamahalleh, Najafpour-Darzi, Rahimnejad, Moghadamnia, & Valizadeh Kiamahalleh, 2016) take a long time and require several steps. Some studies applied response surface methodology (RSM) to optimize the dynamic maceration of curcumin from turmeric using ethanol as a solvent (Başpınar, Üstündaş, Bayraktar, & Sezgin, 2018; Paulucci, Couto, Teixeira, & Freitas, 2013). Residual solvent in the extract is another drawback of the solid-liquid extraction method (Chassagnez-Méndez, Corrêa, França, Machado, & Araújo, 2000).

Curcuminoid extraction is mostly conducted using organic solvents, with residual solvent in the extract removed by evaporation using a rotary evaporator or other suitable equipment or techniques. For cosmetic preparation, the extract is premixed with additives such as glycerin, ethanol and oil as oleaginous bases before adding other ingredients. Thus, the oil might be an alternative solvent for the extraction of curcuminoids from turmeric to prepare ready-to-use curcuminoid-oil mixtures. However, oil might extract fewer curcuminoids compared with organic solvents. To resolve this dilemma, application of RSM in the extraction process offers a suitable approach.

Recently, microwave-assisted extraction (MAE) has gained prominence as a green method to extract plant bioactive compounds. MAE has several advantages including high reliability, high efficiency, lower cost, high stability, and good reproducibility. Nevertheless, there are some disadvantages of MAE such as poor performance with non-polar solvents and low selectivity (Lopez-Avila & Luque de Castro, 2014). Conventional methods of decoction, infusion, reflux, or Soxhlet extraction involve heating from the outside to the inside of the plant matrix, while for MAE heating occurs from the inside to the outside. In MAE, microwave energy influences the molecules by two mechanisms of ionic conduction and dipole rotation. In the case of ionic conduction, the ions in the solution migrate when an electromagnetic field is applied. Ions in the solution that resist the flow cause friction and this generates heating. Dipole rotation involves realignment of the dipoles in the applied field. This forced movement produces molecular friction and the solution is heated (Lopez-Avila & Luque de Castro, 2014).

Here, ready-to-use curcuminoid-oil mixtures were prepared for use as an ingredient in cosmetic formulations. Extraction of curcuminoids by MAE using oils as the solvent shortens the preparation time for cosmetic ingredients. Eight oil types comprising 11 oil samples as almond oil, castor oil, coconut oil, olive oil, peanut oil, rice bran oil, sesame oil, and

sunflower oil were selected. These oils are all mentioned in the Handbook of Pharmaceutical Excipients as cosmetic ingredients (Rowe, Sheskey, Cook, & Fenton, 2012). Rice bran oil is also used in cosmetic products and has a good safety profile (Cosmetic Ingredient Review Expert Panel, 2006) since it is composed of fatty acids, γ-oryzanol, tocopherols and tocotrienols (Cassiday, 2018) that benefit the skin. Different oil types composed of different saturated-, monounsaturated-, and polyunsaturated fatty acids as well as other constituents also affect the stability of the formulation.

2. Objectives

The MAE of organic *C. longa* was investigated to maximize curcuminoid content, and the extraction efficiency of various oil types that could be used as cosmetic ingredients was determined. The stability of curcuminoids in oil types that gave the highest total curcuminoid content as well as production yields was also evaluated.

3. Materials and methods

3.1 Materials

Rhizomes of *C. longa* were collected from a certified organic farm in Lop Buri Province. Standard BDMC, DMC, and CUR were purchased from Chengdu Biopurify Phytochemicals Ltd., China. Acetonitrile (HPLC grade) was purchased from RCI Labscan Co., Ltd., Thailand. Methanol (AR grade) was purchased from Honeywell-Burdick & Jackson, USA. Acetic acid (AR grade) was purchased from Carlo Erba Reagents, Italy. Almond oil, olive oil (A), sesame oil (A), and sunflower oil (A) were purchased from Chemipan Corporation Co., Ltd., Thailand. Castor oil and coconut oil were purchased from Krungthepchemi, Thailand. Olive oil (B) was purchased from Naturel, Spain. Peanut oil and sesame oil (B) were purchased from Lemon Farm, Thailand. Rice bran oil was purchased from Rizi, Thailand. Sunflower oil (B) was purchased from Joe & Co S.R.L., Italy. Almond oil, castor oil, sesame oil (A), and sunflower oil (A) were cosmetic grade, while coconut oil, olive oil (A), olive oil (B), peanut oil, rice bran oil, sesame oil (B), and sunflower oil (B) were food grade.

3.2 Experimental design

A preliminary study was performed to investigate suitable parameters as solid amount, duration time, and number of irradiation cycles. The highest solid amount that did not cause an extremely viscous mixture, duration time and number of irradiation cycles that did not burn the extract were selected to investigate in the experimental design. The Box-Behnken design was applied in the work. Three factors as solid amount (X_1), duration time (X_2), and number of irradiation cycles (X_3) were studied. Five responses as production yield (Y_1), bisdemethoxycurcumin (BDMC) content (Y_2), demethoxycurcumin (DMC) content (Y_3), curcumin (CUR) content (Y_4), and total curcuminoid content (Y_5) were monitored. Microwave power was fixed at 800 W. The factors were varied at three levels; solid amounts were 2, 4, and 6 g/20 g coconut oil, duration times were 0.5, 1, and 1.5 min, with irradiation cycles as 1, 2, and 3. The stop period between cycles was 0.5 min. Fourteen conditions were obtained as shown in Table 1. Condition 13 and Condition 14 were repeated at the center point of the design.

Table 1 Coded value and experimental value of the Box-Behnken design.

Condition	Coded value			Experimental value		
	X_1	X_2	X_3	Solid amount (g/20 g oil)	Duration time (min)	No. of irradiation cycles
1	-1	-1	0	2	0.5	2
2	1	-1	0	6	0.5	2
3	-1	1	0	2	1.5	2
4	1	1	0	6	1.5	2
5	-1	0	-1	2	1	1
6	1	0	-1	6	1	1
7	-1	0	1	2	1	3
8	1	0	1	6	1	3
9	0	-1	-1	4	0.5	1
10	0	1	-1	4	1.5	1
11	0	-1	1	4	0.5	3
12	0	1	1	4	1.5	3
13	0	0	0	4	1	2
14	0	0	0	4	1	2

3.3 Extraction procedure and optimization

Organic *C. longa* rhizomes were harvested from Lop Buri Province, Thailand. They were cleaned, sliced, dried using a hot air oven (60°C for 20 h), pulverized, and passed through a 60-mesh sieve. The rhizomes were weighed as solid amounts of 2, 4 and 6 g into 250-mL Erlenmeyer flasks (n = 3). Coconut oil (20 g) was added and mixed. Then, the flasks were placed in a microwave oven (Sharp, model: R-270, Japan) with the power set at 800 W and microwaved for specific duration time and cycles as shown in Table 1. After that, they were immediately vacuum filtered to collect the extract using two-layer polyester cloths. The obtained oil extracts were weighed to record production yield. Mean and standard deviation (SD) were reported.

Oil extract (100 mg) was added to a 10-mL volumetric flask and the volume was adjusted by adding methanol with vigorous shaking. The solutions were filtered through a nylon syringe filter with 0.45 µm pore size and analyzed for individual and total curcuminoid content by high-performance liquid chromatography (HPLC). Mean and SD values were reported.

Data were analyzed using Design-Expert version 11 (Stat-Ease Inc., USA), and prediction equations, contour plots, and the correlation between predicted values and actual values were reported. The optimum criterion as the maximum total curcuminoid content was selected based on the highest desirability value. Accuracy of the software prediction was confirmed by re-extracting the curcuminoids using the optimum condition following the same extraction procedure. Errors between the predicted values reported by the software and the experimental values were calculated.

3.4 Preparation of standard solution

Stock solutions of each standard were prepared by dissolving 10 mg standard in a 10-mL volumetric flask using methanol as a solvent. One milliliter of stock solution of each standard was added to a 10-mL volumetric flask to prepare mixed standards at concentrations of 100 µg/mL. Then, these were diluted to prepare concentrations of 50, 25, 12.5, 6.25, and 3.125 µg/mL by a two-fold dilution technique. The diluted standards were filtered through a nylon syringe filter with 0.45 µm pore size and analyzed using HPLC. Each concentration was analyzed in triplicate and calibration curves of each standard were produced.

3.5 HPLC condition

Curcuminoid content was analyzed using HPLC (Agilent 1260 Infinity, Agilent Technologies, USA). The HPLC condition was performed following (Monton, Chuanchom, Popanit, Settharaksa, & Pathompak, 2021;

Monton, Luprasong, & Charoenchai, 2019b). An ACE Generix 5 C18 column (150×4.6 mm, i.d., 5 µm) was controlled at 30°C, with acetonitrile and 1% acetic acid aqueous solution in the ratio of 55:45 at a flow rate of 1 mL/min. The injection volume was 10 µL and detection wavelength was set at 425 nm.

3.6 Comparison of oil extraction efficiencies

The optimum condition was used to extract curcuminoids in almond oil, castor oil, two olive oils (A and B), peanut oil, rice bran oil, two sesame oils (A and B), and two sunflower oils (A and B). Extractions were performed according to the above procedure. Production yield was collected and curcuminoid content was analyzed using HPLC. Production yield, individual curcuminoid content, and total curcuminoid content of the various oils were compared with coconut oil.

3.7 Stability test

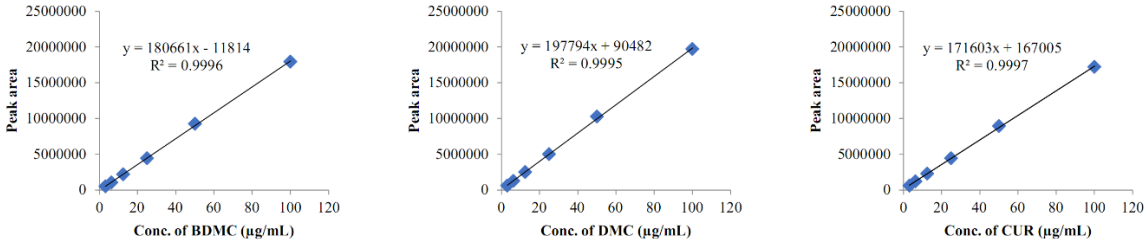
The three oil types which gave the highest total curcuminoid content were used to extract curcuminoids from *C. longa*. If the total curcuminoid content was comparable, production yield was also taken into account and the oil type that provided higher production yield was selected. The obtained mixtures were kept in air-tight containers to protect them from light in a climate chamber (Memmert, Germany) at 30°C/75%RH and 40°C/75%RH for three months. The remaining curcuminoid content was analyzed by HPLC and the result was compared with the initial time point.

3.8 Statistical analysis

Differences in production yield, individual curcuminoid content, and total curcuminoid content between the various oils compared with coconut oil were analyzed by SPSS software version 22 (IBM, USA). The Student's t-test was used to compare differences between the two groups. Data were significantly different when the p-value was less than 0.05 at 95% confidence interval.

4. Results and discussion

Curcuminoid content was analyzed by HPLC. Calibration curves of BDMC, DMC, and CUR in Figure 1 show high R^2 values, indicating that concentration of curcuminoids and peak area had good correlation and could be used for the determination of curcuminoids. HPLC chromatograms of mixed standard curcuminoids and *C. longa* extract in coconut oil are shown in Figure 2.



(a) (b) (c)

Figure 1 Calibration curves of (a) BDMC, (b) DMC, and (c) CUR.

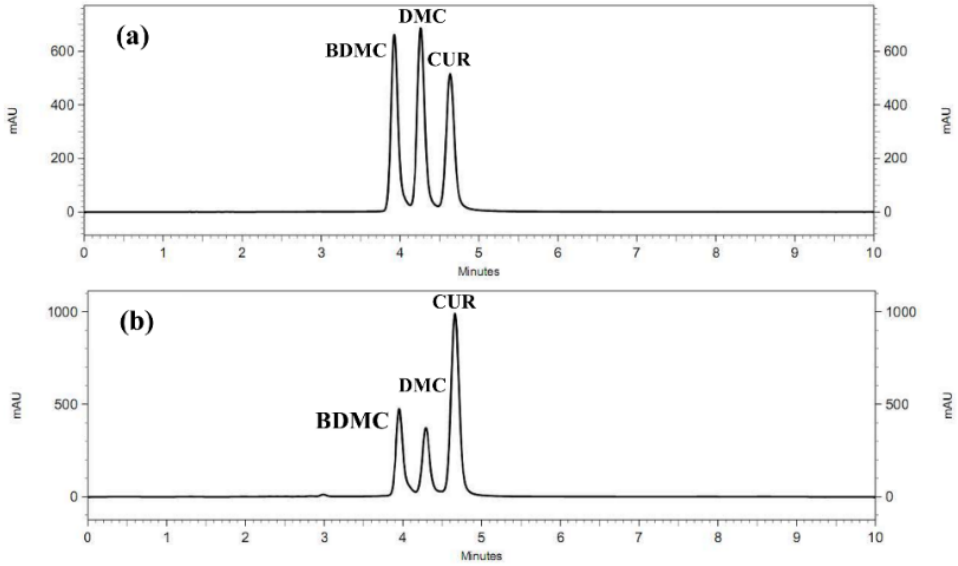


Figure 2 HPLC chromatograms of (a) mixed standard curcuminoids in a concentration of 50 µg/mL and (b) *C. longa* extract in coconut oil obtained from the optimum condition (10 mg/mL).

Table 2 shows production yield and individual and total curcuminoid contents when coconut oil was used as a solvent. Production yield ranged at 12.31-16.87 g (equivalent to 61.58-84.38%). Condition 6 and Condition 3 provided the lowest and highest production yields, respectively. The BDMC, DMC, CUR and total curcuminoid contents ranged at 0.96-4.36 mg/g, 0.50-2.96 mg/g, 1.28-8.03 mg/g, and 2.75-15.37 mg/g, respectively. Individual and total curcuminoid content had the lowest and the highest values in Condition 1 and Condition 8, respectively.

Table 2 Responses of production yield and curcuminoid content obtained from the model when coconut oil was used (n = 3).

Condition	Production yield		Curcuminoid content (mg/g)			
	g*	%	BDMC	DMC	CUR	Total
1	15.80 ± 0.26	79.00 ± 1.28	0.96 ± 0.05	0.50 ± 0.04	1.28 ± 0.13	2.75 ± 0.21
2	12.74 ± 0.20	63.70 ± 1.01	3.53 ± 0.07	1.57 ± 0.76	5.28 ± 0.17	10.39 ± 0.87
3	16.87 ± 0.33	84.38 ± 1.66	1.73 ± 0.13	1.12 ± 0.07	3.46 ± 0.20	6.33 ± 0.40
4	13.17 ± 0.80	65.85 ± 3.99	3.11 ± 0.11	1.63 ± 0.13	4.10 ± 0.48	8.85 ± 0.70
5	16.26 ± 0.39	81.32 ± 1.94	1.15 ± 0.06	0.58 ± 0.03	1.47 ± 0.10	3.21 ± 0.19
6	12.31 ± 0.41	61.58 ± 2.05	3.31 ± 0.03	1.85 ± 0.06	4.88 ± 0.24	10.05 ± 0.32
7	16.82 ± 0.25	84.12 ± 1.23	1.67 ± 0.03	1.06 ± 0.01	3.23 ± 0.04	5.96 ± 0.09
8	13.22 ± 0.36	66.12 ± 1.80	4.36 ± 0.08	2.96 ± 0.05	8.03 ± 0.16	15.37 ± 0.28
9	14.25 ± 1.21	71.27 ± 6.07	1.76 ± 0.06	0.75 ± 0.02	1.58 ± 0.03	4.10 ± 0.11
10	14.69 ± 0.40	73.47 ± 1.98	2.85 ± 0.07	1.74 ± 0.06	4.99 ± 0.18	9.58 ± 0.31
11	14.51 ± 0.05	72.55 ± 0.26	2.64 ± 0.06	1.58 ± 0.05	4.52 ± 0.15	8.75 ± 0.25
12	14.85 ± 0.09	74.28 ± 0.46	3.22 ± 0.38	2.21 ± 0.30	6.62 ± 0.81	12.06 ± 1.49
13	14.70 ± 0.02	73.50 ± 0.10	2.99 ± 0.05	1.93 ± 0.04	5.71 ± 0.11	10.64 ± 0.20
14	14.88 ± 0.76	74.43 ± 3.81	3.03 ± 0.07	1.94 ± 0.06	5.69 ± 0.21	10.66 ± 0.34

*Weight of obtained oil mixture after filtration

Data in Table 2 were analyzed by the Design-Expert program to generate prediction equations as shown in Equations 1-5. The solid amount had a negative effect on production yield, while duration time and number of irradiation cycles had a positive effect. Duration time had a large effect on production yield compared to numbers of irradiation cycles. BDMC content was mostly affected by solid amount, duration time, and irradiation cycles, while DMC content, CUR content, and total curcuminoid content were mostly affected by duration time, followed by number of irradiation cycles and solid amount.

Production yield (%) = 85.93 – 4.47(solid amount) + 2.86(time) + 1.18(cycle) Eq. 1
BDMC content (mg/g) = -0.81 + 0.54(solid amount) + 0.51(time) + 0.35(cycle) Eq. 2
DMC content (mg/g) = -0.95 + 0.30(solid amount) + 0.58(time) + 0.36(cycle) Eq. 3
CUR content (mg/g) = -2.85 + 0.80(solid amount) + 1.63(time) + 1.18(cycle) Eq. 4
Total curcuminoid content (mg/g) = -4.62 + 1.65(solid amount) + 2.71(time) + 1.90(cycle) Eq. 5

Contour plots of production yield are shown in Figure 3. The first column revealed that production yield was high at low solid amount and long duration time. When irradiation cycle numbers increased, production yield increased. The center column revealed that production yield was high at low solid amount and high irradiation cycles. When duration time increased, production yield increased. The last column revealed that production yield was high at long duration time and high irradiation cycles. When solid amount decreased, production yield increased. Results indicated that high production yield was achieved at low solid amount, long duration time, and high irradiation cycles.

Contour plots of BDMC, DMC, CUR, and total curcuminoid content are shown in Figures 4-7, respectively. The first column of each figure revealed that contents were high at high solid amounts and long duration time. When the number of irradiation cycles increased, contents increased. The center column of each figure revealed that contents were high at high solid amount and high irradiation cycles. When duration time increased, contents increased. The last column of each figure revealed that contents were high at long duration time and high irradiation cycles. When solid amount increased, contents increased. Results indicated that high BDMC, DMC, CUR, and total curcuminoid contents were achieved at high solid amount, long duration time, and high irradiation cycles.

Correlation between predicted and experimental values was medium to high because of the relatively high R^2 values (Figure 8). Results indicated that the data were precise and reliable (Monton, Luprasong, et al., 2019a, 2019b; Monton, Settharaksa, Luprasong, & Songsak, 2019; Monton, Wunnakup, Suksaeree, Charoenchai, & Chankana, 2020).

These results showed that all factors: solid amount, duration time and irradiation cycle positively affected all responses; production yield, BDMC content, DMC content, CUR content, and total curcuminoid content, while solid amount impacted production yield. High solid amount absorbed the oil into the plant powder, and production yield decreased when solid amount increased.

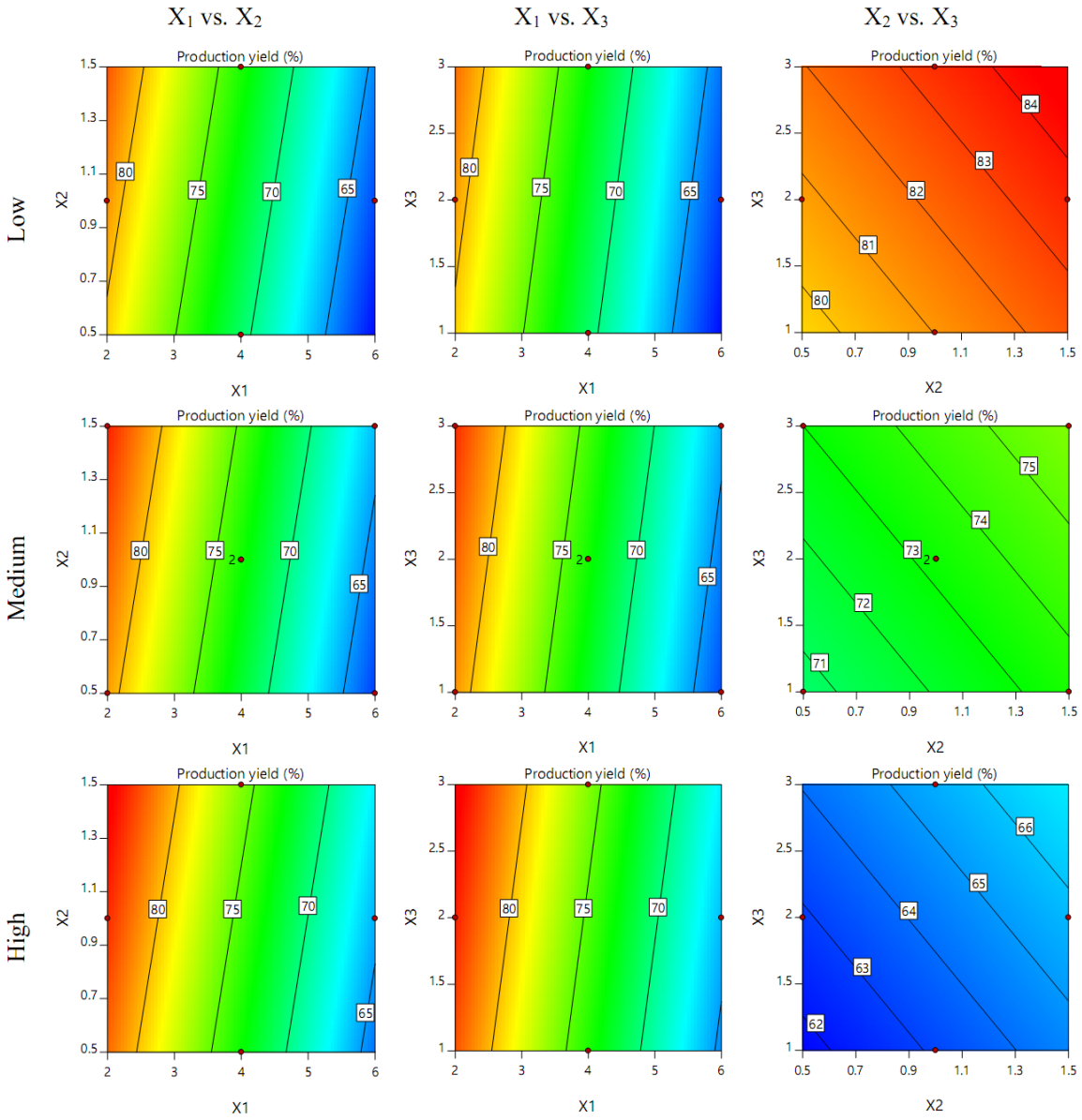


Figure 3 Contour plots of production yield. Different factors; solid amount vs. duration time (left column), solid amount vs. irradiation cycle (center column), and duration time vs. irradiation cycle (right column) at different levels of the third factor;low (top), medium (center), and high (bottom).

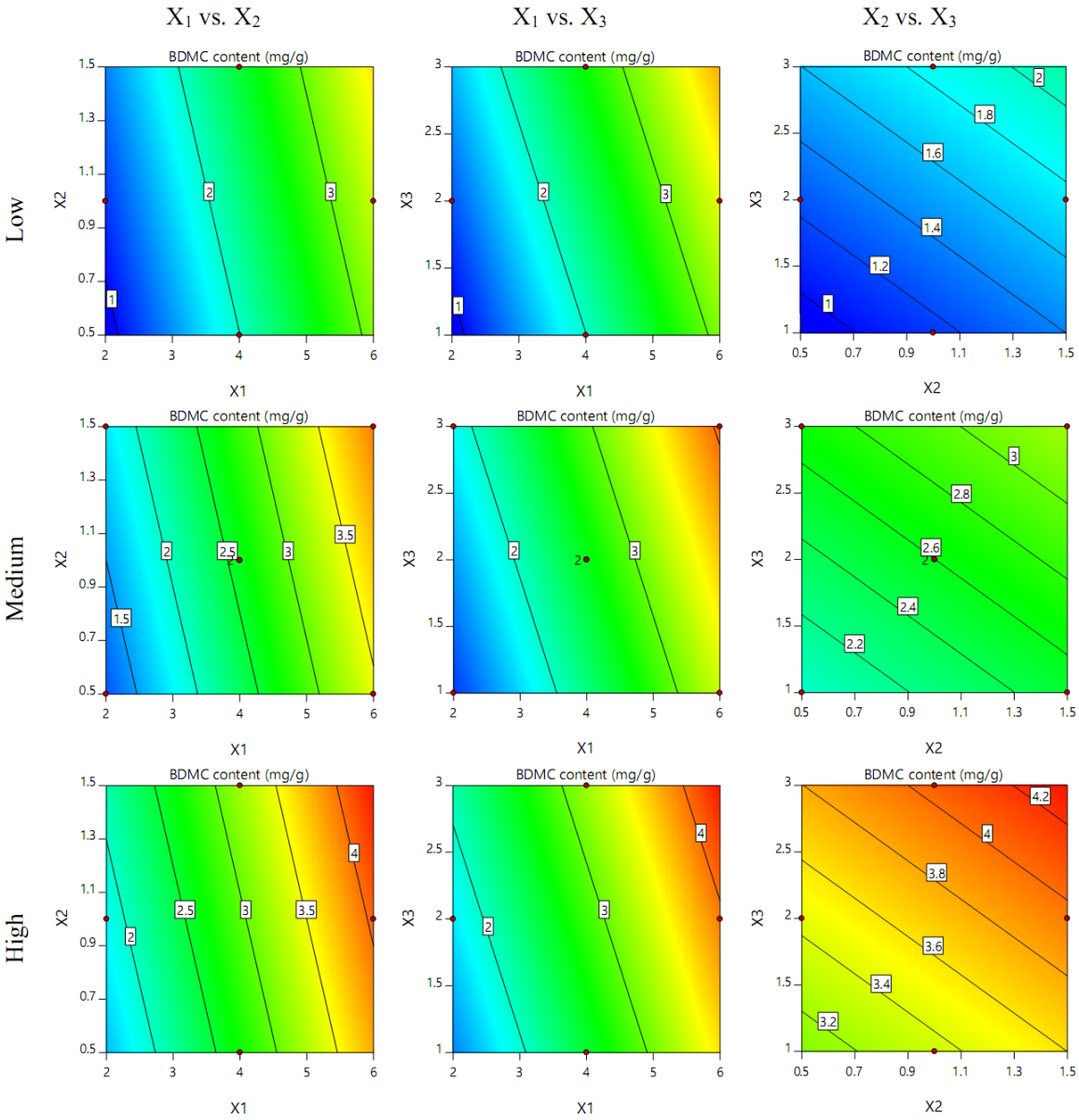


Figure 4 Contour plots of BDMC content. Different factors; solid amount vs. duration time (left column), solid amount vs. irradiation cycle (center column), and duration time vs. irradiation cycle (right column) at different levels of the third factor; low (top), medium (center), and high (bottom).

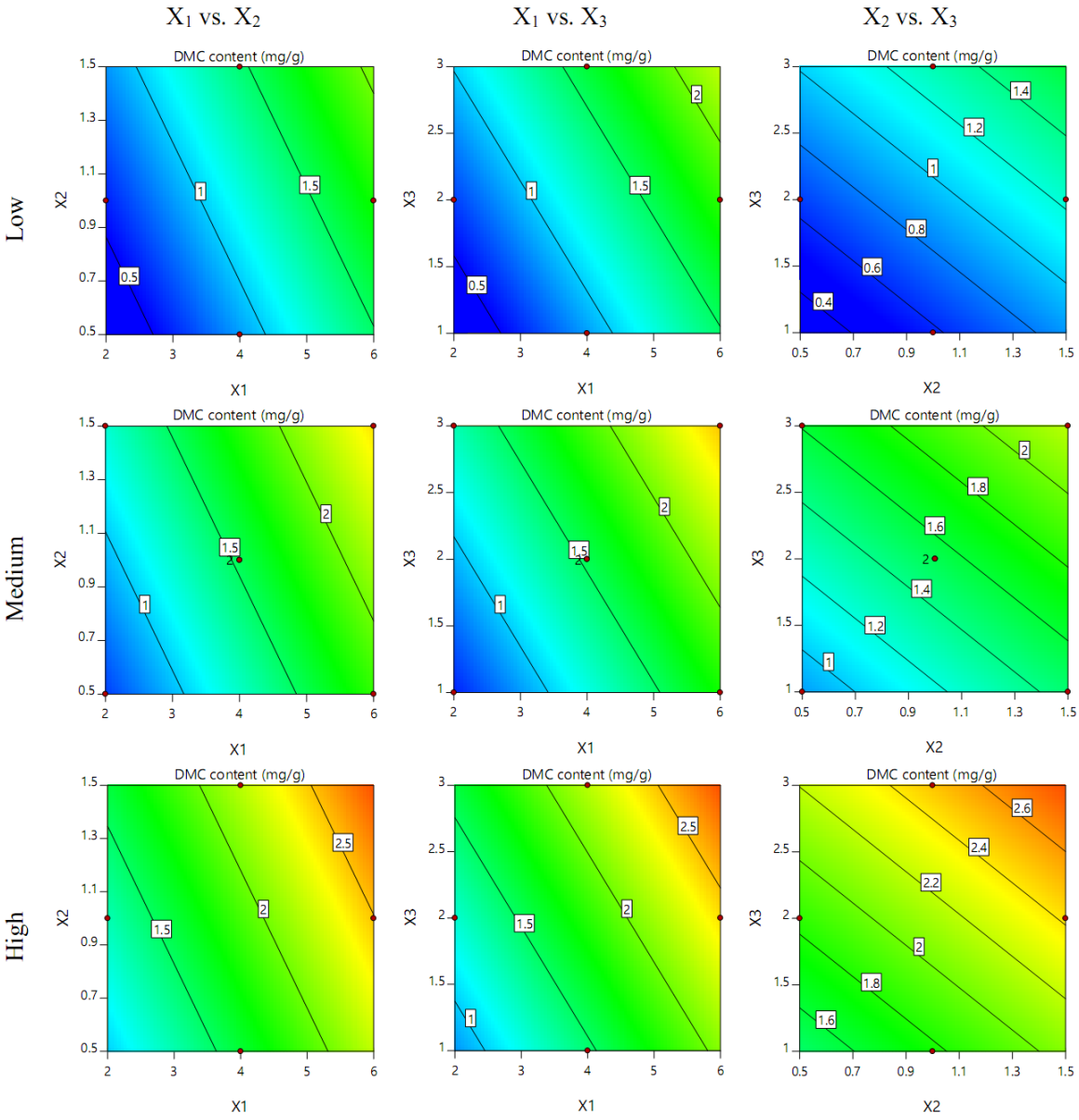


Figure 5 Contour plots of DMC content. Different factors; solid amount vs. duration time (left column), solid amount vs. irradiation cycle (center column), and duration time vs. irradiation cycle (right column) at different levels of the third factor; low (top), medium (center), and high (bottom).

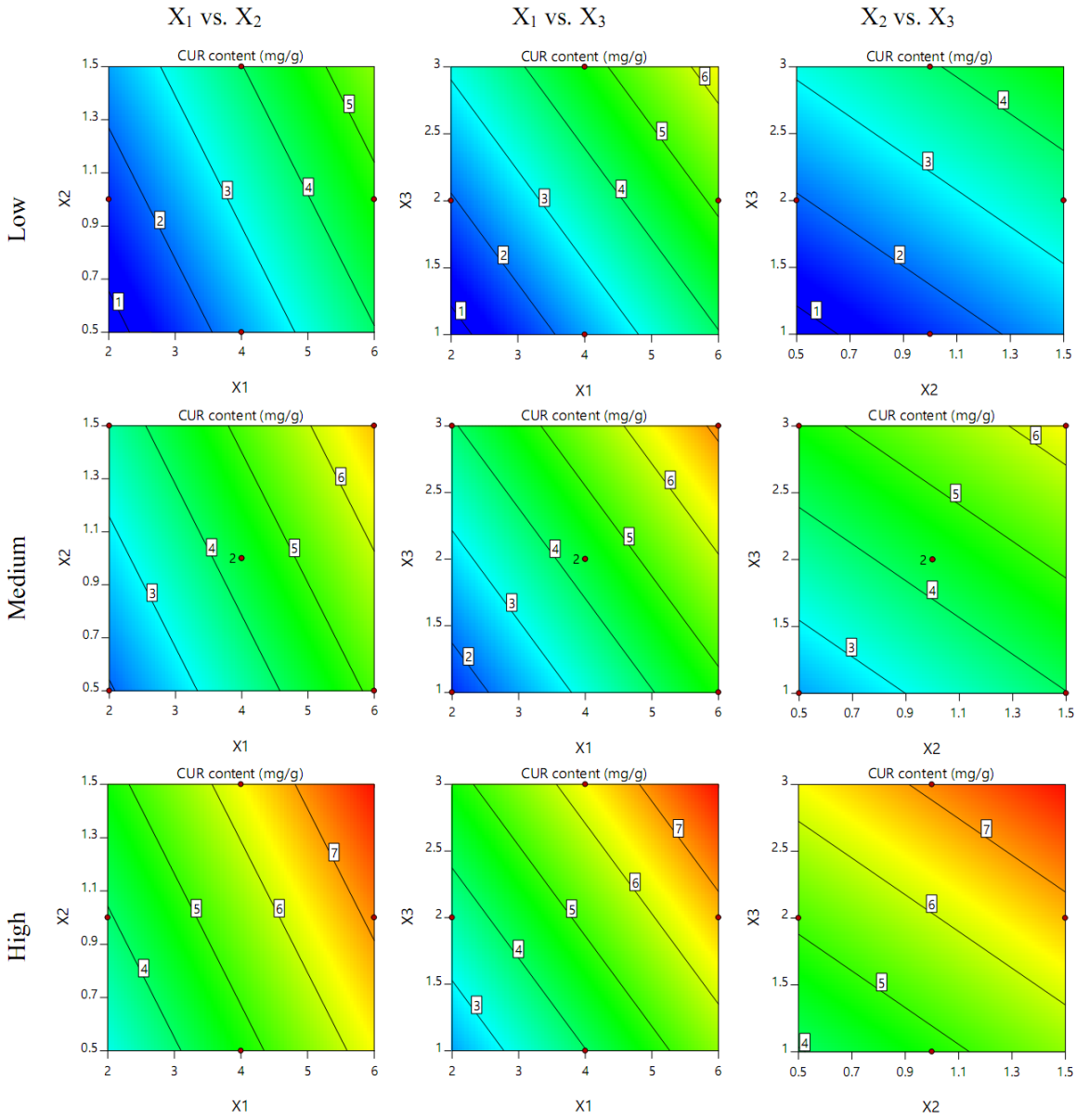


Figure 6 Contour plots of CUR content. Different factors; solid amount vs. duration time (left column), solid amount vs. irradiation cycle (center column), and duration time vs. irradiation cycle (right column) at different levels of low (top), medium (center), and high (bottom).

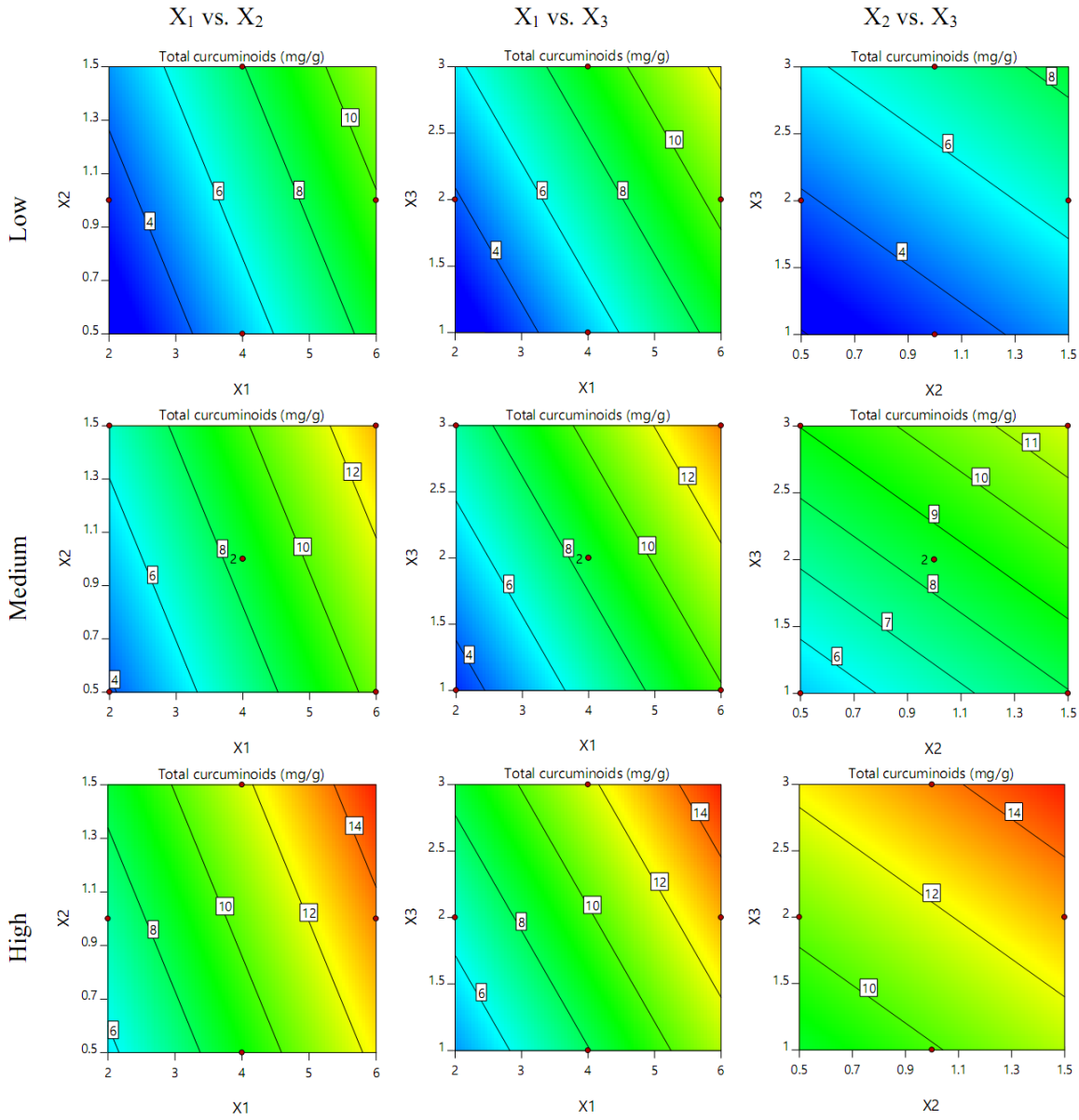


Figure 7 Contour plots of total curcuminoid content. Different factors; solid amount vs. duration time (left column), solid amount vs. irradiation cycle (center column), and duration time vs. irradiation cycle (right column) at different levels of the third factor; low (top), medium (center), and high (bottom).

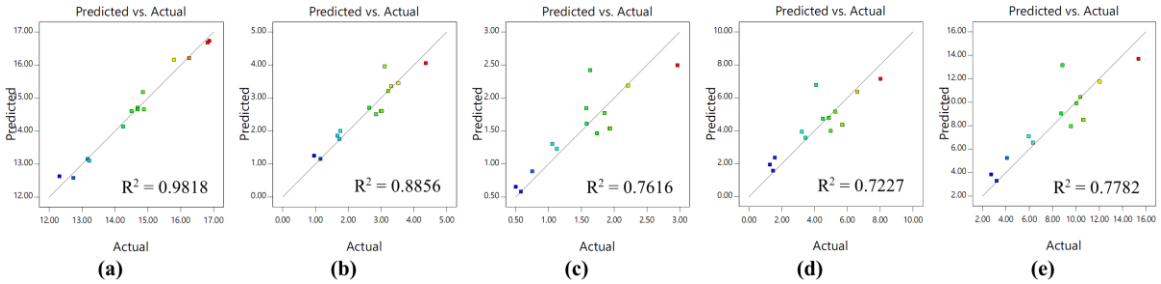


Figure 8 Predicted vs. actual value plots of (a) production yield, (b) BDMC content, (c) DMC content, (d) CUR content, and (e) total curcuminoid content.

Increasing solid amount and microwave time gave high percentage extraction of curcuminoids from *C. longa* (Dandekar & Gaikar, 2002). Singh, Simapaisan, and Utama-ang (2017) reported that at 800 W, increasing microwave time from 1 to 3 min increased individual and total curcuminoid contents. However, when microwave time was increased from 3 to 5 min, individual and total curcuminoid contents decreased. This result suggested that long microwave time destroyed plant bioactive compounds. They also evaluated the effect of solid amount. Increasing turmeric powder from 0.5% to 2.0% increased individual and total curcuminoid contents. Lateh, Yuenyongsawad, Chen, and Panichayupakaranant (2019) showed that when solid amount increased from 1 to 2.5 g/ 20 mL, production yield decreased, while BDMC, DMC, CUR, and total curcuminoid contents increased. When the number of irradiation cycles was increased from 1 to 4, production yield did not alter, while an increase from 1 to 3 cycles increased BDMC, DMC, CUR, and total curcuminoid contents. However, when irradiation cycles increased from 3 to 4, individual and total curcuminoid contents decreased. Sae-Lim, Yuenyongsawad, and Panichayupakaranant (2019) reported that when solid amount increased from 10 to 100 g/100 mL oil, production yield decreased and bioactive compound content in oil increased. The effect of solid content on bioactive compounds could be driven by the concentration gradient between plant matrix and solvent. High solid amount produced a high concentration gradient that promoted dissolution of plant bioactive compounds to the solvent. All the above data suggest that microwave-assisted extraction affected production yield and curcuminoid content. Thus, the optimization of extraction conditions is a very important step for maximizing production yield and plant bioactive compounds.

The optimum condition that provided the maximum curcuminoid content, as predicted by Design-Expert software, was solid amount of 6 g/20 g oil, duration time 1.5 min, and three irradiation cycles. The desirability value of this condition was 0.973. Prediction accuracy by the software was confirmed by re-extracting the *C. longa* using the optimum condition. The HPLC chromatogram of *C. longa* extract in coconut oil using the optimum condition is shown in Figure 2b. Errors between predicted values reported by the software and experimental values are shown in Table 3. Results revealed that the error of all responses was less than 10%, indicating that the prediction of the Design-Expert software was accurate (Monton, Luprasong, et al., 2019a, 2019b; Monton, Settharaksa, et al., 2019; Monton et al., 2020).

Table 3 Predicted values, experimental values, and percentage error of the prediction of various responses.

Response	Predicted value	Experimental value	Percentage error*
Production yield (%)	66.90	66.10 ± 1.80	-1.21
BDMC content (mg/g)	4.30	4.37 ± 0.08	1.49
DMC content (mg/g)	2.78	2.97 ± 0.05	6.34
CUR content (mg/g)	7.95	8.03 ± 0.16	1.02
Total curcuminoid content (mg/g)	15.04	15.37 ± 0.28	2.18

*Percentage error = (Experimental value – Predicted value) ×100/Experimental value

The optimum condition providing the maximum curcuminoid content using coconut oil as a solvent was selected to extract curcuminoids by the other oils. Tables 4 and 5 show production yield and curcuminoid content when extracting *C. longa* using the various oils and their statistical analyses. All oil types gave production yield higher than coconut oil, with almond oil and sesame oil A giving significantly high production yield. Castor oil gave significantly high BDMC content and non-significantly high DMC, CUR, and total curcuminoid contents when compared with coconut oil, while the other oils gave significantly low BDMC, DMC, CUR, and total curcuminoid contents. These results suggested that castor oil provided high production yield and the highest total curcuminoid content.

Table 4 Effect of oil types on production yield compared with coconut oil

Oil type	Production yield		p-value
	g	%	
Almond oil	14.47 ± 0.45	72.33 ± 2.26	0.022*
Castor oil	13.68 ± 0.87	68.40 ± 4.33	0.268
Coconut oil	12.90 ± 0.59	64.52 ± 2.94	-
Olive oil A	13.16 ± 0.61	65.80 ± 3.05	0.628
Olive oil B	12.34 ± 0.61	61.70 ± 3.07	0.315
Peanut oil	13.87 ± 0.58	69.35 ± 2.92	0.114
Rice bran oil	13.59 ± 0.70	67.95 ± 3.49	0.263
Sesame oil A	14.46 ± 0.23	72.28 ± 1.15	0.013*
Sesame oil B	13.56 ± 0.97	67.82 ± 4.83	0.369
Sunflower oil A	13.23 ± 0.62	66.15 ± 3.12	0.545
Sunflower oil B	13.63 ± 0.76	68.15 ± 3.79	0.26

Significant value: p-value < 0.05 when compared with coconut oil

Table 5 Effect of oil types on curcuminoid content compared with coconut oil

Oil type	Curcuminoid content (mg/g)							
	BDMC	p-value	DMC	p-value	CUR	p-value	Total	p-value
Almond oil	3.09 ± 0.17	0.003*	2.30 ± 0.09	0.001*	7.76 ± 0.33	0.003*	13.15 ± 0.57	0.002*
Castor oil	4.83 ± 0.29	0.016*	3.06 ± 0.19	0.202	9.38 ± 0.52	0.898	17.27 ± 0.99	0.184
Coconut oil	4.03 ± 0.20	-	2.88 ± 0.09	-	9.33 ± 0.29	-	16.23 ± 0.54	-
Olive oil A	3.23 ± 0.25	0.012*	2.50 ± 0.12	0.013*	8.55 ± 0.27	.027*	14.27 ± 0.62	0.015*
Olive oil B	2.95 ± 0.26	0.004*	2.29 ± 0.09	0.001*	7.84 ± 0.13	0.001*	13.09 ± 0.47	0.002*
Peanut oil	3.17 ± 0.06	0.002*	2.39 ± 0.05	0.001*	8.01 ± 0.18	0.003*	13.57 ± 0.29	0.002*
Rice bran oil	3.22 ± 0.16	0.005*	2.46 ± 0.09	0.006*	8.28 ± 0.22	0.007*	13.97 ± 0.47	0.006*
Sesame oil A	3.40 ± 0.16	0.012*	2.44 ± 0.13	0.010*	7.99 ± 0.45	0.012*	13.83 ± 0.74	0.010*
Sesame oil B	3.47 ± 0.10	0.011*	2.52 ± 0.11	0.012*	8.27 ± 0.40	0.020*	14.26 ± 0.60	0.013*
Sunflower oil A	2.69 ± 0.05	< 0.0001*	2.08 ± 0.02	< 0.0001*	7.21 ± 0.09	< 0.0001*	11.98 ± 0.12	< 0.0001*
Sunflower oil B	3.04 ± 0.26	0.006*	2.32 ± 0.11	0.003*	7.92 ± 0.21	0.002*	13.28 ± 0.57	0.003*

Significant value: p-value < 0.05 when compared with coconut oil

Organic *C. longa* was determined for its curcuminoid content following the method reported by Monton, Luprasong, et al. (2019b), with results of BDMC 26.6 ± 0.02 mg/g, DMC 18.1 ± 0.00 mg/g, CUR 58.9 ± 0.10 mg/g, and total curcuminoid content 103.5 ± 0.10 mg/g. Curcuminoid extraction recovery ranged from 25.52 ± 0.25% to 38.05 ± 2.18%. Lowest and highest curcuminoid recoveries were found in sunflower oil A and castor oil, respectively. Some oils and curcuminoids remained in the marc and re-extraction of the marc or compression using a mechanical press increased production yield and curcuminoid content with increased recovery.

All selected oils, except for rice bran oil, are reported in the Handbook of Pharmaceutical Excipients (Rowe et al., 2012) as possible cosmetic ingredients, while rice bran oil is also used in cosmetic products and has a good safety profile (Cosmetic Ingredient Review Expert Panel, 2006). Using MAE to extract curcuminoids from organic *C. longa* avoids the evaporation of organic solvent and shortens the extraction step. Different oil types gave diverse solubility data and curcuminoid extraction. Anjana et al. (2012) showed that curcumin solubility in almond oil, castor oil, coconut oil, olive oil, peanut oil, sesame oil, and sunflower oil was comparable at 0.04%. Comparison of different grades of coconut oil revealed that virgin coconut oil solubilized curcumin at 0.06%, higher than coconut oil at 0.04%. Takenaka et al. (2013) revealed that solubility of curcumin in olive oil was 0.45 mg/g, and lower than our results, while Karthika, Sureshkumar, and Suhail (2019) demonstrated that the solubility of curcumin in olive oil and peanut oil was comparable at 3.8 mg/mL vs. 3.7 mg/mL. Higher, curcumin content was extracted by edible oil by increasing the temperature from room temperature to 50°C (Sobankumar, Rajan, Christudhas, & GnanaRaj, 2018). Results indicated that oil types, oil grades, and temperature affected the solubility of curcumin in various oils; however, oil solubility of other curcuminoids was limited.

Three oil types as castor oil, coconut oil, and sesame oil B were selected to evaluate the stability of curcuminoids in curcuminoid-oil mixtures. Results showed that castor oil promoted the highest stability of individual and total curcuminoids for at least three months at 30°C/75%RH and 40°C/75%RH (Figure 9), while coconut oil and sesame oil gave unstable curcuminoids. Sesame oil stabilized only BDMC but not DMC, CUR, and total curcuminoids. The higher stability shown by BDMC than DMC and CUR might relate to the methoxy group. CUR contains two methoxy groups, DMC contains one methoxy group, while BDMC has no methoxy group in its structure (Monton et al., 2016). The presence of the methoxy group had a negative effect on the stability of curcuminoids in coconut oil and sesame oil. This finding was fitted to the stability data of BDMC, DMC, and CUR under stress conditions as reported by Peram, Jalalpure, Palkar, and Diwan (2017). Among the oil types, castor oil showed the highest potential for selection as a solvent for extraction of curcuminoids from organic *C. longa* to prepare cosmetic ingredients. Castor oil gave high production yield, high individual and total curcuminoids, and provided stable formulation. Different oils are composed of diverse types and amounts of fatty acids and other compositions (Sae-Lim et al., 2019) that affect the stability of curcuminoids and curcuminoid-oil mixtures. However, here, fatty acid profiles of the different oil samples were not determined.

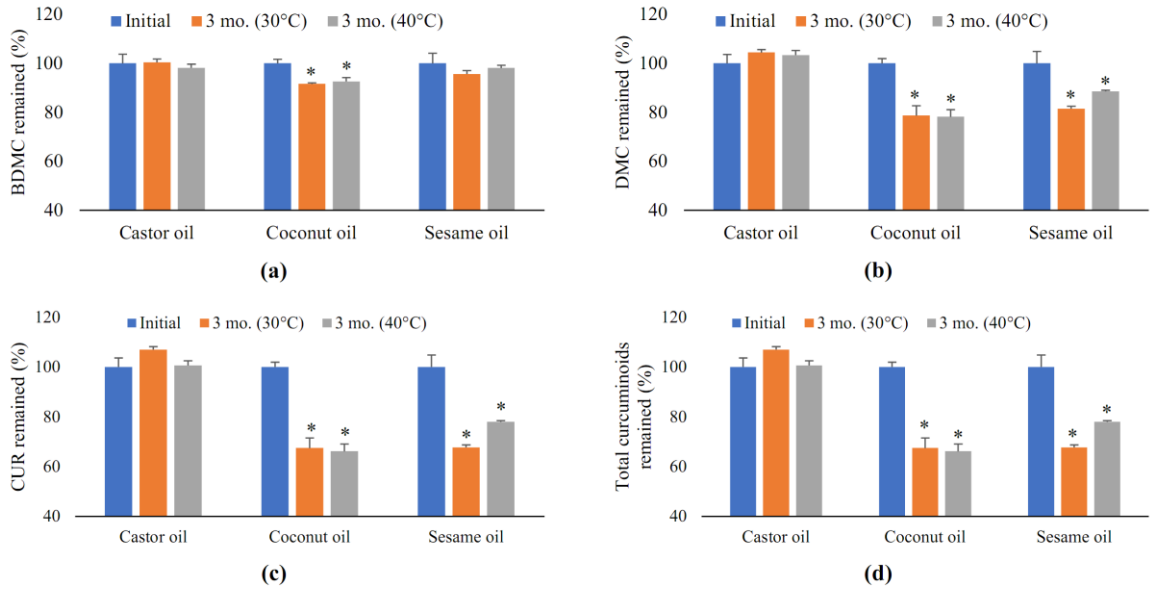


Figure 9 Stability of (a) BDMC, (b) DMC, (c) CUR, and (d) total curcuminoids stored at 30°C/ 75%RH and 40°C/ 75%RH. *indicates significance at $p < 0.05$ compared with the initial time point of each oil type.

5. Conclusions

Microwave-assisted extraction parameters of organic *C. longa* were optimized to maximize curcuminoid content. The Box-Behnken design was applied to evaluate the effect of solid amount, duration time, and number of irradiation cycles on production yield, individual curcuminoid content, and total curcuminoid content. Using coconut oil as a solvent gave high individual curcuminoid content, and total curcuminoid content at high solid amount, long duration time, and high number of cycles. Production yield was high at low solid amount, long duration time, and high number of cycles. Low percentage error recorded by computer software indicated that prediction values were accurate. Almond oil and sesame oil A gave significantly high production yield compared with coconut oil, while castor oil gave highest contents of individual and total curcuminoids. Castor oil stabilized curcuminoids kept at 30°C and 40°C for at least three months. Results can be used as a guide when selecting microwave-assisted extraction parameters and oil types for preparation of ready-to-use curcuminoid-oil mixtures as ingredients in cosmetic formulations.

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7. References

Anjana, D., Nair, K. A., Somashekara, N., Venkata, M., Sripathy, R., Yelucheri, R., Parmar, H., Upadhyay, R., Rama Verma, S., & Ramchand, C. N. (2012). Development of curcumin based ophthalmic formulation. *American Journal of Infectious Diseases, 8*(1), 41-49. DOI:10.3844/ajidsp.2012.41.49

Arct, J., Ratz-Łyko, A., Mieloch, M., & Witulska, M. (2014). Evaluation of skin colouring properties of *Curcuma longa* extract. *Indian Journal of Pharmaceutical Sciences, 76*(4), 374-378.

Başpınar, Y., Üstündaş, M., Bayraktar, O., & Sezgin, C. (2018). Response surface methodology for extraction of curcumin from turmeric and piperine from black pepper *Celal Bayar University Journal of Science, 13*(3), 747-754.

Binello, A., Grillo, G., Barge, A., Allegrini, P.,

Ciceri, D., & Cravotto, G. (2020). A cross-flow ultrasound-assisted extraction of curcuminoids from *Curcuma longa* L.: Process design to avoid degradation. *Foods, 9*(6), 743. DOI: 10.3390/foods9060743

Cassiday, L. (2018). Unconventional oils. *INFORM, 29(6)*, 5-13. Retrieved October 15, 2020, from http://www.fao.org/fileadmin/templates/library/pdf/Inform.pdf

Chassagnez-Méndez, A. L., Corrêa, N. C. F., França, L. F., Machado, N. T., & Araújo, M. E. (2000). A mass transfer model applied to the supercritical extraction with CO_2 of curcumins from turmeric rhizomes (*Curcuma longa* L). *Brazilian Journal of Chemical Engineering, 17*, 315-322.

Cosmetic Ingredient Review Expert Panel. (2006). Amended final report on the safety assessment of *Oryza sativa* (rice) bran oil, *Oryza sativa* (rice) germ oil, rice bran acid, *Oryza sativa* (rice) bran wax, hydrogenated rice bran wax, *Oryza sativa* (rice) bran extract, *Oryza sativa* (rice) extract, *Oryza sativa* (rice) germ powder, *Oryza sativa* (rice) starch, *Oryza sativa* (rice) bran, hydrolyzed rice bran extract, hydrolyzed rice bran protein, hydrolyzed rice extract, and hydrolyzed rice protein. *International Journal of Toxicology, 25*(Suppl 2), 91-120. DOI: 10.1080/10915810600964626

Daily, J. W., Yang, M., & Park, S. (2016). Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: A systematic review and meta-analysis of randomized clinical trials. *Journal of Medicinal Food, 19*(8), 717-729. DOI: 10.1089/jmf.2016.3705

Dandekar, D. V., & Gaikar, V. G. (2002). Microwave assisted extraction of curcuminoids from *Curcuma longa*. *Separation Science and Technology, 37*(11), 2669-2690. DOI: 10.1081/SS-120004458

Department of Medical Sciences. (2019). *Thai Herbal Pharmacopoeia 2019*. Bureau of Drug and Narcotic, Department of Medical Sciences, Ministry of Public Health, Thailand.

Gonçalves, G. M. S., Silva, G. H. d., Barros, P. P., Srebernich, S. M., Shiraishi, C. T. C., Camargos, V. R. d., & Lasca, T. B. (2014). Use of *Curcuma longa* in cosmetics: extraction of curcuminoid pigments, development of formulations, and in vitro skin permeation studies. *Brazilian Journal of Pharmaceutical Sciences, 50*, 885-893. DOI: 10.1590/S1984-82502014000400024

Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A review of its' effects on human health. *Foods, 6*(10), 92. DOI: 10.3390/foods6100092

Karthika, C., Sureshkumar, R., & Suhail, A. (2019). Formulation development and in vitro evaluation of curcumin-loaded solid self-nanoemulsifying drug delivery system for colon carcinoma. *Asian Journal of Pharmaceutical and Clinical Research, 12*(7), 243-247.

Kaur, C. D., & Saraf, S. (2011). Topical vesicular formulations of *Curcuma longa* extract on recuperating the ultraviolet radiation–damaged skin. *Journal of Cosmetic Dermatology, 10*(4), 260-265. DOI: 10.1111/j.1473-2165.2011.00586.x

Kongkaneramit, L., Aiemsum-ang, P., & Kewsuwan, P. (2016). Development of curcumin liposome formulations using polyol dilution method. *Songklanakarin Journal of Science and Technology, 38*(6), 605-610.

Lateh, L., Yuenyongsawad, S., Chen, H., & Panichayupakaranant, P. (2019). A green method for preparation of curcuminoid-rich *Curcuma longa* extract and evaluation of its anticancer activity. *Pharmacognosy Magazine, 15*(65), 730-735. DOI: 10.4103/pm.pm_162_19

Lobo, R., Prabhu, K., Shirwaikar, A., Shirwaikar, A., & Ballal, M. (2011). Formulation and evaluation of antiseptic activity of the herbal cream containing *Curcuma longa* and tea tree oil. *Journal of Biologically Active Products from Nature, 1*(1), 27-32. DOI: 10.1080/22311866.2011.10719070

Lopez-Avila, V., & Luque de Castro, M. D. (2014). Microwave-assisted extraction. In *Reference Module in Chemistry, Molecular Sciences and Chemical*

Engineering: Elsevier.

Mandal, V., Dewanjee, S., Sahu, R., & Mandal, S. C. (2009). Design and optimization of ultrasound assisted extraction of curcumin as an effective alternative for conventional solid liquid extraction of natural products. *Natural Product Communications, 4*(1), 95-100.

Monton, C., Charoenchai, L., Suksaeree, J., & Sueree, L. (2016). Quantitation of curcuminoid contents, dissolution profile, and volatile oil content of turmeric capsules produced at some secondary government hospitals. *Journal of Food and Drug Analysis, 24*(3), 493-499. DOI: 10.1016/j.jfda.2016.01.007

Monton, C., Chuanchom, P., Popanit, P., Settharaksa, S., & Pathompak, P. (2021). Simplex lattice design for optimization of the mass ratio of *Curcuma longa* L., *Curcuma zedoaria* (Christm.) Roscoe and *Curcuma aromatica* Salisb. to maximize curcuminoids content and antioxidant activity. *Acta Pharmaceutica, 71,* 445-457. DOI: 10.2478/acph-2021-0025

Monton, C., Luprasong, C., & Charoenchai, L. (2019a). Acceleration of turmeric drying using convection and microwave-assisted drying technique: An optimization approach. *Journal of Food Processing and Preservation, 43*(9), e14096. DOI: 10.111/jfpp.14096

Monton, C., Luprasong, C., & Charoenchai, L. (2019b). Convection combined microwave drying affect quality of volatile oil compositions and quantity of curcuminoids of turmeric raw material. *Revista Brasileira de Farmacognosia, 29*(4), 434-440. DOI: 10.1016/j.bjp.2019.04.006

Monton, C., Settharaksa, S., Luprasong, C., & Songsak, T. (2019). An optimization approach of dynamic maceration of *Centella asiatica* to obtain the highest content of four centelloids by response surface methodology. *Revista Brasileira de Farmacognosia, 29*(2), 254-261. DOI:10.1016/j.bjp.2019.01.001

Monton, C., Wunnakup, T., Suksaeree, J., Charoenchai, L., & Chankana, N. (2020). Investigation of the interaction of herbal ingredients contained in Triphala recipe using simplex lattice design: Chemical analysis point of view. *International Journal of Food Science, 2020*, 5104624. DOI: 10.1155/2020/5104624

National Drug System Development Committee. (2018). National List of Essential Medicines. In Thai: *Royal Thai Government Gazette, 19 January 2018*, p. 260. Retrieved August 22, 2020, from http://www.fda.moph.go.th/sites/drug/Shared%20Documents/New/nlem2561.PDF

Patel, N. A., Patel, N. J., & Patel, R. P. (2009). Formulation and evaluation of curcumin gel for topical application. *Pharmaceutical Development and Technology, 14*(1), 83-92. DOI: 10.1080/10837450802409438

Paulucci, V. P., Couto, R. O., Teixeira, C. C. C., & Freitas, L. A. P. (2013). Optimization of the extraction of curcumin from *Curcuma longa* rhizomes. *Revista Brasileira de Farmacognosia, 23*, 94-100. DOI: 10.1590/S0102-695X2012005000117

Peram, M. R., Jalalpure, S. S., Palkar, M. B., & Diwan, P. V. (2017). Stability studies of pure and mixture form of curcuminoids by reverse phase-HPLC method under various experimental stress conditions. *Food Science and Biotechnology, 26*(3), 591-602. DOI: 10.1007/s10068-017-0087-1

Perkins, K., Sahy, W., & Beckett, R. D. (2017). Efficacy of *Curcuma* for treatment of osteoarthritis. *Journal of Evidence-based Complementary and Alternative Medicine, 22*(1), 156-165. DOI: 10.1177/2156587216636747

Rowe, R. C., Sheskey, P. J., Cook, W. G., & Fenton, M. E. (2012). *Handbook of Pharmaceutical Excipients* (7th ed.). London, UK: Pharmaceutical Press.

Sae-Lim, P., Yuenyongsawad, S., & Panichayupakaranant, P. (2019). Chamuangone-enriched *Garcinia cowa* leaf extract with rice bran oil: Extraction and cytotoxic activity against cancer cells. *Pharmacognosy Magazine, 15*(61), 183-188. DOI: 10.4103/pm.pm_472_18

Saraf, S., Jeswani, G., Kaur, C. D., & Saraf, S. (2011). Development of novel herbal cosmetic cream with *Curcuma longa* extract loaded transfersomes for

antiwrinkle effect. *African Journal of Pharmacy and Pharmacology, 5*(8), 1054-1062.

Sasidharan, S., Chen, Y., Saravanan, D., Sundram, K. M., & Yoga Latha, L. (2010). Extraction, isolation and characterization of bioactive compounds from plants' extracts. *African Journal of Traditional, Complementary and Alternative Medicines, 8*(1), 1-10.

Singh, K., Simapaisan, P., & Utama-ang, N. (2017). Effect of microwave-assisted extraction on curcuminoid from turmeric and application in germinate-coated rice. *Food and Applied Bioscience Journal, 5*(1), 11-22.

Sobankumar, D. R., Rajan, A., Christudhas, J., & GnanaRaj, A. (2018). Process for the extraction and encapsulation of curcumin in nanoemulsion using edible oils. *International Journal of Advanced Scientific Research and Management, 3*(7), 11-15.

Takenaka, M., Ohkubo, T., Okadome, H., Sotome, I., Itoh, T., & Isobe, S. (2013). Effective extraction of curcuminoids by grinding turmeric (*Curcuma longa*) with medium-chain triacylglycerols. *Food Science and Technology Research, 19*(4), 655-659.

Ungphaiboon, S., Supavita, T., Singchangchai, P., Sungkarak, S., Rattanasuwan, P., & Itharat, A. (2005). Study on antioxidant and antimicrobial activities of turmeric clear liquid soap for wound treatment of HIV patients. *Songklanakarin Journal of Science and Technology, 27*(Suppl. 2), 569-578.

Valizadeh Kiamahalleh, M., Najafpour-Darzi, G., Rahimnejad, M., Moghadamnia, A. A., & Valizadeh Kiamahalleh, M. (2016). High performance curcumin subcritical water extraction from turmeric (*Curcuma longa* L.). *Journal of Chromatography B, 1022*, 191-198. DOI: 10.1016/j.jchromb.2016.04.021

Zaman, S. u., & Akhtar, N. (2013). Effect of turmeric (*Curcuma longa* Zingiberaceae) extract cream on human skin sebum secretion. *Tropical Journal of Pharmaceutical Research, 12*(5), 665-669. DOI: 10.4314/tjpr.v12i5.1

Zamarioli, C. M., Martins, R. M., Carvalho, E. C., & Freitas, L. A. P. (2015). Nanoparticles containing curcuminoids (*Curcuma longa*): development of topical delivery formulation. *Revista Brasileira de Farmacognosia, 25*, 53-60. DOI: 10.1016/j.bjp.2014.11.010