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Optimising Palm Olein-Based Betamethasone 17-Valerate Emulsions for Scalable Manufacturing and Stability

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Abstract

Introduction: Palm olein has been used as an excipient in the formulation of topical emulsions due to its rich source of natural antioxidants that can lead to better skin health and higher stability upon storage. Despite its potential as a topical drug delivery vehicle, the practical implementation of manufacturing 20% (w/w) palm olein-in-water emulsions for commercial purposes has not been explored extensively, and obtaining experimental data on scale-up studies would be helpful in facilitating this realisation. **Methods:** This research work established and optimised the manufacturing process parameters for the production of cream and lotion formulations containing betamethasone 17-valerate, utilising palm olein as the vehicle, with scale-up from lab-scale 5 kg batches to pilot-scale 80 kg batches. Design of experiments (DoE) where response surface methodology as well as three-level, two-factors (32) full factorial design were used to develop statistical models for representing the possible relationships between factors: homogenisation time and speed, and responses: particle size and phase separation. **Results:** The findings established that the quadratic model was the most suitable model as it could predict the interactions between factors and responses in an accurate manner as well as suggest the optimum operating conditions. The optimum homogenisation time and speed were found to be 40 minutes and 3400 rpm, respectively. These conditions produced emulsions with the smallest particle size (3.2 μm ± 0.03) and the least phase separation value (29.7% ± 0.35). **Conclusion:** The study successfully demonstrated the potential to scale up the manufacturing of 20% (w/w) palm olein-in-water emulsions for commercial purposes. The optimised parameters, obtained through DoE, facilitate the large-scale production of stable emulsions containing betamethasone 17-valerate.

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Introduction

Palmisone® products are topical cream and lotion of betamethasone 17-valerate (BV17) which are developed for treating corticosteroid-responsive skin diseases such as eczema and psoriasis. Unlike conventional BV17 products which were prepared using mineral oils as drug delivery vehicle, Palmisone® products were prepared using palm olein, which is the liquid-fractionated part of palm oil extracted from the mesocarp of *Elaeis guineensis*. In order to be used as the drug delivery vehicle, palm olein was homogenised into an oil-in-water emulsion consisting of 20 % (w/w) palm olein-in-water emulsion stabilised with 25 % (w/w) of Span® 20 and Tween® 20 non-ionic surfactant mixture at an effective hydrophile-lipophile balance (HLB) value of 10. The use of palm olein as topical drug delivery emulsion is advantageous since it contains natural antioxidants that can lead to better skin health. It is also stable upon storage due to the presence of natural anti-oxidants (Ramli et al., 2017).

Previous research works have witnessed the superior stabilities and efficacies of 20 % (w/w) palm olein-in-water emulsion when compared to three commercial samples utilising conventional vehicle bases, such as white soft paraffin and liquid paraffin (Ahmad et al., 2018). The present study aims to establish and optimise the manufacturing process parameters for pilot-scale production of topical cream and lotion of BV17 with consistent quality using palm olein as drug delivery vehicle. Since the study comprehensively outlines the practical procedures employed for process optimisation, the research described here serves as a practical reference for optimising procedures in similar processes.

In this research, we used 67.36 kg of 20 % (w/w) palm olein-in-water emulsion to produce 80 kg of Palmisone® products. Response surface methodology (RSM) in conjunction with full factorial design (FFD) was employed to study the influences of two factors (homogenisation speed and time) on two critical responses - particle size and phase separation. These parameters are crucial as they directly impact the stability, bioavailability, and overall performance of the emulsion. The aim was to develop statistical model equations for estimating the optimum conditions in order to generate the smallest particle size and the least percentage of phase separation. RSM demonstrates the relationship between factors and responses by interpreting the effect of factors on responses or processes through mathematical models whereas FFD is used to investigate the importance and the ranges of factors. Despite its low resolution, FFD is a simple and sufficient method for screening a large numbers of experimental parameters (Jankovic et al., 2021, Ćurić et al., 2013, Singh et al., 2011).

Materials and methods

Materials

Refined, bleached and deodorised palm olein, propylene glycol, chlorocresol and BV17 powder were purchased from Plant Succeed Engineering Sdn. Bhd. Tween® 20 and triethanolamine were supplied by Merck Sdn. Bhd. Carbopol® 940 powder was provided by Eurochemo Pharma Sdn. Bhd. Span® 20 was purchased from Hefei TNJ Chemical Industry Co., Ltd. Honey melon fragrance oil was generously provided by IKOP Pharma. All the starting materials used were pharmaceutical grade.

Method

The process optimisation study was performed in the following steps, which were adapted from the methodology outlined by Singh, Ćurić and their co-workers (Singh et al., 2011, Ćurić et al., 2013). The emulsions were prepared using the homogenous mixing equipment (HME) (YC-HM-100, Yenchen, China) available in the Production Department at IKOP Pharma.

Step 1: Define critical formulation stages

Palmisone® products were formulated using four sequential stages: preparation of 1 % (w/w) Carbopol® 940 stock solution (Stage 1), preparation of BV17 slurry (Stage 2), preparation of 20 % (w/w) palm olein-in-water emulsion (Stage 3) and preparation of Palmisone® products (Stage 4).

According to the earlier formulation developmental studies conducted by Win (2015), the

preparation of 20% (w/w) palm olein-in-water emulsion (Stage 3) is the most critical part because it is the base vehicle in which active pharmaceutical ingredient and all other pre-mixed excipients are finally incorporated to obtain the final product. Moreover, the critical quality attributes of finished product are closely derived from the parent base emulsion. For instance, the particle size has a great impact on the diffusion of BV17 from the vehicle into the stratum corneum which in turn affects the therapeutic efficacy of Palmisone® products (Ahmad et al., 2018). Therefore, it is important to determine the best possible manufacturing process parameters in Stage 3 in order to produce 80 kg pilot batch of Palmisone® products with consistent quality and stability.

Step 2: Select critical manufacturing parameters

The purpose of this phase is to determine the appropriate design factors ((Singh et al., 2011, Ćurić et al., 2013). The particle size of the dispersed phase and the phase separation are amongst the most vital parameters in determining the stability of an emulsion (Faria-Silva et al., 2020). These two parameters were chosen as the responses in this study and the factors were further determined based on the manufacturing parameters which had the most influential effect on the chosen responses.

Win (2015) and Mohd Nawi (2018) had reported that homogenisation process parameters such as homogenisation temperature, speed, duration and depth of emulsifier shaft embedded inside the emulsion would greatly influence the properties of palm olein emulsion. Since the emulsifier shaft of the homogenous mixing equipment (HME) cannot be adjusted due to the built-in equipment design, the depth of emulsifier shaft was treated as constant in this research work. Similarly, the homogenisation temperature was maintained at 25 ± 5 ºC as recommended by Win (2015). Therefore, the adjustable parameters, such as homogenisation speed and duration were chosen as the independent variables or factors. The ranges of independent variables were selected based on the HME's homogenising capacities as suggested by the equipment's manufacturer and knowledge attained from trial experiments.

Step 3: Establish experimental model using RSM

The experimental model for the optimisation of homogenisation process was established using the Design-Expert® Software Version 7.0.0 (Stat-Ease Inc., Minneapolis, USA). RSM and three-level, two-factor (32) FFD were used to establish the suitable experimental model (Singh et al., 2011, Ćurić et al., 2013).

Step 4: Finalise experimental design and parameter specifications

The units, notations and targeted values of both independent and dependent variables shown in Table 1(a) were specified in the Design-Expert® software environment and the design matrix is shown in Table 1(b).

Table 1: (a) Variable inputs for the determination of experimental model, and (b) Design matrix for pilot-scale production (67.36 kg) of 20% (w/w) palm olein-in-water emulsion.

(a).

Independent variables	**Unit**	**Notation**	**Coded levels**		
			-1	**0**	**1**
Homogenisation speed	rpm	A	1400	2400	3400
Homogenisation time	min	B	30	40	50
Dependent variables			**Targeted values**		
			Min		**Max**
Particle size	µm	R 1	3.01		5
Phase separation	%	R 2	28.00		40

(b).

Run no.	**A (rpm)**	**B (min)**	**R 1 (µm)**	**R 2 after 24 h (%)**
1	3400	40	3.01	28
2	1400	40	12.54	55
3	3400	30	3.69	40
4	2400	40	3.72	30
5	2400	40	3.73	30
6	2400	40	3.76	30
7	3400	50	3.58	35
8	2400	50	3.91	40
9	1400	30	12.99	60
10	2400	40	3.71	30
11	2400	40	3.83	30
12	1400	50	13.04	59
13	2400	30	3.95	35

Step 5: Perform statistical analysis

The values for coefficient of determination (R^2), predicted and adjusted coefficient of determinations (predicted R^2 and adjusted R^2) were analysed to evaluate the fit quality of the selected model. The residual plots were also visually analysed to examine the goodness of the chosen model. Furthermore, analysis of variance (ANOVA) test was employed to determine the significance of the chosen model based on F-test. In this context, the model was considered significant if the probability associated with the F-test was greater than 0.05 at a 95% confidence interval (i.e. Prob > F). The generated quadratic equations were analysed for suitability in representing the relationship between the chosen factors and each response. For visual representation, the fitted equations for both responses were represented in the forms of contour and response surface plots (Yolmeh et al., 2017).

Step 6: Optimise homogenisation process

To prepare the emulsion, the temperature of HME was maintained at 60 ± 5 °C before commencing the homogenisation. The following starting materials, i.e. 16 kg of palm olein, 3.32 kg of Span® 20 and 0.68 kg of Tween® 20 were mixed with the HME. The mixture was heated to the set temperature and stirred for 15 minutes until the oil and surfactant were homogenous. Upon mixing, the HME was cooled down to 25 ± 5 ºC using a recirculating cooler (HL-35H, Lab Companion, Jeio Tech, Korea) before the addition of 47.36 kg purified water into the mixed oil phase. The stock emulsion was then homogenised.

The experiments were carried out with the parameters as shown in Table 1(b) and the samples were withdrawn at 10-minutes interval throughout the experimental periods (50 minutes) for measuring the particle size and the percentage of phase separation.

In order to measure phase separation, emulsion samples were stored inside 100-mL graduated cylinders to visually monitor the phase separation at room temperature. The mouths of the graduated cylinders were closed with caps to prevent the evaporation of water from the formulations throughout the study period. The percentage of phase volume to total volume of emulsion was determined as the percentage of phase separation of the formulation. In order to investigate the particle size of dispersed phase or palm olein, a calibrated laser particle size analyser (BT-9300H, Dandong Baite Instruments Ltd., China) was used and the result was displayed as D (v,50), i.e. the point at which 50 % of the sample volume possess the same particle size (Win, 2015, Mohd Nawi, 2018).

The measurements were triplicated to determine the average values for each response at specific time and the values were expressed as mean ± standard deviation. The observed average values were then compared against the predicted values generated by the Design-Expert® software.

Step 7: Validate the optimised parameters

When the optimum conditions were determined, three batches of 67.36 kg of 20 % (w/w) palm olein-in-water emulsion were prepared using the optimum homogenisation speed and time obtained from the studies conducted in Step 6. The mean response values were compared to that of the predicted values given by the Design-Expert® software in order to confirm the accuracy, validity and suitability of the optimised parameters (Yolmeh et al., 2017).

Results

The model summary statistics given by the Design-Expert® software shows information such as coefficient of determination (R^2), predicted coefficient of determination (predicted R^2) and adjusted coefficient of determination (adjusted R^2) for linear, interactive (denoted as 2F1) and quadratic models as presented in Table 2. The quadratic model was chosen by the software since this model exhibited the highest R^2.

Additionally, the adequacy of quadratic model was confirmed using ANOVA test. The quadratic equations for particle size (R 1) and phase separation (R 2) given by the ANOVA test were as follow:

$$R\,1 = 3.69 - 4.71*A - 0.017*B - 0.04*A*B + 4.20*A^2 + 0.36*B^2 \quad (1)$$

$$R\,2 = 30.07 - 11.83*A - 0.17*B - 1*A*B + 11.26*A^2 + 7.26*B^2 \quad (2)$$

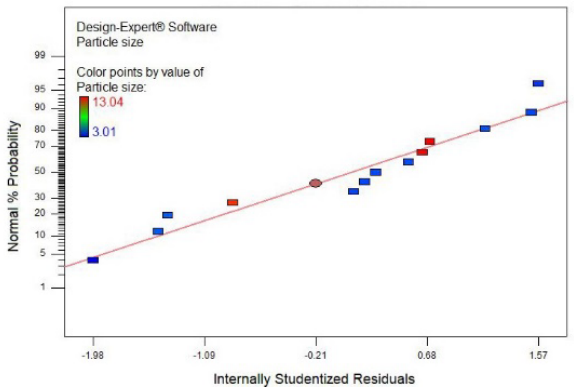
where A is homogenisation speed and B is homogenisation time. The above equations are mathematical descriptions on the true relationship between factors and responses which simulate the possible interactions between factors or combinations of factors on responses (Maran et al., 2013).

Following the ANOVA test, the Fisher's statistical test or F-test was performed to determine the significance of each response using the F-value. The outcomes are summarised in Table 3.

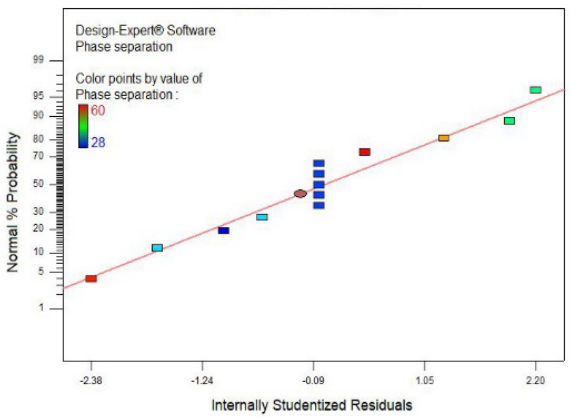
For model validation purpose, statistical parameter such as R^2 is widely used to indicate the suitability of a chosen model. In order to enhance the confidence level of the result, graphical tool was used as well whereby the normal plots of the residuals were constructed to confirm the suitability of quadratic model (Mohr et al., 2022).

Normal probability plots or normal plots are graphical interpretations of how well the data from fitted models are normally distributed. The data can be either raw data or residuals. Residuals from fitted models are the difference between experimental responses and theoretical responses whereas studentised residuals are residuals which are expressed in their standard deviations. Normal plot of residuals is obtained when the normal % probability (y-axis) is plotted against internally studentised residuals (x-axis). The normal plot of residuals for both responses are given in Fig. 1, whereas the predicted against actual plots of both responses are depicted in Fig. 2.

Fig. 3 and Fig. 4 show the visual depiction of the relationship between factors and responses using two-dimensional contour plots as well as three-dimensional response surface plots. Contour plots are simpler interpretations of response surface plots. The contour lines delineate the response which contours both factors at a time. On the other hand, the gridded response surface plots briefly describe the impact of factors on responses from the best-fitted model with a map of contour lines in three-dimensional design. These plots could lead to the identification of optimum operating parameters (factors) for producing the most desirable outcomes (responses) (Lamidi et al., 2023, Singh et al., 2011). In the context of Design-Expert® software, blue zone represents the zone for favourable responses while red zone represents the zone for undesired responses. Factors A and B were plotted at x- and y-axes, respectively for both contour and response surface plots. Unlike contour plots, individual response was plotted at z-axis in each response surface plot. Both contour plots (Fig. 3) and response surface plots (Fig. 4) showed similar trend in which both particle size (R 1) and phase separation (R 2) decreased with increasing homogenisation speed (A) and homogenisation time (B).



(a)



(b)

Fig. 1: Normal plots of residuals for (a) particle size (R 1) and (b) phase separation (R 2) showing normal distribution of studentised residuals and goodness of fit of quadratic model.

Table 2: Results for model summary statistics of both responses (R 1 and R 2) provided by Design-Expert® software.

Model	Particle size (R 1)			Phase separation (R 2)		
	R^2	Predicted R^2	Adjusted R^2	R^2	Predicted R^2	Adjusted R^2
Linear	0.6850	0.6220	0.3646	0.5077	0.4093	-0.0073
2F1	0.6851	0.5801	-0.3907	0.5101	0.3469	-1.4018
Quadratic	0.9994	0.9990	0.9962	0.9820	0.9691	0.8168

Table 3: Analysis of variance results for (a) particle size (R 1), and (b) phase separation (R 2).

(a).

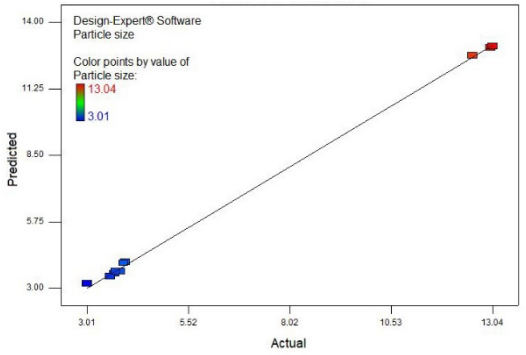
Source	Sum of squares	df	*F*-value	*p*-value (Prob > F)	SE
Model	194.61	5	2446.90	< 0.0001	0.0524
A	133.39	1	8385.59	< 0.0001	-
B	0.00	1	0.10	0.7556	-
A*B	0.01	1	0.40	0.5460	-
A^2	48.80	1	3068.14	< 0.0001	-
B^2	0.36	1	22.33	0.0021	-

A = homogenisation speed, B = homogenisation time, df = degree of freedom, SE = standard error

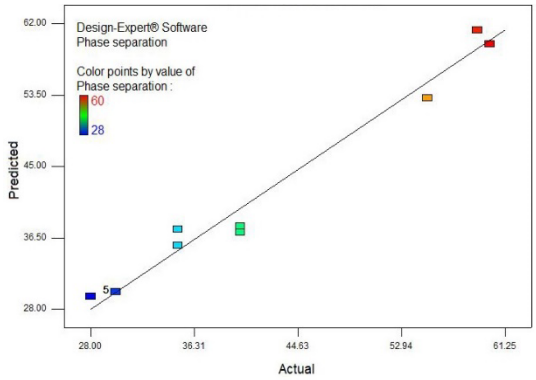
(b).

Source	Sum of squares	df	*F*-value	*p*-value (Prob > F)	SE
Model	1625.24	5	76.25	< 0.0001	0.8573
A	840.17	1	197.10	< 0.0001	-
B	0.17	1	0.04	0.8489	-
A*B	4.00	1	0.94	0.3650	-
A^2	350.09	1	82.13	< 0.0001	-
B^2	145.52	1	34.14	0.0006	-

A = homogenisation speed, B = homogenisation time, df = degree of freedom, SE = standard error

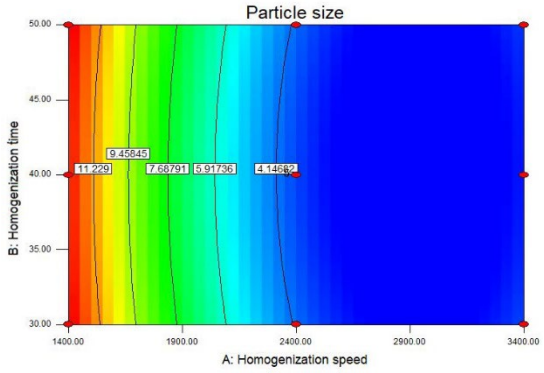


(a)

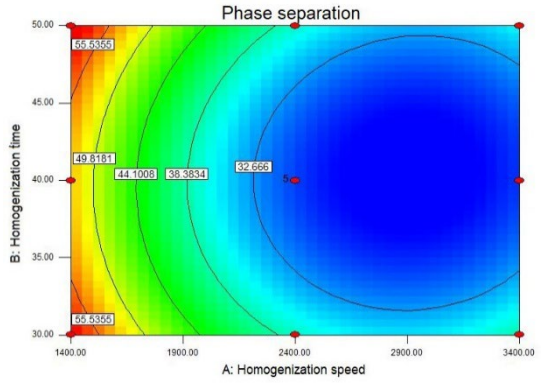


(b)

Fig. 2: Plots of predicted against actual for (a) particle size (R 1) and (b) phase separation (R 2).

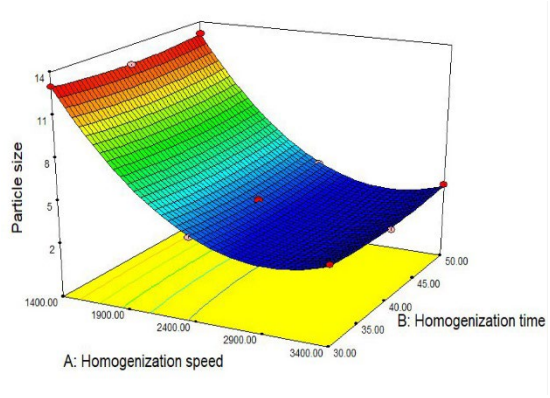


(a)

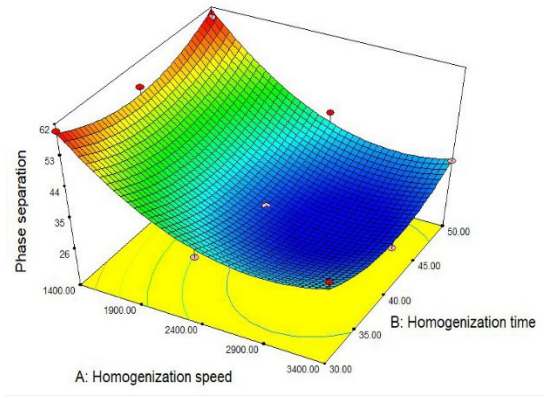


(b)

Fig. 3: Two-dimensional contour plots for (a) particle size (R 1) and (b) phase separation (R 2) against homogenisation speed (A) and homogenisation time (B).



(a)



(b)

Fig. 4: Three-dimensional response surface plots for (a) particle size (R 1) and (b) phase separation (R 2) versus homogenisation speed (A) and homogenisation time (B).

Selection of optimum operating parameters

The Design-Expert® software has provided seven check point batches. The actual responses together with standard deviation values and percentage errors for all check point batches were recorded and summarised in Table 4. Furthermore, the desirability ramp of the optimised process variables for both responses, which focuses on selecting values that maximise the desirability score, is shown in Fig. 5.

Fig. 5: Desirability ramp of optimised process variables for particle size and phase separation.

Table 4: Results for predicted responses, actual responses and percentage errors (values are mean ± SD).

No	Factors		Predicted responses		Actual responses		Error (%)		D
	A (rpm)	B (min)	R 1 (μm)	R 2 (%)	R 1 (μm)	R 2 (%)	R 1	R 2	
1	3400	31	3.54	36.68	3.60 ± 0.10	38.34 ± 0.54	1.65	4.53	1.0000
2	3400	40	3.19	29.45	3.20 ± 0.31	29.66 ± 0.60	0.46	0.71	1.0000
3	3400	44	3.23	30.27	3.25 ± 0.69	30.58 ± 0.19	0.73	1.01	1.0000
4	3400	33	3.41	33.92	3.44 ± 0.43	35.57 ± 1.98	1.02	4.87	1.0000
5	2719	30	3.01	35.18	3.57 ± 0.63	36.13 ± 0.89	18.60	2.69	0.6597
6	2692	50	3.01	34.37	3.59 ± 0.41	38.79 ± 2.52	19.27	12.86	0.6462
7	2664	32	3.01	32.97	3.63 ± 0.55	40.21 ± 2.00	20.60	21.96	0.6322

A= Homogenisation speed, B= Homogenisation time, R 1= Particle size, R 2= Phase separation, D= Desirability

Table 5: Results for the confirmation studies of 67.36 kg of 20 % (w/w) palm olein-in-water emulsions homogenised at 3400 rpm (optimum homogenisation speed) for 40 min (optimum homogenisation time).

Batch No.	Predicted responses		Actual responses	
	Particle size (μm)	Phase separation (%)	Particle size (μm)	Phase separation (%)
1	3.19	29.45	3.20	30.05
2			3.18	29.38
3			3.23	29.56
Mean	-	-	3.20	29.66
Standard deviation	0.13	2.06	0.03	0.35
Percentage error	-	-	0.42	0.72

Validation of optimum operating parameters

The results for three confirmation batches were compared with predicted responses and presented in Table 5.

Discussion

In this study, the quadratic model has been identified as the most suitable model since it gave the highest R^2 for both responses as shown in Table 2. R^2 indicates the total variance in the dependent variables given by the model. Low R^2 implies that there are variations which cannot be explained by the model. Another good indication of significant model is having a difference of 0.2 or less between the predicted and adjusted R^2. It is also a great advantage to have higher adjusted R^2 value than the corresponding predicted R^2 value for a model since it assures high correlation between the theoretical and experimental values (Karch, 2020, Maran et al., 2013). Based on Table 2, it was observed that the quadratic model satisfied the above conditions; hence, it was chosen for the current process optimisation study of 20% (w/w) palm olein-in-water emulsion.

The quadratic equations (1) and (2) were found to effectively capture the relationship between independent and dependent variables since the complete equations including all possible interactions were given by the ANOVA test. It was also observed that homogenisation speed had greater impact on both particle size and phase separation (-4.71 for R 1 and -11.83 for R 2) in comparison to homogenisation time (-0.017 for R 1 and -0.17 for R 2). Owing to the negative signs, larger factors would lead to lower (better) responses (Karch, 2020).

Table 3 shows that the F-value of R 1 (2446.9) was higher than that of R 2 (76.25). The larger the F-values, the better the fitted quadratic equation in describing the variance in the response. The related p-value for each F-value confirms the significance of F-value. The F-value is considered statistically

significant when the value is large and the related p-value is less than 0.05 (Maran et al., 2013). The p-values of approximately 0.0001 were seen for terms such as A, A^2 and B^2, thus showing that they were highly significant statistically. However, low F-value (B = 0.1, A*B = 0.4 for R 1 and B = 0.04, A*B = 0.94 for R 2) and p-values of > 0.05 (B = 0.7556, A*B = 0.546 for R 1 and B = 0.8489, A*B = 0.365 for R 2) were seen in some factors (B and A*B for both responses), thus indicating that these factors were statistically insignificant in the equation although the entire model was proven to be significant. Similar observation was reported by Abdulwahab and Saidat (2013). This happened due to the hierarchical problem which occurred when the developed model contained some factors that were aliased with one another. Nonetheless, the developed model was still applicable since the overall p-value of the model was less than 0.05 (Abdulwahab & Saidat, 2013). Furthermore, the standard error (SE) of R 1 model (0.0524) was found to be lower than that of R 2 (0.8573).

Fig. 1 reveals that all studentised residuals were normally distributed since they were fitted to the diagonal lines for both responses which indicated the goodness of fit of the quadratic model (Maran et al., 2013, Singh et al., 2011). As observed, the internally studentised residuals of R 1 followed the diagonal line more perfectly than R 2. These findings were also verified using predicted against actual plots, as presented in Fig. 2, from which the developed models were proven to be adequate since the data points were distributed along the straight line (Maran et al., 2013). On the other hand, both Fig. 3 and Fig. 4 suggest that higher factors would lead to better responses.

Effect of homogenisation speed and time

The rotor and stator of the homogenising head of HME induced extremely powerful shear forces which can break down the bigger oil droplets into smaller ones and homogenise the emulsion at the same time. The shear force increases with respect to the homogenisation speed. On the other hand, longer homogenisation time would lead to smaller particle size due to longer period of exposure to shearing forces (Win, 2015). This explains the condition where higher factors would lead to lower hence better responses as shown in Fig. 4.

However, it was observed that there was a slight increase in both responses at the end of the experiments (50 minutes). This could be due to the shear-induced flocculation mechanism in which electrical charges appeared on the smaller particles which attracted the adjacent oil droplets and flocculated into bigger particles (Li et al., 2016). In order to avoid this mechanism, homogenisation is routinely carried out at optimum homogenisation speed and time at which emulsions with the smallest droplet size and the least phase separation are produced (Win, 2015). From the visual observation of contour and response surface plots, it was estimated that the optimum homogenization conditions for producing 67.36 kg of 20% (w/w) palm olein-in-water emulsion could be roughly over 3000 rpm for homogenisation speed (A) and approximately 40 minutes for homogenisation period (B). This hypothesis was further confirmed by performing the following studies.

Selection of optimum operating parameters

The percentage error indicates the difference between experimental and predicted values. Lower percentage error dictates higher accuracy of the chosen experimental design. From Table 4, it was found that the least percentage errors recorded were 0.46 % for particle size (R 1) and 0.71 % for phase separation (R 2) in Batch 2. Therefore, the factors from Batch 2 were chosen as the optimum operating parameters because they would lead to the smallest percentage errors in both responses. The batches in which the emulsions were homogenised at speeds of 3400 rpm (i.e. batches 1 - 4) were seen to exhibit higher desirability values in comparison to those with the homogenisation speeds of over 2600 rpm (i.e. batches 5 – 7). Nonetheless, Batch 2 was finally chosen since it had added advantages such as producing emulsions with the smallest particle size (3.20 ± 0.31 μm) and the least percentage of phase separation (29.66 ± 0.60 %) in addition to having the lowest percentage error. Smaller percentage of phase separation was expected from the emulsion having smaller particle size since smaller oil droplets would take longer to undergo aggregation, i.e. the so-called Ostwald's ripening that triggers the phase separation (Zwicker et al., 2015).

On the other hand, higher percentage errors as well as lower desirability values were exhibited by batches where the emulsions were homogenized at speeds less than 600 rpm. High percentage error was generated when the process parameters could not reproduce the predicted response values given by the software. The big difference in predicted and observed responses was attributed to the fact that the homogenisation speed of < 3000 rpm could not produce emulsions of particle size ≤ 3 μm in practical milieu (i.e. 67.36 kg of emulsions). This

phenomenon was caused by the relationship between homogenisation conditions and homogenisation volume. Higher homogenisation volume requires higher homogenisation speed and/or longer homogenisation time to produce emulsion with smaller particle size (Win, 2015). Mohd Nawi (2018) reported that the homogenisation conditions could vary according to the homogenisation volume; therefore, the optimum homogenisation parameters should be customised based on the prepared emulsion amount.

Since the findings of Batch 2 were satisfactory, the optimised homogenisation speed and time were chosen as 3400 rpm and 40 minutes (Batch 2), respectively for preparing 67.36 kg of 20% (w/w) palm olein-in-water emulsion stabilised with 25% (w/w) to oil of Span® 20 and Tween® 20 mixture with effective HLB value of 10. Based on the multiple response optimisation, the chosen optimum operating conditions yielded a desirability value of 1 for both responses. The desirability value ranges from 0 (least desirable) to 1 (most desirable), whereby the value of 1 indicates that the chosen optimum conditions are highly satisfactory to yield the desired outcomes (Shokri et al., 2020).

The results from the validation studies in Table 5 proved that the observed data showed reasonable agreement with the predicted data. This favourable outcome indicated the suitability of quadratic models. These observations also indicated the reproducibility of responses if the optimum homogenisation process parameters were controlled during batch-to-batch operations.

Conclusion

It was evident that the developed quadratic models were able to represent the relationship between process parameters and properties of emulsions. The study revealed that the characteristics of the 20 % (w/w) palm olein-in-water emulsions, such as particle size and phase separation were affected by both speed and duration at which the emulsions were homogenised. Both attributes were found to be inversely proportional to the process variables within certain limits. This study also demonstrated that the favourable outcomes, such as smallest particle size and lowest percentage of phase separation were obtained when the homogenisation speed was set at 3400 rpm for a duration of 40 minutes. These operating parameters were considered as optimum operating conditions which should be controlled for future pilot-batch production of emulsions having similar characteristics.

Authors contributions

Conceptualisation, M.R.A.B. and T.W.; performed the experiments, analysed the data and drafted the paper, T.W.; reviewed and edited the paper, M.R.A.B.; supervision, M.R.A.B., F.M., M.T. and M.Z.I.S. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that they have no conflicts of interest to disclose.

Declaration of generative AI and AI-assisted technologies in the writing process

The authors declare that ChatGPT was used to assist in improving the readability and language in certain parts of this work. The authors have reviewed and edited the content as necessary and take full responsibility for the final content of the publication.

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