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*Original Article*

# Iconographic correlation analysis for optimization of high caloric density enteral nutrition formulation

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## Abstract

High caloric density enteral nutrition contains high amounts of carbohydrates, proteins and fats. Therefore, it is likely to have either too high viscosity or unstable emulsion if not optimally formulated. Response surface methodology (RSM) is a tool for optimization. To obtain the optimal formula, numerous formulas are needed to be prepared and determined if classical RSM using a central composite design (CCD) is used since there are many involving factors. For this reason, the Iconographic Correlation (IC) could be compromising. In this study, 9 influencing factors were optimized. The desired response was the complex viscosity and a degree of emulsion separation. By using the IC, the number of experiments was reduced from 524 treatments if the CCD was used to 17 treatments. The model describing significant logical interactions between factors toward each response was proposed with excellent correlation, $R^2$adj = 0.99, and 0.93 for complex viscosity, and emulsion separation, respectively.

**Keywords:** iconographic correlation, response surface methodology, optimization, enteral nutrition

## 1. Introduction

Enteral nutrition is one kind of nutrition supports for patients that can be introduced either by tube or oral (Frias, Peñas, & Vidal-Valverde, 2009; Hebuterne *et al.*, 2003; Rufián-Henares, Guerra-Hernandez, & García-Villanova, 2006). Oral enteral nutrition in the form of thickened liquid is more frequently used in hospital (Robbins *et al.*, 2002; Sura, Madhavan, Carnaby, & Crary, 2012) since it can prevent aspiration during administration (Gallegos, Brito-de la Fuente, Clavé, Costa, & Assegehegn, 2017). However, formulating this kind of product is complicated because the nutritional and organoleptic aspects are both the main consideration. Enteral nutrition normally contains several kinds of protein, carbohydrate, and fat source (Fávaro, Iha, Mazzi, Fávaro, & Bianchi, 2011). The composition of the formula determines its organoleptic and nutritional characteristics. Additionally, other ingredients are also necessary to develop the acceptable quality and sensory characteristic, e.g. emulsifier, flavoring, colorant. A physical treatment, such as heating also exerts an impact on the final attributes of the product. The extent of impact of heating on the final attributes of the product also

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depends on the initial composition of the formula. It is, therefore, important to consider the effect of different ingredients and their proportion in the formula so that the transformations during heating have the least possible impact on the organoleptic and nutritional characteristics of the final product. According to consumers, organoleptic qualities such as viscosity and visual aspects are essential for product acceptance. As a result, various types of ingredients and their application level are needed to be optimized. Two important characteristics influenced by the composition of the formula, namely the viscosity and the emulsion stability, may cause issues after heating. Preliminary tests have shown that a too viscous and/or shifting formula before heat treatment tends to emphasize these characteristics after heating. Therefore, to obtain a final product with good characteristics, an optimum formula should be found for the product before the heat treatment.

The search for the best possible formula that can satisfy several characteristics can be done using different optimization techniques. The most common is the Response Surface Methodology (RSM) based on a quadratic model that links the responses and the influencing factors. Many authors have used this approach for the formulation of a product (Arteaga, Li-Chan, Vazquez-Arteaga, & Nakai, 1994; Odun tan & Arueya, 2018) or the optimization of a process (Devi & Das, 2018; Douiri-Bedoui *et al.*, 2011; Tan, Ying-Yuan, & Gan, 2014). Various experimental designs can be used to explore the relationship between influencing factors and responses. If a curvature in a response with regard to influencing factors is expected, a design that yields a second-order model such as Doehlert matrix, Box-Behnken design, or Central Composite design should be used. This method is indeed very effective for the search for an optimal point in the case of problems where a few factors, less than 4, influence the responses studied. Beyond that, the large number of tests to be carried out can become prohibitive. Iconographic Correlation (IC) method (with CORICO software) is another way to carry out optimization. This method can make it possible to circumvent this difficulty by considerably reducing the number of tests to be carried out when the number of factors is greater than or equal to 4 compared to a Doehlert design (Jouquand *et al.*, 2015). IC has been previously employed to investigate the optimum condition for cooking fish by microwave heating (Laguerre *et al.*, 2013) and find the optimized condition for microwave combined with hot air drying (Laguerre, Ratovoarisoa, Vivant, Gadonna, & Jouquand, 2017). Both works showed that the model proposed by the IC was predictable and accurate.

The aim of this study was, thus, to find optimal enteral nutrition formulas in terms of viscosity and emulsion stability using the iconographic correlation.

## 2. Materials and Methods

### 2.1 Ingredients

Maltodextrin, which has the dextrose equivalent (DE) 10-12 from corn starch, was purchased from Nutrition SC Co., Ltd. Soy protein isolate (SPI), which has 86% protein, 0.5% carbohydrates, and 0.5% fat, was obtained from Mighty international Co., Ltd. Whey protein isolate (WPI), which has 89% protein, 0.6% carbohydrates, and 1.3% fat, and Whey protein concentrate (WPC) containing 79% protein, 7.39% carbohydrates, and 5.49% fat, were from Vicchi Enterprise Co., LTD. Hydrolyzed whey protein (without flavor), which has 80% protein, 3.2% carbohydrates, and 1.6% fat, was purchased from Myprotein. Soy lecithin, malic acid, citric acid, and high fructose syrup 42% were obtained from Chemipan Cooperation Co., Ltd. Coconut oil (CCO) and rice bran oil (RBO) were purchased from local supermarkets in Thailand.

### 2.2 Sample preparation

The formulation was based on the caloric distribution by fixing the calorie from protein at 20% and varying the calorie from fat and from carbohydrates according to the experimental design. All calculated amounts of the ingredients were added and mixed with a blender (Moulinex®) at the lowest speed for 5 minutes. The samples were stored in a plastic bottle and kept refrigerated before the measurements.

### 2.3 Experimental design

#### 2.3.1 Factors

There were 9 factors to be optimized in this research, which were type of oil, lecithin concentration in % (w/w), caloric density [caldens] in kcal/g, amount of solid in high fructose syrup to acid ratio [FStoAcid], percentage of hydrolyzed whey protein to total protein [Hydrolyzed], percentage of calorie from fat to total calorie [Calfat], percentage of calorie from high fructose syrup to total calorie [CalFS], whey protein concentration [WPconc] in % (w/w), and percentage of whey protein isolate to total whey protein [WPI toWP]. Table 1 shows the level of each factor used in the study. It is noted that three macro nutrients, which are fat (rice bran oil and coconut oil), carbohydrates (fructose syrup), and protein (whey protein isolate, whey protein concentrate, and hydrolyzed whey protein) was set to contribute to 50%-60%, 5%-15% and 25%-45% of the total caloric density, respectively.

Two kinds of design, which are response surface methodology (RSM) with Doehlert matrix (DM) and IC using CORICO or CORICO design (CD), were compared in term of the number of trial needed for optimization.

The calculation for the number of trials was conducted following Equation 1 for DM according to Ferreira *et al.* (2017). CD was set to fit economic occupation of corners and economic space filling. The number of trials required for DM was 524 trials while CD proposed only 17 experiments. Therefore, CD was selected as the means for experimental design.

$$N = 2^k + k + Co \tag{1}$$

where N is the number of experiment, k is the number of factors, and $C_o$ is the number of central of central points developed.

Indeed, CORICO designs are more efficient than classical ones when the factors to be studied are four or higher. Jouquand *et al.* (2015) found out that using a 4-factors CD for the optimization of microwave cooking of beef

Table 1. Definition, range and levels of 9 influencing factors used in the study.

| Variable | Definition | Range | Levels |
|---|---|---|---|
| Oil | Oil type (rice bran oil or coconut oil) | - | 2 levels (defining CCO as 1, and RBO as 2) |
| Lecithin (% (w/w)) | Lecithin concentration | 0.5 to 1 | 5 |
| Caldens (kcal/g) | Caloric density | 3.5 to 4 | 5 |
| FstoAcid | Ratio of solid in high fructose syrup and acid (1:1 citric acid and malic acid) | 10 to 30 | 5 |
| Hydrolyzed (%) | Percentage of hydrolyzed whey protein to total protein | 0 to 25 | 6 |
| CalFat (%) | Percentage of calorie from fat to total calorie | 50 to 60 | 7 |
| CalFS (%) | Percentage of calorie from high fructose syrup to total calorie | 5 to 15 | 7 |
| WPconc (% (w/w)) | Whey protein concentration | 1 to 8 | 7 |
| WPItoWP (%) | Ratio of whey protein concentrate to total complex whey protein | 0 to 100 | 7 |
| LogVis | Log of viscosity in cP | | (Response) |
| Emul_Sep (%) | Percentage of emulsion separation | | (Response) |

burgundy needed only 12 experiments while a Doehlert matrix design required 21 experiments.

### 2.3.2 Response measurement

Two responses, which were percentage of emulsion separation and viscosity, were needed to be optimized. After the preparation, the percentage of emulsion separation was determined following the method described by Antes *et al.* (2017) with some modifications by using an ultrasonic bath (Bandelin Sonorex, Berlin, Germany) that was operated at 35 kHz. The sample was filled in a 15-mL plastic tube before it was tempered at 60 °C for 1 hour and sonicated at 35 KHz and 60 °C for 2 hours. The height of the separated oil was recorded, and emulsion separation was calculated following Equation (2).

$$\text{Emul Sep} = \frac{H_o}{H_t} \times 100 \tag{2}$$

where, $H_o$ and $H_t$ is the height of oil separated from the emulsion and the height of the sample, respectively.

The sample's viscosity was measured at 50 Hz and 25 °C using a remote (Anton Paar, Austria, model MCR-92) with 50-millimeter parallel plate geometry. The linear visco-elastic range (LVR) was determined by an amplitude sweep test. The sample's viscosity was determined using the de-formation in the LVR from 5 Hz to 100 Hz.

## 2.4 Data analysis

Correlation analysis, model regression, optimiza-tion, and response surface methodology were carried out by CORICO ($p < 0.01$). Model regression was set to find the model with the least standard error. The model from CORICO contains logical interactions such as those shown in Equation (3).

$$Y = a_0 + a_1X_1\&X_2 + a_2X_1\wedge X_2 + a_3X_1\&\text{-}X_2 + a_4 X_1\text{-}X_2 + a_5 X_1]X_2 + a_6 X_1\#\text{-}X_2 + a_7 X_1\{X_2 + a_8 X_1\text{-}X_2\} \tag{3}$$

where $a_0$, $a_1$, $a_2$… are coefficients, $X_1$, $X_2$ are factors, and Y is a response. The meaning of each logical interaction is as follows.

$X_1\&X_2$ means that Y is high when the value of both $X_1$ and $X_2$ are high,

$X_1\wedge X_2$ means that Y is high when the value either or both $X_1$ and $X_2$ are high,

$X_1\&\text{-}X_2$ means that Y is high when the value of $X_1$ is high and $X_2$ is low,

$X_1\text{-}X_2$ means that Y is high when the difference between $X_1$ and $X_2$ is high,

$X_1]X_2$ means that Y correlates with $X_1$ when $X_2$ is high,

$X_1\#\text{-}X_2$ means that Y is high when $X_1$ did not vary as $X_2$,

$X_1\{X_2$ means that Y is high when $X_1$ is at average and $X_2$ is high, and

$X_1\{\text{-}X_2$ means that Y is high when $X_1$ is at average and $X_2$ is low.

Sometimes, CORICO proposes a model showing logical interaction of its own. For instance, $X_1{*}X_1$ means that $X_1$ affects the response in the pattern of the square of the factor.

## 2.5 Determination of optimal conditions and model validation

CORICO facilitates the optimization to find the condition that gives responses closest to the targeted value or range. In this research, CORICO was employed to optimize emulsion separation and viscosity of the enteral nutrition. For percentage of emulsion separation, it was not noticeable when the value was lower than 1%; consequently the optimal value was set from 0 to 1. According to Gallegos *et al.* (2017), the viscosity of enteral nutrition should be around 1,750 cP (or 3.24 log value) at 50 Hz and 25 °C, thus the optimal value range was set to 3.2 to 3.3 log value. Validation of the optimal formulas yielding the desirable responses was carried out. The predicted responses were compared to those obtained by the measurements detailed in Section 2.3.2.

# 3. Results and Discussion

## 3.1 Experimental design and responses

Table 2 shows the design arrangement along with the responses from formula optimization using CORICO. The viscosity value ranged from 3.08 log value or 1,202 cP (trial

Table 2. Design arrangement from IC and responses.*

| Trial | Oil | Lecithin | Caldens | FstoAcid | Hydrolyzed | CalFat | CalFS | WPconc | WPItoWP | LogVis | Emul_Sep |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | RBO | 0.75 | 3.75 | 20 | 20 | 54 | 13 | 5.2 | 40 | 3.43 ± 0.07 | ND |
| 2 | CCO | 1 | 3.75 | 15 | 15 | 56 | 9 | 2.4 | 20 | 3.59 ± 0.33 | ND |
| 3 | CCO | 0.625 | 4 | 20 | 5 | 52 | 11 | 6.6 | 60 | 4.33 ± 0.77 | ND |
| 4 | RBO | 0.75 | 3.625 | 30 | 10 | 58 | 7 | 3.8 | 80 | 3.13 ± 0.16 | 1.72 ± 0.51 |
| 5 | CCO | 0.625 | 3.625 | 15 | 5 | 52 | 7 | 2.4 | 20 | 3.58 ± 0.12 | ND |
| 6 | CCO | 1 | 4 | 30 | 20 | 58 | 13 | 6.6 | 80 | 3.51 ± 0.03 | ND |
| 7 | RBO | 0.75 | 3.75 | 20 | 15 | 55 | 10 | 4.5 | 50 | 3.57 ± 0.03 | ND |
| 8 | RBO | 1 | 4 | 10 | 0 | 50 | 15 | 8 | 100 | 4.66 ± 0.01 | 3.57 ± 0.28 |
| 9 | RBO | 0.5 | 4 | 30 | 0 | 50 | 5 | 8 | 100 | 5.09 ± 0.84 | ND |
| 10 | CCO | 1 | 3.5 | 30 | 25 | 50 | 5 | 1 | 100 | 3.96 ± 0.05 | ND |
| 11 | RBO | 1 | 4 | 10 | 25 | 60 | 5 | 1 | 0 | 3.60 ± 0.03 | 2.08 ± 0.70 |
| 12 | CCO | 0.875 | 3.875 | 30 | 0 | 60 | 15 | 1 | 0 | 4.43 ± 0.19 | 3.87 ± 0.35 |
| 13 | RBO | 0.5 | 3.875 | 25 | 25 | 50 | 15 | 8 | 0 | 4.37 ± 0.14 | ND |
| 14 | CCO | 0.5 | 3.5 | 25 | 25 | 60 | 5 | 8 | 100 | 3.17 ± 0.05 | 1.11 ± 0.08 |
| 15 | RBO | 0.5 | 3.5 | 10 | 25 | 60 | 15 | 1 | 100 | 3.08 ± 0.25 | ND |
| 16 | CCO | 0.875 | 3.5 | 10 | 0 | 60 | 15 | 8 | 0 | 3.13 ± 0.04 | ND |
| 17 | CCO | 0.875 | 3.875 | 25 | 25 | 60 | 15 | 8 | 100 | 3.39 ± 0.18 | 1.43 ± 0.30 |

*See Table 1 for the meaning of the acronyms.

15) to 5.09 log value or 123,037 cP (trial 9). Caloric density (Caldens) and calorie from fat (CalFat) affected the viscosity. Higher caloric density tended to increase the viscosity value. On the other hand, more calories from fat reduced it.

The percentage of emulsion separation was varied from "not detected" in trial 1 to 3, 5 to 7, 9 to 10, 13, and 15 to 16 to the highest separation observed in trial 12 with 3.86% separation. This response did not show a clear correlation with any influencing factors. More discussion is given in section 3.4.

## 3.2 Correlation analysis

Figure 1 (a) shows the result of correlation analysis by CORICO program in the form of sphere, only the significant links ($p < 0.01$) are shown in figures (b) and (c). CORICO showed relationships between each variable by using solid lines for positive correlation ($r > 0$) and dotted lines for negative correlation ($r < 0$). The longer solid lines explicit stronger positive correlation while shorter dotted lines describe stronger negative correlation.

The Pearson correlation coefficient is displayed in Table 3 for significant links from each response. From Table 3, viscosity appeared to positively relate with caloric density, and negatively relate to calorie from fat $(|r| > 0.5)$. As a result, reducing caloric density and increasing calorie from fat lowered viscosity due to 2 reasons. Firstly, adding more fat could directly reduce the product's viscosity (Ariffin, Yahya, & Husin, 2016). Ariffin *et al.* (2016) investigated the effect of oil fraction on the viscosity of water-in-oil emulsion. The result from this study was consistent with the stated research. Secondly, the formula with more fat contained more moisture content since fat has a higher caloric value (9 kcal/g) compared with other macronutrients. Therefore, when adding more fat, other composition could be reduced and water could be added which yielded lower product's viscosity (Yanniotis, Skaltsi, & Karaburnioti, 2006). The work from Yanniotis *et al.* (2006) also reported that the viscosity of honey with higher moisture content was lower. Other links, where the correlation coefficient was in the range between -0.5 and 0.5, had weak correlations. Thus, it could be drawn that there was no clear trend for factor-response of each link.

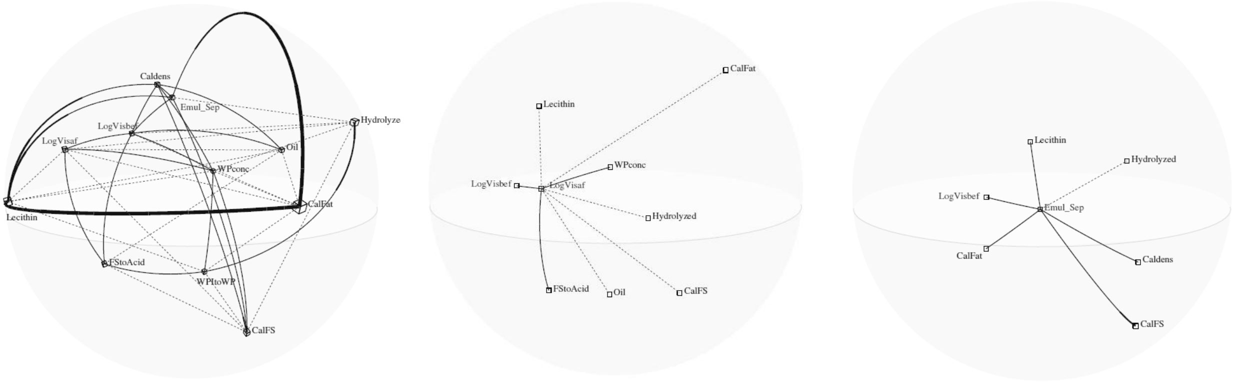
## 3.3 Model and response surface of logarithm of viscosity from IC

CORICO proposed the model for logarithm of viscosity (ModelLogVis) with 9 terms, which comprised a constant and other 8 factors that showed logical interactions. The model is shown in Equation 4 with $R^2_{adj} = 0.99$.

$$\begin{aligned}\text{ModelLogVis} = {} & 3.766 + 1.796\ \text{Caldens-CalFat} - 1.015 \\ & \text{Hydrolyzed*Hydrolyzed} - 0.4357 \\ & \text{WPconc]CalFS} + 0.4818\ \text{CalFS*WPItoWP} + \\ & 0.4038\ \text{Hydrolyzed\{-Hydrolyzed} + \\ & 0.1003\text{Caldens\^{}FStoAcid} + 0.1308\text{Caldens\}-} \\ & \text{Oil} + 0.3515\text{Caldens\^{}Hydrolyzed} \qquad (4)\end{aligned}$$

From regression analysis, the experimental values and the predicted values had a strong correlation with an R value of 0.998, slope of 0.996 and Y-intercept of 0.0143. It could be concluded that the predicted value agrees well with that observed from the experimental.

According to Equation 4, the response mostly depended on the "Caldens-CalFat" term. This term is defined as Caldens "minus" CalFat, which means that Logvis value was high when the difference between Caldens and CalFat was high. This also means that the viscosity increased when the caloric density was provided by other ingredients than fat or that the viscosity was low when the caloric density was mostly contributed by fat. Moreover, the term "Hydrolyzed*Hydrolyzed" also affected this response. This term is described as the square of the percentage of hydrolyzed whey protein with respect to the total amount of protein. The negative coefficient means that change in the percentage of hydrolyzed protein resulted in a decreasing log value of viscosity in the downward concave manner.




(a) (b) (c)

Figure 1. CORICO spheres show positive correlation with solid lines and negative correlation with dotted lines for (a) full sphere with all links, (b) significant link ($p < 0.01$) with log viscosity (LogVisbef), and (c) significant link ($p < 0.01$) with percentage of emulsion separation (Emul_Sep).

Table 3. Pearson correlation coefficient of significant links, p< 0.01, from correlation analysis.

| Variable 1 | Variable 2 | Pearson correlation coefficient ($p < 0.01$) |
|---|---|---|
| LogVisbef | Caldens | 0.64 |
| LogVisbef | FStoAcid | 0.25 |
| LogVisbef | Emul_Sep | 0.25 |
| LogVisbef | WPconc | 0.21 |
| LogVisbef | Oil | 0.16 |
| LogVisbef | CalFat | -0.69 |
| LogVisbef | Hydrolyzed | -0.47 |
| Emul_Sep | Lecithin | 0.36 |
| Emul_Sep | LogVisbef | 0.25 |
| Emul_Sep | CalFat | 0.25 |
| Emul_Sep | Caldens | 0.17 |
| Emul_Sep | CalFS | 0.17 |
| Emul_Sep | Hydrolyzed | -0.28 |

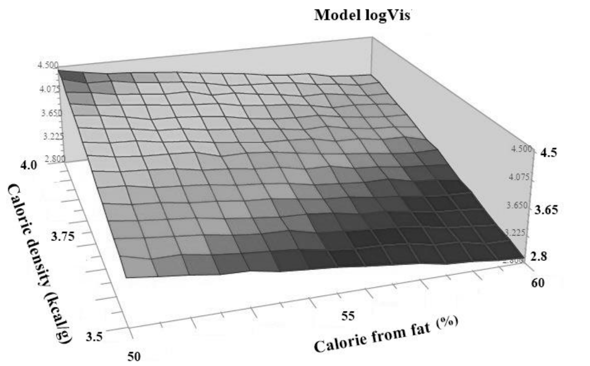



Figure 2. 3D response surface for logarithm of viscosity (Model logVis) with caloric density (kcal/g) and calorie from fat (%).

To develop a response surface, the most important interaction with the highest absolute value of coefficient was selected (Jouquand *et al.*, 2015). In this study, logarithm of viscosity values (Model logVis) was plotted with calorie from fat and caloric density as illustrated in Figure 2. Figure 2 shows that the response relied on both the caloric density of the enteral nutrition and the calorie from fat as explained earlier by Equation 4. Furthermore, viscosity decreased with decreasing caloric density and increasing calorie from fat as discussed in Section 3.2.

## 3.4 Model and response surface of percentage of emulsion separation from IC

IC suggested the model for the percentage of emulsion separation with 7 factors which are displayed in Equation 5 with $R^2_{adj} = 0.93$.

$$\text{Emul\_Sep} = 0.8106 - 3.681\ \text{FStoAcid\#-CalFat} + 2.128\text{Caldens\&-WPconc} - 1.803\text{CalFS\&-CalFS} + 0.9670\ \text{Lecithin}\{\text{CalFat} - 0.8741\ \text{WPconc}\{-\text{Oil} + 0.8154\ \text{FStoAcidCaldens}\} \quad (5)$$

The experimental value and the predicted value had a strong correlation, but a bit weaker than that for the logarithm of viscosity with an R value of 0.978, slope of 0.957 and Y-intercept of 0.0346. However, this still shows the consistency between the predicted values and the experimental observations.

From Equation 5, "FStoAcid#-CalFat" had a stronger effect on the percentage of emulsion separation but with a negative coefficient. This term is defined as FStoAcid "as not" CalFat, which means that the emulsion separation was high when the solid in high fructose syrup to acid ratio did not vary the same way as the calorie from fat. In the other word, the response was high when either the solid in high fructose syrup to acid ratio was high while the calorie from fat was low or vice versa. However, the response inversely depended on this interaction. Therefore, the value was transposed between high and low. In addition, the term "Caldens&-WPconc" also impacted the percentage of emulsion separation. This term is described as Caldens "and not" WPconc, which indicates that the response was high only when the caloric density was high, and the concentration of whey protein was low.

The percentage of emulsion separation (Model Emulsion separation) was plotted against the solid in high fructose syrup to acid ratio and the calorie from fat. The resulted response surface is shown in Figure 3. Figure 3 shows the relationship between the percentage of emulsion separation, the solid in high fructose syrup to acid ratio, and the calorie from fat as mention earlier in Equation 5. A study on the emulsion's viscoelasticity (Figure 4) revealed that the emulsion separation was related to the sample's viscoelastic property. Dominating viscous behavior was found in the sample that showed high oil separation, while dominating elastic behavior at low frequencies was observed for stable, no oil separation, samples. Emulsion with viscous or fluid-like behavior allowed the oil droplet to accumulate and resulted in oil separation. On the other hand, elastic or solid-like emulsion could not flow well and obstruct coalescence that leads to emulsion's breakdown (Xiong *et al.*, 2018). Tzoumaki, Mos chakis, Kiosseoglou, and Biliaderis (2011) studied the effect of chitin-stabilized oil-in-water emulsion with various added chemical compounds. It was noted that the emulsion with a lower stability had more viscous characteristic. Tadros (2015) collected the data on the relationship between emulsion stability and viscoelasticity of the system. It was indicated that the emulsion with lower volume fraction or a lower stability tended to have more viscous behavior. Xiong *et al.* (2018) conducted a study on the emulsion with ovalbumin/chitosan complex. They reported that the emulsion with fluid-like pattern had lower stability.

Lecithin could be another reason that impacted the stability of the emulsion as the correlation analysis pointed out a slight positive correlation between emulsion separation and lecithin concentration (Table 3). Adding too much lecithin into emulsion system can cause rapid coalescence that, in turn, yields an emulsion breakdown (Muhamad, Quin, & Selva kumaran, 2016). McCrae (1999) studied the efficiency of lecithin in stabilizing different kinds of milk products. They found that increasing lecithin in whole milk samples reduced their stability. Dammak and José do Amaral Sobral (2018) investigated the effect of lecithin addition on the stability of pickering emulsion for hesperidin encapsulation. They indicated that the increasing lecithin concentration in a low range can increase emulsion stability. However, adding too much lecithin could make the system unstable.

## 3.5 Optimal formulas and validation

By setting the targeted response range for each response as detailed in Section 2.5, the optimal conditions for each kind of oil were suggested as shown in Table 4. These formulas would yield the enteral nutrition that has the viscosity in the 3.2-3.3 log value range, or around 1585 to 1995 cP, with low oil separation. Both conditions did not have a high caloric density and low calorie from fat that resulted in too high viscosity. In addition, both formulas had high fructose syrup to acid ratio and calorie from fat in the range that gave low emulsion separation. It is noteworthy that the predicted formulas would yield an enteral nutrition that contains more than 3.5 kcal/g caloric density, which is much higher than the formulas patented by Maldonado, Smith, and Nguyen (2008) and Fuente, Keim, and Pestana (2016) which contain 1.4 to 2.1 and 0.8 to 1.5 kcal/ml, respectively.

IC proposed the value of responses at each optimal condition as shown in Table 5. IC calculated the viscosity value of the optimal formula obtained for rice bran oil in a close proximity with the experimental data, which were 2.90

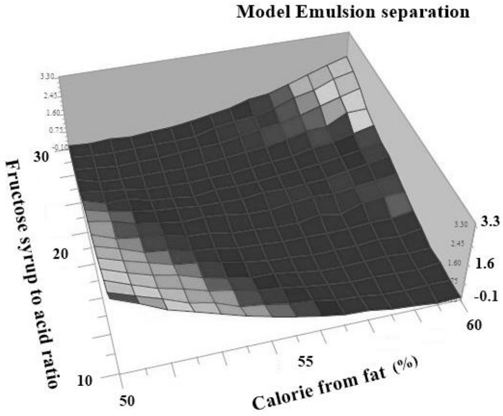



Figure 3. 3D response surface for the percentage of emulsion separation (Model Emulsion separation) versus solid in high fructose syrup to acid ratio and calorie from fat (%).

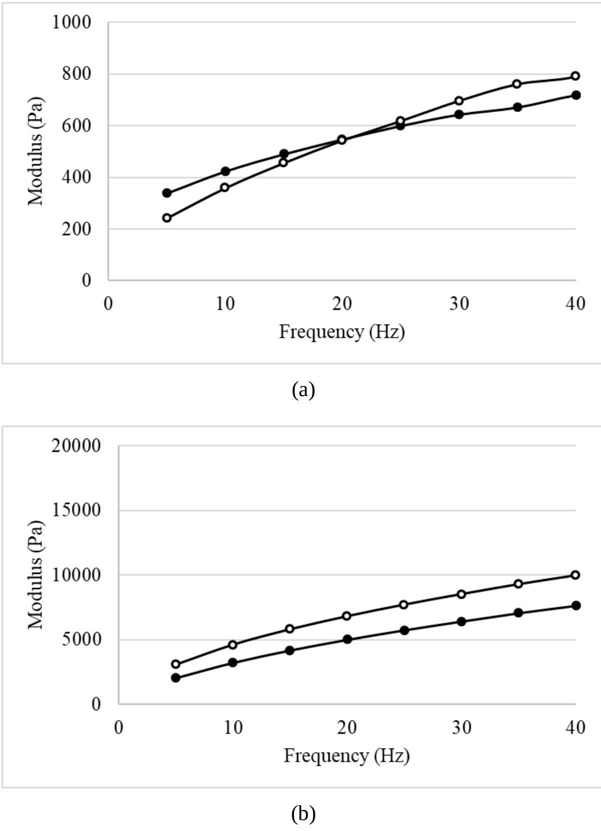



Figure 4. Storage modulus (G′) in black circle (●) and loss modulus (G″) in white circle (O) of samples (a) with unnoticeable separation (trial 2), and (b) with 3.57% separation (trial 8).

and 3.33 in log value range, or around 794 to 2140 cP, for the formula with coconut oil and rice bran oil, respectively. The predicted viscosity value of the optimal formula with coconut oil showed higher difference from the experimental data. On the other hand, values for percentage of emulsion separation were not much different since they were all unnoticeable; thus, they were noted as less than 1 or "not detected".

Table 4. Optimal formulas calculated from IC.

| Factor* | Formula 1 | Formula 2 |
|---|---|---|
| Oil | Coconut oil | Rice bran oil |
| Lecithin (%w/w) | 0.82 | 0.77 |
| Caldens (kcal/g) | 3.89 | 3.58 |
| FstoAcid | 12.88 | 29.10 |
| Hydrolyzed (%) | 17.09 | 20.15 |
| CalFat (%) | 59.51 | 53.17 |
| CalFS (%) | 14.46 | 11.80 |
| WPconc (%w/w) | 5.74 | 5.31 |
| WPItoWP (%) | 83.05 | 63.81 |

*See Table 1 for the meaning of the acronyms.

Table 5. Predicted value using IC method compared with experimental data, n =3, of each response for formula for each oil.

| Response | Predicted value | Experimental data (n = 3) |
|---|---|---|
| Formula with coconut oil | | |
| Log value of viscosity in centipoise | 3.23 | 2.90 ± 0.01 |
| Percentage of emulsion separation | 0.15 | Not detected |
| Formula with rice bran oil | | |
| Log value of viscosity in centipoise | 3.30 | 3.33 ± 0.00 |
| Percentage of emulsion separation | 0.01 | Not detected |

## 4. Conclusions

This study showed that the iconographic correlation (IC) method using CORICO software was applicable for optimization with nine factors. The method offers a more economical but efficient way for optimization that involves many factors. The models proposed by IC gave a good correlation between the experimental data and the predicted value. The result also showed that viscosity mainly depended on caloric density and calorie from fat. Further, emulsion separation was mostly affected by fructose syrup to acid ratio and calorie from fat. The optimal conditions were proposed and validated.

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