

REVIEW RESEARCH

**OPTIMIZATION OF DIFFERENT CHEMICAL PROCESSES USING
RESPONSE SURFACE METHODOLOGY - A REVIEW**

*Hiba Zaid¹

Zainab T. Al-Sharify^{2,3}

*Hamzah, M.H^{4,5}

Salih Rushdi⁶

- 1) Chemical Engineering Department, College of Engineering, University of Al-Qadisiyah, Diwaniya, Iraq.
- 2) Department of Environmental Engineering, College of Engineering, Mustansiriyah University, Baghdad, Iraq
- 3) School of Chemical Engineering, University of Birmingham, Edgbaston B15 2TT, Birmingham, United Kingdom
- 4) Department of Biological and Agricultural Engineering, Faculty of Engineering, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia.
- 5) Smart Farming Technology Research Centre, Faculty of Engineering, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia.
- 6) Chemical Engineering Department, College of Engineering, University of Al-Qadisiyah, Diwaniya, Iraq.

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Abstract: Several chemical and biological processes have been investigated and predicted using Response Surface Methodology (RSM) models. Response Surface Methodology is a useful instrument for designing laboratory-scale experiments that optimize and support the research outcomes with statistical analysis. It is a powerful statistical technique for complex variable study systems. The standard optimization (one component at a time) strategy is well-studied. However, it has significant drawbacks, such as requiring more experimental runs and time and failing to reveal the synergistic impact of processing parameters. It is a valuable instrument for process improvement. Recent research has shown, for instance, that RSM successfully optimizes biodiesel in fats and oils generated from diverse feedstocks. According to this study, Response Surface Methodology is the best cost-effective technique for maximizing environmentally friendly and sustainable methods applied to different experimental procedures. The current review reported RSM's application, theory, methodology, advantage, and limitations for different processes using different oil sources.

Keywords: Response surface methodology; optimization; extraction; microwave; olive oil; palm oil.

1. Introduction

Cost reduction and improved system and process performance are of paramount importance.

*Corresponding Author: eng.chem.20.post.10@qu.edu.iq

Optimization is employed where one parameter changes the typical procedure of acquiring optimum operating conditions. The approach requires focusing on a single factor at a time [1-4].

The primary shortcoming of the optimization method is that it ignores variable interaction effects and hence fails to portray all of the parameters' impacts on the process. Optimization research based on response surface techniques (RSM) might help tackle this challenge [5-9].

RSM combines statistical and mathematical methods to improve processes. For example, RSM may build or improve products. It studies the impact of factors alone or in combination on processes. This approach assesses independent variables to simulate chemical or biological processes [5, 10-13]. It was developed by Box and Wilson (1951) to quantify the impact of operating factors as well as their effects on response factors [14]. RSM develops, optimizes, and improves processes using statistical and

mathematical methods [15]. Some examples of these processes include the extraction of oil from fruits [16], evening primrose meal [17], anthocyanins from black currants [18], sunflower hull [19], vitamin E from wheat germ [20], and palm oil extraction [13]. RSM is used in the creation, formulation, and enhancement of products. Also, RSM is used in chemical and biological processes and wastewater treatment applications. Therefore, it is crucial to examine RSM applications for many chemical engineering processes, such as optimizations of the extraction of olive oil from olive wastes toward a sustainable approach it describes how different influences impact processes and produces a mathematical chemical or biological model [11, 21].

RSM was used to investigate the kinetics of alcohol dehydrogenase [22]. It is commonly used in modern chemical and biological processes. However, some studies have disregarded RSM's limitations [23-25].

Sinha et al. [26] used a response surface technique to improve biodiesel production. The transesterification of peanut and rapeseed oils was explored. It has high oil content, great fatty acid composition, low agricultural input costs, a predictable seed maturity rate, and a defined growing season.

The technique uses potassium hydroxide (KOH) and sodium hydroxide (NaOH) as catalysts. RSM improved the parameters of the transesterification reaction. Their models matched the experimental data well, demonstrating the effectiveness of this optimization method. The variation in response to three process factors was described using RSM models [27-30].

Hence, it is necessary to find the optimum chemical engineering process design from the above, and it needs further studies. This work

aims to review the use of RSM and highlight this methodology's applications in the chemical engineering field [31, 32].

2. RSM applications

RSM is increasingly used for optimization studies [5, 10-18], for example, the epoxidation of rapeseed oil [33] and castor oil and vegetable oil derivatives such as sucrose soyate and methyl esters derived from castor oil, jatropha oil, and waste cooking oil, was optimized using RSM, a statistical method used in chemical and biochemical engineering. This method cuts down on the time it takes to figure out the best process parameters for optimizing epoxy output [34]. In addition, RSM has been used to find the optimum conditions for oil extraction, biodiesel fuel, renewable energy, and other applications [33-37].

Valdivia et al. [38] employed the Response Surface Methodology to examine the impacts of talc during olive paste malaxation, water addition throughout the same stage, and short-term olive paste storage. 0-2 percent talc, 0-20 percent water, 0 to 36 hours storage. Using mathematical models and statistical analysis, they examined olive oil output and quality (ANOVA). Oil productions, peroxide index, K270, acidity, and chlorophyll models are crucial with 95% confidence. Adding talc affects oil quality, yet all olive oil produced is extra virgin under EU guidelines.

Many applications, particularly olive oil, demand the usage of optimal processes for creating consistently higher yields. Delil et al. [39] investigated the effects of malaxation on olive oil production and the phenolic transition. According to the models, regular malaxation conditions should be monitored for oil production and quality.

Rising energy demand from industrialization and population growth generated interest in renewable energy. Several authors used RSM to research renewable energy situations. Naveenkumar and Baskar [40] studied ultrasonic-assisted oil extraction from castor seeds in 2022 and optimized various parameters for maximum oil extraction.

3. Advantages and Limitations of RSM

RSM provides various benefits over one-variable-at-a-time experimental or optimization approaches. First, it provides plenty of information from a few trials, where the classical approaches need numerous experiments to describe a system's behavior. Second, in RSM, the interaction impact of independent factors on the response may be seen [41-43]. Third, to enhance process actions, the RSM can be a beneficial statistical approach for pinpointing diverse influences on a variable yield and dissecting and visualizing a process composed of at least one reaction to a selection of process parameters [40].

Especially in chemical, biochemical, and biomedical processes, the interaction impact of the factors, including synergism, antagonism, and addition, would be more critical. These impacts may be clarified using the model equation, which considers binary combinations of the independent factors [43].

RSM is a valuable technique for optimizing chemical and biological processes in several respects. After decades of fast development, CFD has shown to be a reliable and efficient modeling tool for design and analysis. Visualization of important parameters such as velocity, temperature, and pressure provides even more exact information than practical measuring methods [44].

The central composite or the Box-Behnken experimental design was used in conjunction with the response surface approach. The experimental results show that all the circumstances tested are relevant for the epoxidation process in the applicable ranges. [34]

4. Theory

RSM is a series of mathematical approaches for discovering correlations independent of the studied system's reaction. It outlines how independent factors, individually or collectively, affect processes. The experimental technique examines independent variables and gives a mathematical model, whereas the RSM refers to the graphical model [45, 46]. The equation that describes the connection between the output and the input is written as follows:

$$\eta = f(x_1, x_2, \dots, x_n) + \varepsilon \quad (1)$$

Where:

η = the answer,

f = unknown response function,

x_1, x_2, \dots, x_n = independent variables,

n = the total number of independent variables.

ε = the statistical error that shows other reasons for variability. It has a zero-mean, one-variance normal distribution.

RSM allows for three phases of optimization. The first step is to define independent criteria and levels. The second step is to design an experiment and anticipate and validate model equations. Finally, they created the response surface and contour plots as a function of independent factors and determined the optimal placements. The stage specs are shown below [47-49].

4.1. Identifying the Different Factors and Their Significance Levels

Parameters influence chemical and biological processes. Because determining the effects of all characteristics is complex, the most important ones must be selected. Independent parameters are discovered via screening tests. There are factorial designs used. Improvement paths and parameter values are chosen after choosing critical parameters. These levels determine the success of the optimization procedure. Failure occurs when levels are not optimized [44, 50].

The independent variables have different unit systems. Despite the fact that several parameters share the similar units, not all of them will be examined throughout the same range. The regression analysis should not be conducted because the parameters in the experimental domain have different units and/or ranges. Instead, before doing a regression analysis, the parameters must be normalized. Since each coded variable must range from -1 to 1, the units of the parameters are useless and have no bearing on how the solution is determined [51, 52]. The following is a commonly used coding equation:

$$X = \frac{x - (x_{max} - x_{min})/2}{(x_{max} - x_{min})/2} \quad (2)$$

Several variables are involved in this equation. The natural variable x is one of them, as is the coded one.

4.2. Prediction and Verification of Model Equations and Experimental Design Choices

Myers [15] specifies ten critical factors when designing a response surface. Some computer programs provide the finest designs depending on the demands and preferences of the user. Each of these designs has different experimental choices and a certain number of runs designs [43, 53].

Previous research has underlined the need to apply RSM methodologies to establish the

optimum process with fewer experimental runs as feasible. The RSM allows for monitoring process variables and studying their combined influence on the final product [43]. When the design is chosen, the model equation is defined, and the model equation coefficients are predicted. The RSM model is just a simplified form of a quadratic equation [54-56]. The second-order model is expressed in this manner.

$$y = \beta_0 + \sum_{j=1}^k \beta_j X_j + \sum_{j=1}^k \beta_{jj} X_j^2 + \sum_{i < j} \beta_{ij} X_i X_j \quad (3)$$

Where

X_i, X_j = coded independent variables, and

$\beta_0, \beta_i, \beta_{ii},$ and β_{ij} = coefficients of regression for linear, quadratic, intercept, and interaction coefficients, respectively.

The model's matrix representation is defined in Eq. (4).

$$y = X\beta + \varepsilon$$

$$\begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix} = \begin{bmatrix} 1 & x_{11} & x_{12} & \dots & x_{1k} \\ 1 & x_{21} & x_{22} & \dots & x_{2k} \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 1 & x_{n1} & x_{n2} & \dots & x_{nk} \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \\ \vdots \\ \beta_n \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix} \quad (4)$$

5. Previous Studies

Various RSM studies published in recent years were covered in this section. RSM applications were separated into two groups. RSM optimizes *Bacillus mojavensis* alkaline protease production [57]. First, R.S.M. was performed to study the influence of independent parameters on protease production in shaking flask cultures. Optimal parameters were then employed in a bioreactor. Five independent variables make up a face-centre design. R^2 is 0.9473 after fitting a second-order polynomial to the experimental data. AAD was 29.7%. Casaminos, inoculum age, and agitation have positive coordinates, whereas two have negative values (glucose and incubation time).

Lower incubation time increases protease synthesis, according to the incubation time influence on the response. Unfortunately, biochemical processes are not feasible. This will be done for the first time in the current work; the incubation period influences reaction in the tested range. In the second half of the research, in bioreactors, incubation time had a favorable influence on protease synthesis between the sixth and 12th hour and after 12 h. In the experimental design, casamino acid doses were 2–8 mg/ml. However, 8 and 12 mg/ml were employed in model validation. Using 12 mg/ml to validate the equation may not be accurate since they got the descriptive equation from low substrate concentrations. (This concentration's reaction requires extrapolation.) At this concentration, a high yield does not always mean that the conditions are ideal for protease production [58, 59].

Senanayake [60] incorporated Dubai Health Authority (DHA) into borage oil using RSM and lipase. Enzyme amount, reaction temperature, and reaction duration affected DHA incorporation yield. Their study helps determine independent components. Early researchers studied the effect of independent qualities on the reaction by changing one aspect at a time. Experimental findings are unaffected by enzyme amount or reaction temperature. In the projected model equation's 3D response surface plot and 2D contour plot, they see the negative effects of these independent variables on response. The projected model equation is not useful for process optimization since it forecasts erroneous data at high enzyme and temperature levels. Also, the data were logarithmically transformed before fitting to the second-order polynomial equation in the experimental design section of the research. However, they saw no change in the model equation prediction.

Ong et al. [12] utilized RSM to examine the ideal circumstances for Soxhlet extraction using n-hexane as the solvent to extract palm oil from oil palm decanter cake. Obtaining the optimal ratio between two factors—reaction time and solid-to-solvent ratio—would enable them to extract the most oil possible. The reaction time of 4.92 hours and the solid-to-solvent ratio of 1:10 produced the best results. An R^2 value of 0.78 for the proposed model shows that the experimental parameters significantly influenced the result. The oil yield for oil palm Decanter cake (OPDC) without microwave pre-treatment was examined using the optimized data.

In contrast to the 3.1070085 grams of palm oil produced by the OPDC without microwave pre-treatment, the OPDC with pre-treatment generated 3.2890.047 g of palm oil. Research using Fourier Transform Infrared Spectroscopy (FTIR) revealed that the presence of fatty acids in the palm oil produced from both samples was indicated by the abundance of two significant functional groups, C-H alkene stretch and C=O stretch. According to scanning electron microscopy (SEM) of decanter cake. According to this research, RSM aids in the optimization of agricultural processing parameters [12, 61].

Ghadge and Raheman [42] used RSM and multiple regression analysis to yield a quadratic polynomial equation for acid value. Verification experiments validated the projected model's correctness. They discovered that 0.32 v/v methanol-to-oil ratio, 1.24 percent v/v H_2SO_4 catalyst, and 1.26 h reaction duration at 60 C were the best combinations for decreasing the acid level of mahua oil to less than 1% following pre-treatment. The fuel characteristics of mahua biodiesel generated met American and European biodiesel standards.

Liu et al. [53] extracted pomegranate seed oil using supercritical CO_2 . They used RSM to

examine the influence of process variables on pomegranate seed oil yield. Their work improved extraction parameters using a central composite design experiment. Supercritical CO₂ pomegranate seed oil was compared to Soxhlet-extracted oil for tocopherol and fatty acid content. The extraction yielded 14 percent more tocopherols than Soxhlet.

Lo et al. [41] employed RSM to optimize Burkholder sp. HL-10 lipase output. Olive oil, tryptone, and Tween-80 significantly affected lipase output. Using a faced-centered central composite design, they established the optimal concentrations of these three components (FCCCD).

Mohammed et al. [44] improved *Jatropha curcas* oil alkaline transesterification. The high cost of edible vegetable oil is a major impediment to biodiesel production. Non-edible oils, such as *Jatropha curcas* oil, are required for biodiesel manufacturing. They ran 20 experiments to see how catalyst concentration (0.25-0.75g), methanol-to-oil ratio (3:1 to 9:1), and reaction duration affected the results (60 - 120 min). A regression model was developed after a statistical analysis of variables and interactions. They achieved 98.80 percent yield using a 6:1 methanol to oil ratio, 0.75g catalyst, and a 90-minute reaction period. The measured value closely fits the model equation simulation. The methanol-to-oil ratio had a greater impact on biodiesel yield than catalyst concentration and reaction duration. Biodiesel compares well to the ASTM standard.

Govedarica et al. [34] modeled and improved the epoxidation of linseed oil using peracetic acid generated in situ from acetic acid and hydrogen peroxide in a heterogeneous catalyst. The temperature was between 65 to 85°C, and the ratio of hydrogen peroxide to oil unsaturation molar ratio (1.1:1 to 1.5:1), catalyst amount (10–

20 wt%), and reaction length (5–13hr) affected epoxy production. The regression model's R² was 98.95% based on the analysis of variance. Using the model, the optimal process conditions were 70.6% oC, a 1.5:1 hydrogen peroxide-to-oil unsaturation molar ratio, 20% by weight catalyst, and a 7-h reaction time. Under these conditions, the epoxy yield was 84.73 0.07 percent, close to the projected 87.60 percent. As a consequence, under usually safe circumstances, isothermally produced epoxidized linseed oil with high epoxy oxygen concentration (8.27, 0.01%) and low iodine number (4.22 0.42 g iodine/100 g oil).

Miladi et al. [43] used n-hexane, a non-polar solvent, to increase specific gravity (SCG) oil extraction. To determine the best extraction L/S ratio, extraction temperature, and solvent contact length, a statistical factorial design was followed by a Central Composite Rotatable Design. They reported that no other study had investigated all three operational factors simultaneously, confirming the study's originality [43]. Delil et al. [39] reported that RSM optimization helps yield quality metrics for extracting olive oil from olive fruit oils. The results show that the optimum condition was 35°C/45 min, 33°C/44 min, and 35°C/24 min for spotted, purple, and black phases.

6. Conclusions and Further Work

Various chemical and biological processes have been analyzed and forecasted using Response Surface Methodology models. Response Surface Methodology is an excellent tool for planning laboratory-scale studies and statistical analysis to back up the results. It is a valuable statistical approach for complicated variable systems used in research. It benefits from requiring a smaller number of experimental runs to acquire sufficient data for statistically acceptable findings. It is a useful tool for improving processes. For example, RSM has recently been shown to

effectively optimize biodiesel in fats and oils derived from various feedstocks. Although the transesterification process is uncomplicated, it is nevertheless important to optimize the processing parameters in order to produce biodiesel at its highest possible yield. The application of RSM for optimizing the creation of biodiesel from different oils was covered in the current review. According to this research, the most cost-effective strategy for optimizing environmentally friendly and sustainable methodologies applied to various experimental procedures is RSM.

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Conflict of interest

The authors confirm that there is no conflict of interest.

Author Contribution Statement

All authors contributed in writing and editing this manuscript. Author Z.T. proposed the research problem and supervised the findings of this work. Authors H. Z, M.H and S. R. A.B.: developed the introduction and the manuscript pattern. All authors discussed the results and contributed to the final manuscript.

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