Research article

Black-box modelling, bi-objective optimization and ASPEN batch simulation of phenolic compound extraction from *Nauclea latifolia* root

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A R T I C L E   I N F O

A B S T R A C T

Nauclea latifolia root (NLR) extract is one of phytochemicals used to treat various ailments in most of developing countries. This investigation focuses on modelling, optimization and computer-aided simulation of phenolic solid-liquid extraction from NLR. The extraction experiments were conducted at extraction temperature (ET: 33.79–76.21 °C), process time (PT: 2.79–4.21 h) and solid-liquid ratio (SLC: 0.007929–0.018355 g/ml). Regression models (RM) were developed, using Response Surface Methodology (RSM) in Design Expert software, for predicting and optimizing total phenolic content (TPC) and total flavonoid content (TFC) and also compared with adaptive neuro-fuzzy inference system (ANFIS) modelling in Matlab environment. Aspen Batch Process Developer (ABPD) V10 was used to simulate phenolic extract production and perform material balance of the process. Both Coefficients of determination (R^2) of RSM (TFC: 0.9996, TPC: 0.9932) and ANFIS models (TFC: 0.99998, TPC: 0.9982) were compared and predicted satisfactorily. Optimization results show: ET (2.79 h), PT (38.8 °C), SLC (0.0198 g/ml), TFC (25.92 25.92 μg RE/g) and TPC (8.47 mg GAE/g). The phenolic extraction base case simulation results gave batch throughput, annual throughput, number of batches per year 0.0089 g/batch, 0.139 g/year and 1019 batches, respectively. The ABPD predicted TPC and experimental TPC results were compared and gave mean relative deviation error of 3.75%. Thus, ABPD simulation model is reasonably reliable for the scale-up design engineering of the phenolic extract production from NLR.

1. Introduction

Most of extracts from the plant material are good sources of phenolic compounds and utilized for healing pathological problems (Alcântara et al., 2019; Garcia-Oliveira et al., 2020; García-Cruz et al., 2017). Consumption of plant materials such as fruits and vegetables contribute to the prevention of many ailments owing to the presence of some phenolics in the plant materials (Septembre-Malaterre et al., 2018). Bioactive compounds present in the plant materials consist of different phenolic compounds and hydroxyl groups. Most of the compounds are soluble (flavonoids, quinones, phenylpropanoids) and insoluble (lignins, condensed tannins and hydroxyl cinnamic acid) which are embedded in cell-wall of the plant materials (Jahromi, 2019).

Nauclea latifolia (NL) is a small tree with average height of 10ft and found in tropical Africa and Asia. It is popularly grown in south-southern,

south-western and north-central part of Nigeria. NL is therapeutically applied in traditional medicine for the treatment of malaria, hypertension, diarrhoea, tuberculosis, dysentery and also as a laxative (Odeniyi et al., 2020; Osamudiamen et al., 2018; Boucherle et al., 2016). Phytochemical analysis identifies indole-quinolizidine, alkaloids (glyco-alkaloids) and saponins as the major components (Ajayi et al., 2020). The extract from solid-liquid extraction of NL root, using water as solvent, showed a high anti-parasitic potential. The aqueous extract also showed effectiveness against chloroquine resistance strains of plasmodium falciparum as well as exhibiting strong antibacterial property (Ogbole et al., 2018). Owing to high consumption of *N. latifolia* root herb and commercialization prospect of the product in most of developing countries; it is necessary investigate phenolic solid-liquid extraction of NLR. The phenolic compounds from plant materials are obtained via leaching or dissolution of plant matrix in extraction solvent.

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Various methods of phenolic compounds extraction from plants include: conventional technique, ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE) and Supercritical fluid extraction (SFE). Conventional extraction method has traditionally been often used to extract the bioactive polyphenolic compounds from the *N. latifolia* root. The extraction technique is based on solid-liquid separation process which is one of the simplest and cheapest methods of the extraction. This method uses various solvents under various polarities, temperature and pH conditions in the extraction of various combinations of phenolic compounds from plants (Vega et al., 2017; Chen et al., 2018). The technique is also utilized for preparing household herbal mixture in most of developing countries due to simple extraction procedures and as a result, various phenolic compounds could be extracted by organic solvents with different polarities (Mumivand et al., 2017). (Oreopoulou et al., 2019) reported that convectional extraction technique has widely been used for optimizing extraction conditions of the laboratory and industrial scale implementations of several aromatic and herbal plant materials.

Modelling of chemical processes is fundamental to process system engineering; owing to its significant roles in process engineering design, optimization and operation. Process modelling has conventionally been achieved via black-box and physics modelling techniques. Solutions of mechanistic modelling, which are based on process physics, are often accurate but characterized with complexity and convergence problems. However, black-box modelling techniques such as soft-computing models namely, artificial neural network (ANN), adaptive neuro-fuzzy inference system (ANFIS), genetic algorithm (GA), support vector machine (SVM) and response surface methodology (RSM), map input variables with process responses without the prior knowledge of the process physics. Previous researchers analysed and predicted phenolic extract production from various plant materials through ANFIS modelling technique (Tao et al., 2017; Kumar and Sharma, 2017; Baskararaj et al., 2019; Kunjiappan et al., 2020). Fuzzy inference system and neural network are integrated as robust ANFIS modelling technique that is capable of analysing complex and vague chemical process system.

RSM is an effective statistical technique and also a critical tool that is used for modelling and analysing the effects of multiple parameters on the process (Derrien et al., 2017). It estimates the complex interaction among the process variables and also used for optimizing chemical process design. Optimizing existing or new facilities in chemical process industry improves performance of process system; it provides optimum parameters values that maximize or minimize the productivity of the process. Optimization of process variables are of great interest in process scale-up and process design engineering. Various studies have been conducted in order to develop optimum envelopes for solid-liquid extraction (Al-Dhabi et al., 2017; Rajha et al., 2014; Nayak and Rastogi, 2013). Process optimization objectives differ and at the same time contrasting in some engineering endeavours; however, process parameters are adjusted in order to achieve target objective functions. Therefore, bi-objective optimization technique is applied to proffer solution to the problem having two contrasting objectives.

This work involves modelling and optimization of total phenolic content (TPC) and total flavonoid content (TFC) from *N. latifolia* root. Previous studies emphasised on application and biological activities of the root extract (Taïwe et al., 2011; Okechukwu et al., 2015; Ekong and Nnalu, 2016; Nwadiogbu et al., 2017); however, scaling-up NL root extract production to commercial production remains the gab to be filled. Product and process scale up need fundamental engineering studies such as computer process engineering simulation and conceptual process design in order to maximize experimentation and production costs. Previous studies used various computer aided commercial simulators such as Aspen Plus, Aspen Hysis, Chemcad and SuperPro Designer for modelling, simulation and conceptual design of various chemical and bio-processes (Parjikolaei et al., 2017; Gebremariam, and Marchetti, 2018; Suharmanto et al., 2020).

This study intends to fill the research lacuna by using Aspen Batch Process Developer (ABPD) for simulating TPC production from *N. latifolia* root. ABPD is a commercial simulator based on the recipe procedure for mass and energy balance as well as equipment capacity sizing (Orozco-Mena et al., 2014). The lab-scale optimum data and information obtained from the experiment were used to develop base case simulation model for TPC production in ABPD environment. Thus, this work is aimed at developing optimum conditions and computer aided simulation of phenolic extract production from *N. latifolia* root. The results of the present simulation are bridging the knowledge gap and also serve as a precursor for techno-economic analysis for the feasibility of phenolic extract production plant in most of developing countries.

2. Materials and methods

2.1. Chemicals and reagents

Analytical grade of the following chemicals: Gallic acid, Folin-Ciocalteu and anhydrous sodium carbonate, Rutin reagent, Aluminium chloride and methanol were procured from the agent of Sigma Aldrich and GFS Chemicals, Inc. Distilled water was processed and obtained from Analytical Laboratory unit of MOUAU, Nigeria.

2.2. Material preparation and Nauclea latifolia root extraction

Nauclea latifolia roots (NLR) were bought from botanical shop in Ogbomosho, Nigeria. The roots were thoroughly examined in order to ascertain their freshness and were subsequently dried. The dried herbs were ground and converted into powder form (0.2mm) and then stored in air-tight container. Hybrid design (HD) of response surface methodology (RSM) was used to design randomized experiments for the optimum process conditions that maximize TFC and TPC extraction from NLR. Extraction time (X_1), extraction temperature (X_2) and (X_3) solid-liquid concentration were the three input independent variables; while total flavonoid content (Y1: TFC) and total phenolic content (Y2: TPC) were considered as dependent parameters for the design. The minimum and maximum RSM design values are indicated in Table 1a. The solid-liquid extraction was carried out by taking certain amount of *Nauclea latifolia* root herb into a conical flask 250-ml. Distilled water was added to the root herb based, in order to obtain solid-liquid concentration, on the experimental design in Table 1b. Then, the mixture was kept in water bath, mechanically shaken and maintained for different periods of extraction time (2.79–4.21 h) and temperature (40–76.2 °C) according to experimental design matrix shown in Table 1b. Then, Whatman No. 1 filter paper was used to filter the mixture and the filtrate was concentrated via rotary evaporator at 40 °C.

2.3. Determination of total phenolics content (TPC)

The TPC was determined using Soto et al. (2014) method: this method involves the formation of Folin – Ciocalteu reagent and Na_2CO_3. 1ml of the NLR extract was dispensed into a clean test tube and 1ml of Folin – Ciocalteu reagent as well as 2 ml of 20% Na_2CO_3 were added. The mixture was centrifuged for 20 min at 4000 rpm, the supernatant was collected by decanting and its absorbance was taken at 765 nm. The standard curve was generated by preparing a stock solution using gallic acid: 1 g of pure gallic acid was weighed accurately, dissolved and made up in 1000 ml volumetric flask to obtain 1000 mg/L solution which was used as stock solution. The standard curve was generated using gallic acid as standard in water (10–50 mg/L). TPC was measured and expressed in mg gallic Acid equivalent (GAE) per g of dry extract.

2.4. Determination of total flavonoid content (TFC)

The flavonoids of the sample were determined by aluminium chloride method using rutin as standard. This method was based on formation of

Table 1. Response Surface Methodology experimental design for phenolics extraction from *Nauclea latifolia* root.

Factor	Name	Unit	Minimum	Maximum
X1	Extraction time	Minutes	2.79	4.21
X2	Extraction temp	(^{0}C)	33.79	76.21
X3	Solid-liquid ratio	g/ml	0.00793	0.0221
Y1	Total Flavonoid Content	μg RE/g dry solid	3	25.93
Y2	Total Phenolic Content	mgGAE/g dry solid	3.5	8.47

flavonoid – aluminium complex (Tlili et al., 2013). 1 ml of the sample filtrate, 3 ml of methanol, 0.2 ml of 10% of aluminium chloride and 0.2ml of 1 M potassium acetate were introduced into a test tube. Rutin was used as standard as obtainable in Kumar and Sharma (2017), measured at 430 nm absorbance and the extract was expressed in μg rutin equivalents (RE) per g of dry extract.

2.5. Extraction modelling and optimization

NLR extraction data were modelled using polynomial regression equation as shown in Eq. (1). The extraction data were fitted into the equation in order to determine the relationship between independent and dependent experimental variables.

$$Z = \alpha_o + \sum_{i=1}^{3} \alpha_i Y_i + \sum_{i=1}^{3} \alpha_{ii} Y_i^2 + \sum \sum_{i<j\leq 1}^{3} \alpha_{ij} Y_i Y_j \tag{1}$$

where Z is the experimental output, α_o, α_i, α_{ii}, and α_{ij} are the constant parameter, linear, polynomial and interactive coefficients of the model, respectively, and; Y_i and Y_j are different independent variables. The variable $Y_i Y_j$ is the first order interaction between Y_i and Y_j for (i < j). The reliability and dependability of the regression equation is measured by coefficient of determination (R^2) and the Fisher test value (F-value) as obtained from the analysis of variance (ANOVA). Statistical importance of the model and independent variables was estimated at the confidence level of 95.0%. Numerical desirability search method was used for the optimization of extraction variables for bi-objective optimization of TFC and TPC extract from NLR. Desired goal (minimize, maximize, range and target) for each variable was selected in numerical optimization environment of RSM. The two response parameters: TPC and TFC were maximized, while extraction time and temperature were minimized and concentration was fixed for the range of experimental design in this study. The objective functions are fused together into an overall function $D(x)$, called desirability function in order to search for the extraction optimum region. The value of desirability function for *n* responses can be defined as:

$$D(x) = (d_1 \times d_2 \times d_3 \ldots\ldots\ldots\ldots\ldots\ldots d_n)^{1/n} \tag{2}$$

An ideal desirability function value is one; while non-desirable desirability function represents zero.

2.6. Neuro-fuzzy structure development

A hybrid learning-reasoning system of intelligent neural network and fuzzy inference reasoning system was developed to predict the complex and vague behaviour of NLR phenolic solid-liquid extraction system. Takagi-Sugeno Fuzzy System Type (TSFST) was used, in this study, to represent the architecture that models the input and output extraction variables in this study. TSFST with two input and one output used five different layers within its architecture for training and testing experimental data as shown in Figure 1. The two inputs and their output are c, d and v respectively. The architecture consists of adaptive nodes represented by square node while fixed nodes symbolised as circle nodes as depicted in figure. The adaptive modes are to be learned and modified; however, fixed nodes are fixed parameters. The rule set of two fuzzy if-then rules is expressed in Eqs. (3) and (4):

Rule 1: If c is A_1 and d isB_1, then

$$f_1 = p_1 c + q_1 c + r_1 \tag{3}$$

Rule 2: If c is A_2 and d isB_2, then

$$f_2 = p_2 c + q_2 c + r_2 \tag{4}$$

where A and B are logical range of values of linguistic terms. Eqs. (5), (6), (7), (8), and (9) are the sequential equations representing five layers in the ANFIS structure:

Layer 1: Square node function in layer 1 is represented in Eq. (5)

$$O_i^L = \mu_{Ai}(c) \tag{5}$$

Input variables c and d are assumed to be fed into input nodes. The input variables are linguistically transformed to input membership
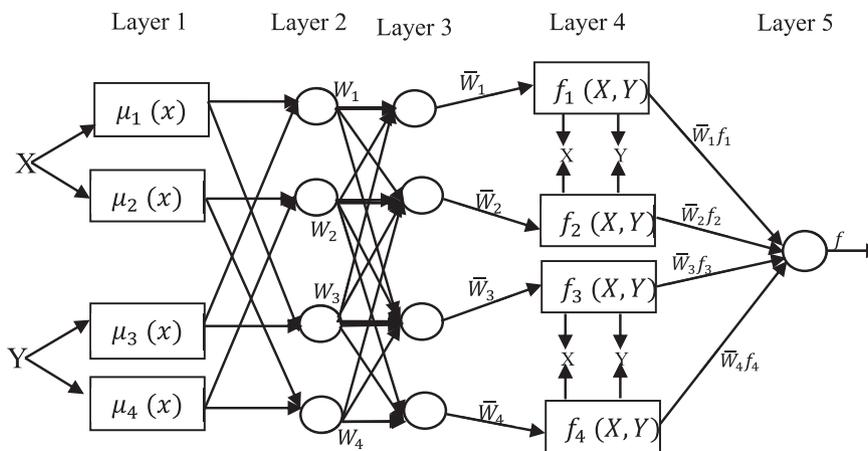
Figure 1. ANFIS architecture representation.
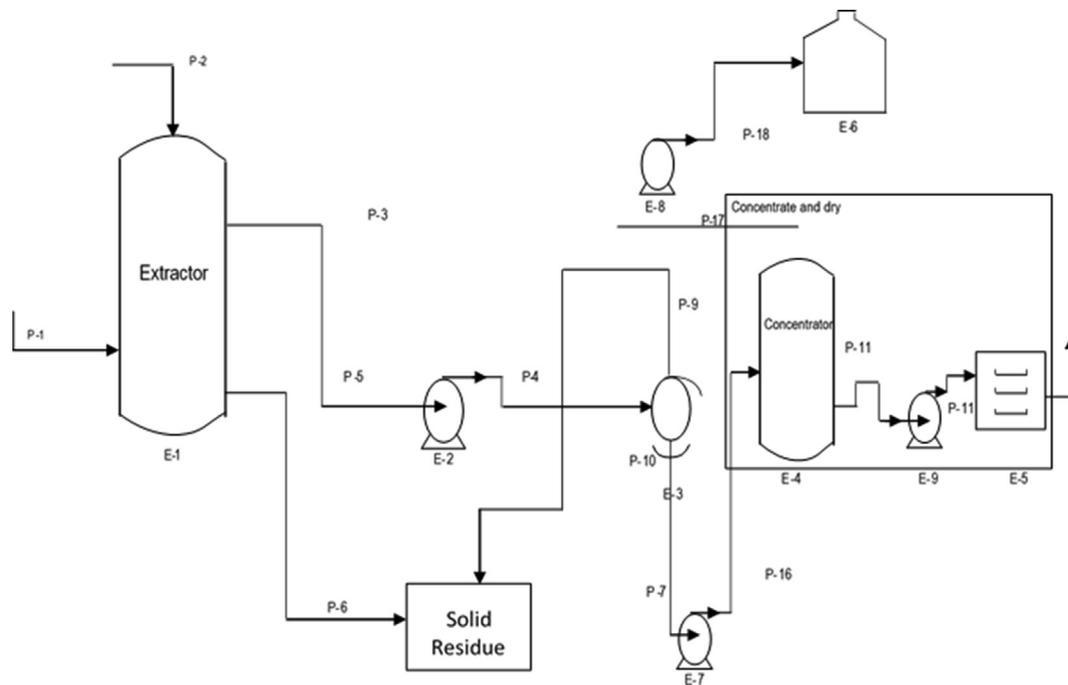
Figure 2. ABPD Flow sheet for Phenolic Extract from NLR.

functions (mfs). Where, O_i^L is the mf of A_i and c is the input parameter to the node.

Layer 2: the node in layer 2 intensifies the bound signal and triggered the product out of the layer:

$$w_i = \mu_{Ai}(x) \times \mu_{Ai}(y), \; i = 1, 2 \tag{6}$$

Layer 3: Circle node. The node relates the i-th rule's firing strength to the sum of all rules' firing strengths and estimates their ratio:

$$w_i' = \frac{w_i}{w_1 + w_2} \; , \; i = 1, \; 2 \tag{7}$$

Layer 4: Square node with node function:

$$O_i^4 = w_i' f_i = w_i'(p_i x + q_i y + r_i) \tag{8}$$

p, q, r – parameter set (consequent, linear parameters).

Layer 5: Circle node. This node shows the overall output of all the incoming signals.

$$O_i^5 = overall \, output = \sum_i w_i' f = \frac{\sum_i w_i f_i}{\sum_i w_i} \tag{9}$$

2.6.1. ANFIS performance assessment

In this study, ANFIS modelling for forecasting TFC and TPC of NLR extract was assessed by RMSE (root mean square error), and the R^2 value (coefficient of determination) as shown below:

$$R^2 = 1 - \frac{\sum_{p=1}^{p}(d_p - O_p)^2}{\sum_{p=1}^{p}(O_p)^2} \tag{10}$$

$$RMSE = \sqrt{\frac{1}{P}\sum_{p=1}^{p}(d_p - O_p)^2} \tag{11}$$

d_p and O_p are the measured and predicted dependent parameters respectively. The RMSE value near zero and the R^2 values close one shows the adequacy of the models (Oke et al., 2014).

2.7. Computer aided simulation

2.7.1. Simulation environment description

Batch lab phenolics *N. latifolia* root extract production was simulated via Aspen Batch Process Developer (ABPD) V10™. ABPD has been explicitly designed for the simulation of pharmaceutical, biotech and agricultural chemical processes and other complex recipe-based batch processes (Orozco-Mena et al., 2014). Raw NLR total extractible (28%), total fibre content (69.99%), moisture content (1.48%) and total extractible TPC (0.53%) from the root values, as obtained experimentally, were firstly declared in user-defined pure and predefined mixture component interface of ABPD. This was done due to the absence of NLR compositions in ABPD data base. However, water, nitrogen and oxygen components are default parameters in pure component interface of the software. Material and energy balance, equipment sizing as well as process scheduling were performed in ABPD environment. ABPD in-built extract model, filter and concentrate shortcut models were used to model the unit operations owing to the availability of required lab data. Modelling a chemical process in ABPD primarily includes identifying the unit procedures and operations that create the step as well as specifying the process parameters for the operations. Then, simulation is run once the environment has been set up and a recipe has been entered for the step. In this study, the operation method was set to be batch mode, in order to simulate lab-scale experiment, with 312 days/year.

2.7.2. Process description

Lab scale optimum conditions were used for base case simulation in this section and the process flow diagram was shown in ABPD environment in conjunction with Visio software as depicted in Figure 2. The extractor (E-1) was charged with 1.9 g of pulverized NLR with 100 ml of water making the biomass to water ratio be 0.019 g/ml based on optimum condition specifications. The solid-liquid mixture was maintained 60 °C for 2.79 h. It was assumed that 95% of the root biomass dissolved during the heating process. For the extract to settle, the content in E-1 was cooled for 10 min. The batch in unit E-1 was filtered in a filter (E-3), the transfer time of the slurry is 5 min. Then, the mother liquor was sent to the concentrator (E-4) in the drying section. The solid residue in the

Table 2. Experimental design for TFC and TPC extract from *Nauclea latifolia* root.

Run	Time (h)	Temperature (C)	Solid ratio (g/ml)	TFC(μg RE/g dry solid)	TPC (mgGAE/g dry solid)
1	3.5	55a	0.015	3	3.5
2	4.21	55	0.01147	22.87	5.77
3	3.5	76.21	0.01147	25.93	8.47
4	3.5	33.79	0.01147	17.13	6.03
5	3.5	55	0.02207	4.77	7.95
6	3	70	0.01854	16.77	6.815
7	4	40	0.01854	17.02	7.965
8	4	70	0.01854	19.59	5.7
9	3	40	0.01854	16.99	6.59
10	2.79	55	0.01147	3.17	5.23
11	3.5	55	0.00793	3.1	6.42

Table 3. Regression coefficient and ANOVA of TFC and TPC.

Factor	TFC(μg RE/g dry solid)	TPC (mgGAE/g dry solid)
Intercept	337.9	1358.11
Linear		
A	-163.3**	-3.211****
B	-65.52*	-36.74****
C	731.07****	2997.95**
Quadratic		
A^2	9.978**	1.27****
B^2	18.48***	3.03**
C^2	398.84****	1658.6**
Interaction		
AB	1.4****	-1.24****
AC	-187.48**	-3.76**
BC	-75.71*	-41.1***
ANOVA		
F value (model)	289.33	116.28
p value (model)	0.042	0.019
R^2	0.9996	0.9932
Adjusted R^2	0.9961	0.932
Press	32447.6	15789.04
CV (%)	3.87	5.76

A = Extraction time, B = Extraction temperature and C = solid-liquid ratio.
*Significant at $p < 0.1$, **Significant at $p < 0.05$, ***Significant at $p < 0.01$, ****$p > 0.1$.

filter is transfer to a solid residue tank where it can be used as livestock feed. The outlet of the filtration section is concentrated in E-4 and dried. The drying operating time is 1 h. The overhead of the evaporator is sent to a recovery tank (E-6).

3. Result and discussion

3.1. Total flavonoid content (TFC)

The total flavonoids content of extract obtained from NLR extraction ranged from 3.0 to 25.93 μg RE/g as indicated in Table 2. The highest TFC is obtained at temperature of 76.21 °C for 3.5 h with solid-liquid concentration ratio of approximately 0.0114 g/ml as revealed in Table 2. The temperature of 55 °C for 3.5 h with the concentration ratio of approximately 0.015 g/ml gave the lowest TFC (3.0 μg RE/g) as also shown in Table 2. The TFC results from this study is similar to TFC extract values from *Colocasia esculenta* in previous work of Kumar and Sharma (2017). The regression analysis of the experimental design gave a second order polynomial model in Eq. (12) for TFC. The reduced quadratic model developed portrays the interaction between the dependent TFC

and the coded values of the independent variables A, B, and C (extraction time, temperature and solid-liquid ratio respectively).

$$\text{TFC} = 3.00 + 5.43A + 3.37B + 0.25C + 9.61A^2 + 19.61B^2 + 0.90C^2 + 1.40AB - 8.87AC - 5.09BC \tag{12}$$

Regression coefficients for each linear, quadratic and interactive variable of polynomial quadratic models for TFC and TPC with the corresponding R^2, adjusted R^2, PRESS and coefficient of variation (CV) are presented in Table 3. The fitness of the TFC model was expressed by the coefficient of determination (R^2) of 0.9996 and the adjusted R^2 of 0.9961 (Table 3). This shows that the R^2 and adjusted R^2 of the model are close to obtained R^2 in Agbede et al. (2020) and Oke et al. (2018). Analysis of variance (ANOVA) in Table 3 revealed that TFC regression model was significant and the model lack of fit is highly non-significant. Therefore, the ANOVA result showed that the model adequately predicted TFC. It was also noticed from Table 3 that extraction time ($p < 0.05$), combined extraction time and solid-liquid ratio ($p < 0.0382$), quadratic extraction time-time ($p < 0.033$) and temperature-temperature ($p < 0.018$) statistically affected TFC extraction from NLR. But linear solid-liquid ratio term, interactive extraction time-temperature and quadratic solid-liquid
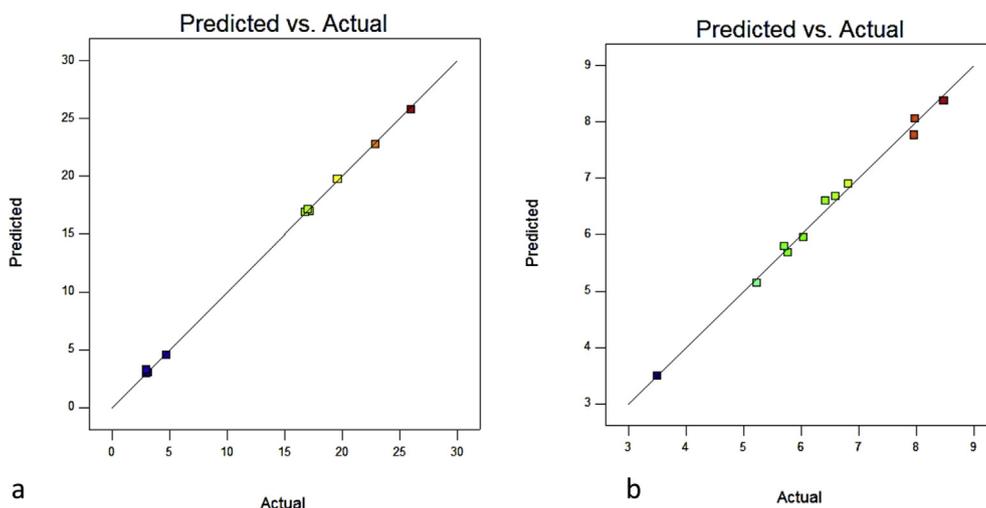
Figure 3. Response Surface Methodology Predicted and Experimental plots a: (TFC(μg RE/g dry solid) b: TPC (mgGAE/g dry solid).

ratio terms are not significantly contributing to TFC extraction from NLR as shown in Table 3.

3.2. Total phenolics content (TPC)

The highest TPC extract (8.47 mg GAE/g solid) from NLR was archived at temperature 76.21 °C, solid-liquid concentration ratio of 0.01147 mg/ml and extraction time 3.5 h, as shown in Table 2. It was noticed that the lowest TPC yield was obtained at process conditions of temperature 55 °C, ratio of 0.015 mg/ml and extraction time 3.5 h, as depicted in Table 2 respectively. The TPC results obtained from this study is comparable to previous works (Ghafar et al., 2017; Kakouri et al., 2019). TPC experimental data were fitted into regression model in RSM and the model correlation parameters for TPC and independent variables are R^2 (0.9932), adjusted R^2 (0.932) and CV (5.76%) as shown in Table 2.

The lack of fit of TPC model is not significant with p and F values 0.019, as well as 116.28, respectively. The multiple regression model that showed the relationship between the dependent variable (TPC) and independent variables (extraction time, temperature and solid-liquid ratio) is represented by Eq. (13):

$$TPC = 31.48 + 1.39A + 1.64B + 0.16C - 21.62A^2 - 17.38B^2 - 26.52C^2 - 3.26AB + 0.24AC - 6.17BC \tag{13}$$

ANOVA results revealed that solid-liquid ratio (p < 0.04), quadratic extraction temperature (0.043) and solid liquid ratio (p < 0.02) terms with interactive extraction time and the ratio (p < 0.028) term influenced the extraction rate of TPC from NLR as shown in Table 3. Figure 3 depicts plot of predicted versus experimental data of TFC and TPC extract from NLR. It is evident from the graph that the data were much closed to the

Table 4. TFC ANFIS model results at different input and output mfs.

Input membership function	RMSE (linear)	R^2 (linear)	RMSE (constant)	R^2 (constant)
Gauss	0.0005	0.9987	0.005	0.879
Gauss2	0.0005	0.9992	0.00499	0.886
Gbell	0.0005	0.9992	0.00497	0.9137
Tri	5.75	0.0443	N/A	N/A
psig	0.0005	0.9983	0.00499	0.899
Pi	N/A	N/A	0.005	0.879
Dsig	0.0005	0.9988	0.00499	0.898
Psig	0.0036	0.991	0.0035	0.991

N/A: Not Available.

Table 5. TPC ANFIS model simulation at different input and output mfs.

Input membership function	RMSE (linear)	R^2 (linear)	RMSE (constant)	R^2 (constant)
Gauss	0.01	0.992	0.11	0.99
Gauss2	0.003	0.99982	0.1	0.994
Gbell	0.01	0.991	0.11	0.99
Tri	N/A	N/A	N/A	N/A
Trap	N/A	N/A	N/A	N/A
Pi	0.01	0.99	0.009	0.991
Dsig	0.01	0.99	0.009	0.992
Psig	0.01	0.992	0.01	0.991

N/A: Not Available.
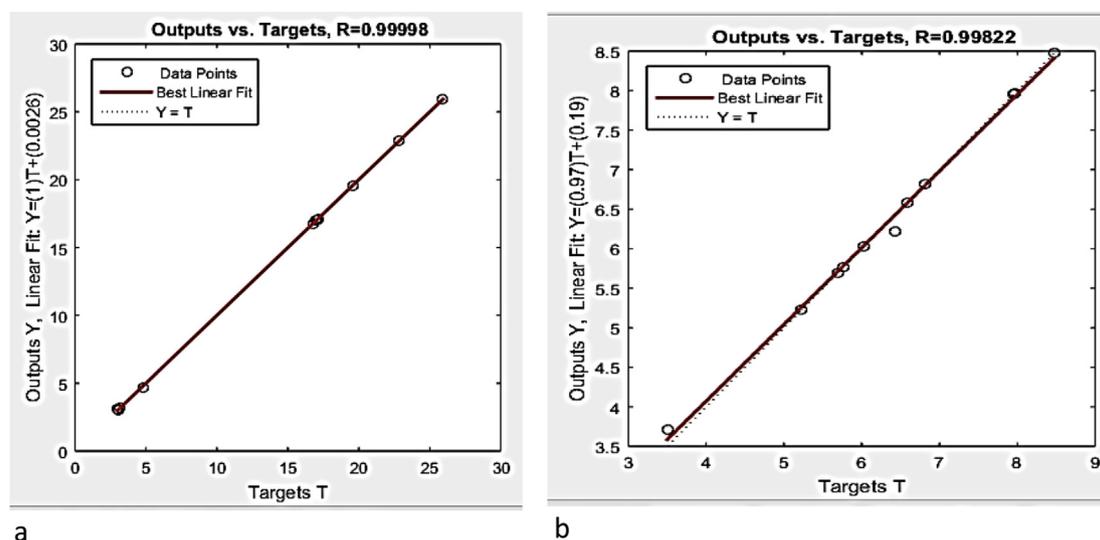
Figure 4. ANFIS Predicted and Experimental plots a: (TFC(μg RE/g dry solid) b: TPC (mgGAE/g dry solid).

straight line as shown in Figures 3a and b. The plotting further revealed correlation of RSM predicted results with experiment data.

3.3. ANFIS modelling results

3.3.1. ANFIS architecture setting

The performance of ANFIS model depends on the input membership function (mf), output mf and number of input mf as well as epoch number (Amir et al., 2016; Oke et al., 2019). Several ANFIS structures were developed in this study at different input mf and output mf. The preliminary investigations (not shown) on the best epoch number and number of input mf were conducted. Therefore, epoch number 50 and three (3) input mf were used for the ANFIS simulation in this study. Different input mfs were also used in order to determine the best input mf for the prediction of TFC and TPC extract from NLR. Table 4 presents results of TFC ANFIS architectures at varying membership functions. For linear output mf, RMSE ranges from 0.0035 to 0.0037 and the corresponding R^2 also ranges from 0.991 to 0.99998 as indicated in Table 4. However, tri and trap membership functions could not model TFC data and consequently gave non-available (N/A) results as also shown in Table 4. This occurrence might be as a result of the fact that the two mfs could not fit and linguistically interpret the TFC data. For constant output mf, the RMSE of the ANFIS ranges from 0.0035 to 0.0057 with corresponding R^2 values from 0.991 to 0.998 as shown in Table 4. It was noticed that all RMSEs are near zero and R^2 are near one for all input and output mfs in Table 4. These values are comparable with previous study result on ANFIS prediction (Amir et al., 2016). Oke et al. (2018) claimed that the closer the R^2 to one (1) and the closer the RMSE to zero, the better the performance of the model. Gaussian input and linear output mf have the highest R^2 and lowest RMSE as shown in Table 4. Therefore, these parameters were used to develop ANFIS structure for the prediction of TFC extract from NLR.

Table 5 shows the results of different ANFIS structures at different input and output (linear and constant) mf. ANFIS model with input mf gauss 2 and linear membership function gave the best prediction of TPC extract from NLR with R^2 0.99982 and RMSE 0.003. The lowest R^2 (0.99) with the highest RMSE (0.01) of TPC model were obtained via pi and dsig input mf as well as linear output mf. The statistical performance parameters (R^2 and RMSE) obtained for the best TPC extract prediction are similar and consistent with previous researches on soft-computing prediction of TPC by Kunjiappan et al. (2020) and Ekici et al. (2014).

Figure 4 a and b show the correlation between predicted and measured data of TFC and TPC. These figures corroborate the degree of predictability of TFC ($R^2 = 0.9998$) and TPC ($R^2 = 0.9982$) extract from NLR.

3.3.2. ANFIS results compared with RSM

The degree of predictability of RSM and ANFIS models for TFC and TPC are compared in this study. Both models predicted well based on the coefficients of determination obtained from Tables 3, 4 and 5 respectively: RSM (TFC: 0.9996, TPC: 0.9932) and ANFIS (TFC: 0.99998, TPC: 0.9982). However, ANFIS models R^2 values are slightly higher than RSM models. Nevertheless, both ANFIS and RSM results (coefficients of determination) were comparable with existing works on ANFIS and RSM models (Mostafaei et al., 2016; Betiku et al., 2016).

Figures 5a-f show the degree of membership of each input, which is input 1, 2 and 3, for the forecast of the phenolic extract from NLR. Membership function revealed the degree of truthfulness of uncertain system ranging from 0 (zero) to 1 (one). The curves in Figures 5a-5f are Gaussian distribution curves representing the logic crisps of gauss and gauss2 membership functions of TFC and TPC prediction, respectively. It was noticed that the curves in the figures are similar to Gaussian membership function curve in earlier studies of ANFIS modelling and prediction (Jaypuria et al., 2020; Sihag et al., 2019). Talpur et al. (2017) also reported that Gaussian membership function is commonly used for ANFIS modelling of complex problem and it also demonstrated higher degree of accuracy as compared with its counterparts.

3.4. Optimization study results

3.4.1. Desirability function bi-objective optimization result

Desirability function algorithm of RSM was applied in order to obtain optimum operating region for simultaneous optimization of TFC and TPC. Table 6 shows the optimization criteria for phenolic maximization. For maximization of the responses, weighted coefficients 1,1,1,1 and 1 were assigned for time, temperature, solid-liquid ratio, TFC and TPC as depicted in Table 6, respectively. The extraction time and temperature were minimized in order to minimize the production cost.

Figure 6 shows optimal ramp of extraction time (2.79 h), extraction temperature (38.8 °C), solid-liquid ratio (0.0198 g/ml), TFC (25.92 µg RE/g) and TPC (8.47 mg GAE/g) with total desirability 0.957. The same optimized process conditions were experimented for the validation. It was observed that verification experiment gave 25.12 µg RE/g and 8.16 mg GAE/g for TFC and TPC, respectively. Both optimized and verification experimental results were compared and gave 3.08 % and 3.65% percentage error for TFC and TPC, respectively. Both dependent and independent variable desirability values of the optimized conditions for maximization of TFC and TPC were presented in Figure 7. It was observed that 0.999, 1, 1, 1 and 1 were desirabilities for extraction time,
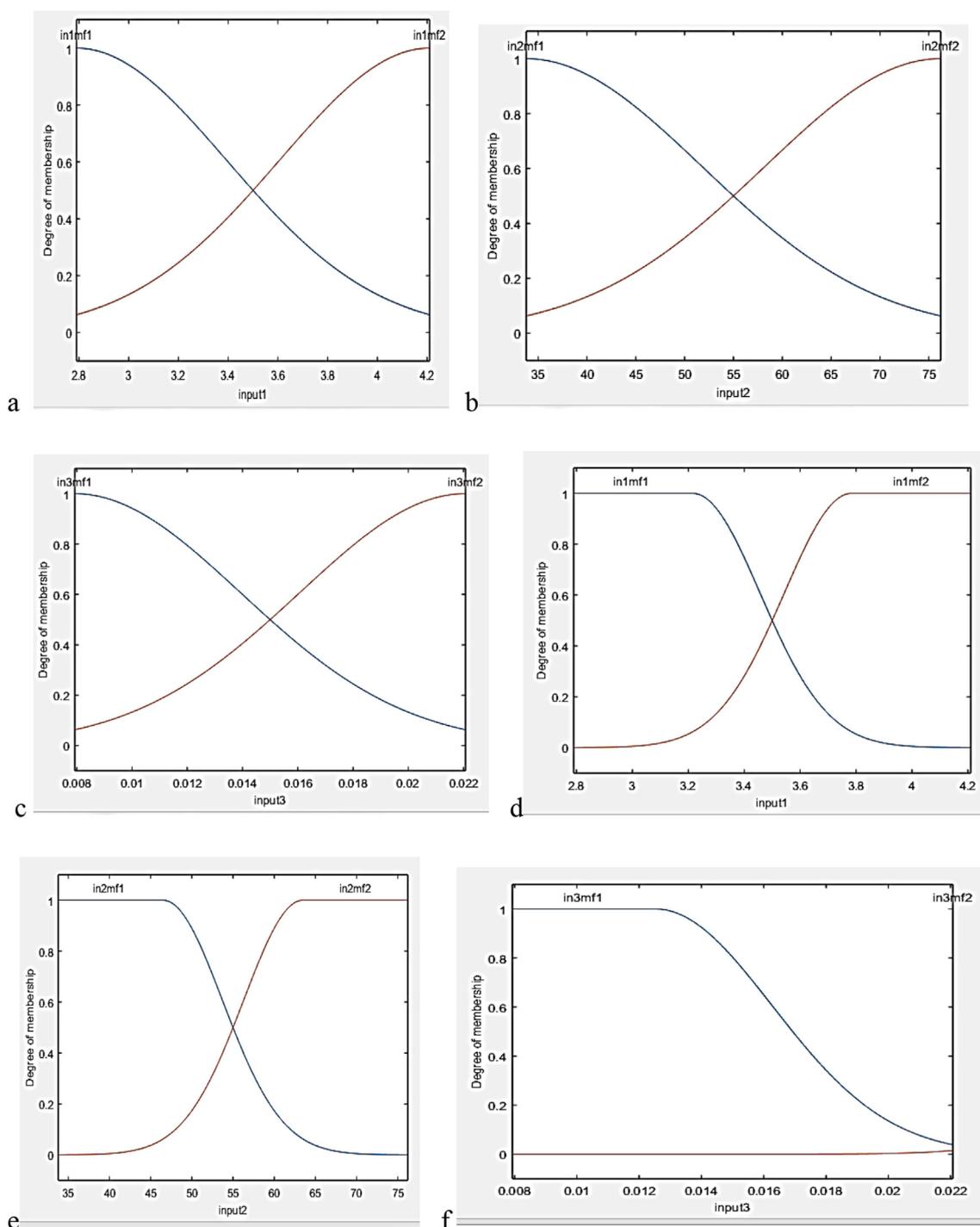
Figure 5. a–c: Neuro-fuzzy Membership Function Degree of TFC; d–f: ANFIS Membership Function Degree of TPC.

process temperature, solid-liquid ratio, TFC and TPC accordingly as revealed in Figure 6. Previous reports documented that the desirability values close to one (1) gave excellent optimality (Pandey et al., 2020). Thus, the obtained desirability values in this study are satisfactory and consistent with existing study.

3.5. ASPEN simulation results

3.5.1. Base case simulation results

Table 7 depicts the phenolic extract production throughput parameters. The base case simulation results (Table 7) shows batch throughput,

annual throughput, number of batches per year, process batch time, cycle time and production rate of 0.0089 g/batch, 0.139 g/year, 1019 batches, 559 min, 439 min and 0.0000159 g/min, respectively. It was observed that the present base case simulation scheme may not be sufficient based on the demand of NLR herbal extract, therefore, further study on scale-up simulation scheme is needed.

3.5.2. Material balance

The stream summary of phenolic NLR extract production is shown in Table 8. The flow of mass of the herbal root (raw material), distilled water, the intermediate unit operation input as well as the final output

Table 6. Desirability search optimization criteria for TFC and TPC.

	Time (h)	Temperature (^{0}C)	S/L ratio (g/ml)	TFC(μg RE/g dry solid)	TPC (mgGAE/g dry solid)
Upper limit	4.21	76.21	0.02	25.93	8.46
Lower limit	2.79	33.79	0.01	3.1	3.5
Weight	1	1	1	1	1
Importance	3	3	3	3	3
Objective/Goal	minimize	minimize	Range	Maximize	Maximize

(TPC), with the respective operating mass flow rate and temperature, are presented in Table 8. However, the last column of the Table 8 revealed the total amount of TPC (0.0088 g GAE/g) as predicted by ABPD simulation. The predicted TPC (0.0088 g GAE/g) result was compared with the experimental data (0.00847 g GAE/g) as obtained from previous section. The deviation error of 3.75% was obtained as the experimental and predicted values were compared. Oke et al. (2014) reported that MRDE with less than 10% is validating the degree of predictability of the simulation model. Therefore, ABPD simulation model for the simulating TPC is satisfactorily validated.

3.5.3. Flow rate sensitivity analysis

Figures 8 and 9 show effect of the crude herbal root and solvent flow rate on the production of TPC extract. It was noticed from Figure 8 that as the flow rate is increasingly tuned, the TPC production is increasing. This

occurrence might be as a result of the increased quantity of the root powder in the solid-liquid mixture system which in turn increased the solid-liquid ratio for the extraction. Generally, Figure 8 shows that the

Table 7. NLR Extract Production throughput parameters.

Process Parameters	Value
Annual throughput (g/year)	0.139
Batch throughput (g/batch)	0.0089
Number of batches per year	1019
Process batch time (min)	559
Minimum cycle time (min)	439
Production rate (g/min)	0.0000159
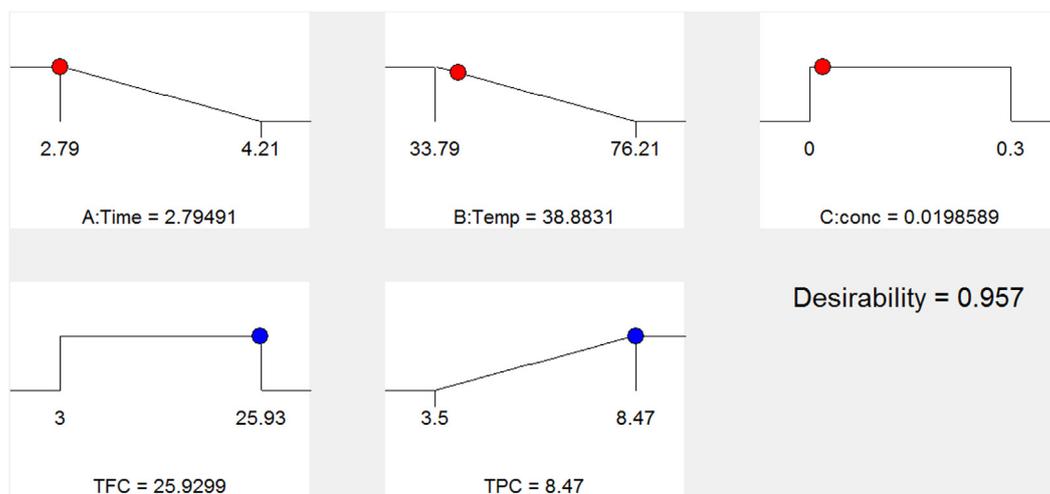
Figure 6. *Nauclea Latifolia* root phenolic extraction optimal conditions profile.
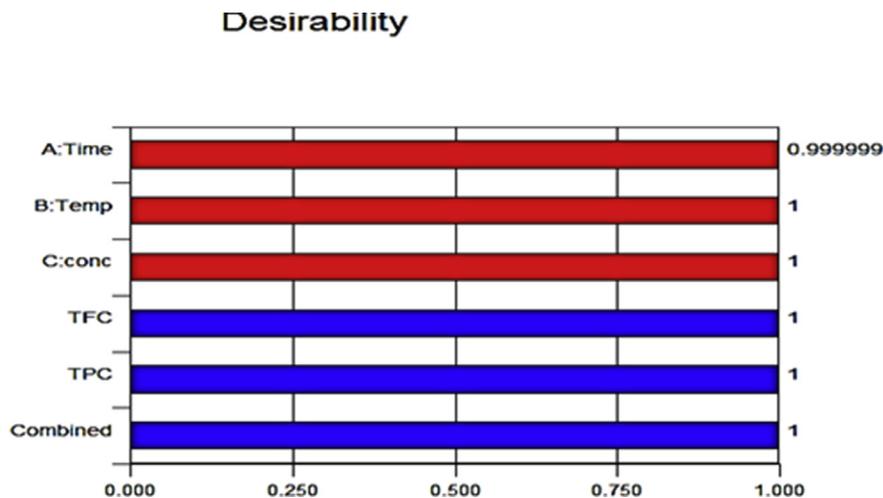
Figure 7. Desirability values for dependent and independent variables.

Table 8. Material balance for NLR phenolics extraction simulation.

From Unit	Solid storage tank	Liquid storage tank	Beaker, 250 ml	Beaker, 250 ml	Filter flask, 125ml	Evaporator flask, 100ml	Evaporator flask, 100ml
To Unit	Beaker, 250 ml	Beaker, 250 ml	Beaker, 250 ml	Filter flask, 125ml	Evaporator flask, 100ml	Evaporator flask, 100ml	Evaporator flask, 100ml
Total	2	99.3814	90.8975	10.4839	10.4828	8.944	1.5565
TPC	0.0106	0	0.0013	0.0093	0.0093		0.0088
Moisture	0.0296	0	0.0296	0	0	0	0
Water		99.3814	89.4433	9.9381	9.9378	8.944	0.9475
Nitrogen	0	0	0	0	0	0	0.0686
Oxygen	0	0	0	0	0	0	0.0208
Nauclea fibre	1.3998	0	1.383	0.0168	0.016	0	0.0152
Extractible	0.56	0	0.0403	0.5197	0.5197	0	0.4955
Mass flow rate (g/min)	0.13	6.63	18.18	2.1	2.1	0.15	0.01
Volumetric flow (l/h)	0.01	0.4	1.13	0.13	0.13	0.01	0.88
Temperature (^{0}C)	25	25	50	50	49.91	100.03	100
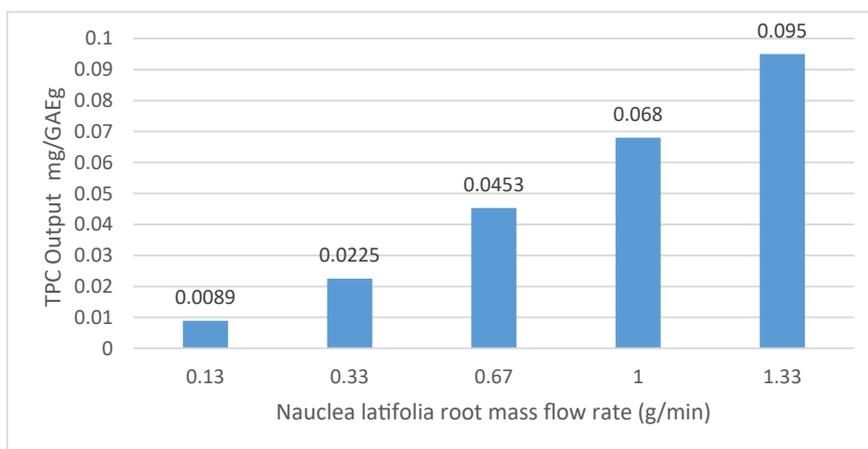
Figure 8. Effect of NLR flow rate on TPC (mgGAE/g dry solid) extract production.
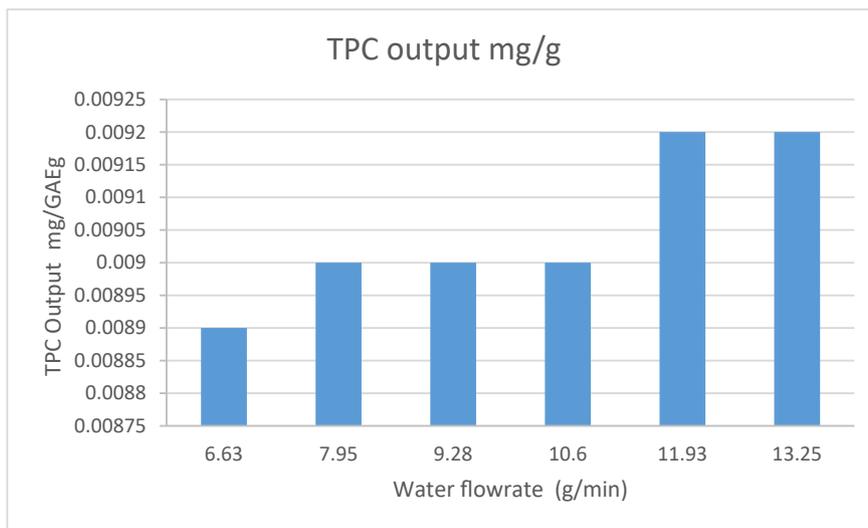
Figure 9. Effect of solvent flow rate on TPC (mgGAE/g dry solid) extract production.

linearity relationship between NLR mass flow rate and the extract production. Figure 9 revealed that increase in the solvent flow rate from 6.63 g/min to 7.95 g/min increased the extraction of TPC. Tuning of flow rate from 9.28 to 10.6 g/min does not show significant difference in TPC production as revealed in Figure 9. The behaviour of TPC production rate to the tuning of solvent flow rate is not linear as represented in Figure 8.

4. Conclusion

Experimentation, desirability function search optimization and ABPD simulation of phenolics extraction from NLR were studied in this work. The highest TFC (25.93 μg RE/g) and TPC (8.47 mg GAE/g) were obtained at temperature of 76.21 °C for 3.5 h with ratio of approximately

0.011 g/ml. The lowest TFC and TPC were extracted at temperature of 55 °C for 3.5 h with ratio of 0.015 g/ml. The TFC and TPC showed coefficients of determination (R^2) of 0.99798 and 0.962874, respectively, depicting the fitness of the model. Optimization result ramp of extraction time (2.79 h), process temperature (38.8 °C), solid-liquid ratio (0.0198 g/ml), TFC (25.92 µg RE/g) and TPC (8.47 mg GAE/g) with total desirability 0.957 were obtained from this investigation. The base case simulation of phenolics extraction from NLR shows batch throughput, annual throughput, number of batches per year, process batch time, cycle time and production rate of 0.0089 g/batch, 0.139 g/year, 1019 batches, 559 min, 439 min and 0.0000159 g/min respectively. The ABPD predicted TPC and optimum TPC results were compared and gave mean relative deviation error of 3.75%. This shows that the degree of ABPD simulation model predictability is reasonably reliable for the scale-up design engineering of TPC extract from NLR. Thus, the results obtained from this study are precursors for scale-up design and techno-economic analysis of phenolic compounds extraction from NLR.

Declarations

Author contribution statement

Oke E.O.: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Okolo B.I., Agbede O.O. & Nnaji P.C.: Contributed reagents, materials, analysis tools or data.

Adeyi O.: Analyzed and interpreted the data.

Adeyi, J. A.: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Osoh, K. A.: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Ude C. J.: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Data availability statement

The data that has been used is confidential.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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