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Artificial intelligence-based approaches for modeling the effects of spirulina growth mediums on total phenolic compounds

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ABSTRACT

Spirulina is a microalga and its phenolic compound is affected by growth mediums. In this study, Artificial intelligence (AI) based models, namely the Adaptive-Neuro Fuzzy Inference System (ANFIS) and Multilayer perceptron (MLP) models, and Step-Wise-Linear Regression (SWLR) were used to predict total phenolic compounds (TPC) of the spirulina algae. Spirulina productivity (P), extraction yield (EY), total flavonoids (TF), percent of flavonoid (%F) and percent of phenols (%P) are considered as input variables with the corresponding TPC as an output variable. From the result, TPC has a high positive correlation with the input variables with $R = 0.99999$. Also, the models showed that the ANFIS and SWLR gives superior result in the testing phase and increased its accuracy by 2% compared to MLP model in the prediction of TPC.

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1. Introduction

Spirulina (*Arthrospira platensis*), commonly known as the blue-green algae representing taxonomically the phylum *Cyanobacteria*, is a microorganism that performs the process of photosynthesis similar to other photosynthetic organisms. It is a helical filamentous, multicellular microalga with a long history as human food in the Azetic peoples of Latin America and Lake Chad communities in African (Belay, 2008). In addition to *Arthrospira platensis*, other species, namely *Arthrospira maxima* also represent the microalgae, Spirulina. At a commercial level, spirulina is considered the top cultured microalga, thereby 30% of worldwide algae biomass production comes from the genus *Arthrospira*. The global interest to this alga is increased because of the multipurpose functions and the high protein, carotenoid, phycocyanin and other bioactive compounds role in different areas (Costa et al., 2019; Paula da Silva

et al., 2021). The global Spirulina market before five years is around 700 million dollars but in the coming five years annually it will grow by 10% and at 2026 the Spirulina market will be projected to a value of around 2 billion dollars, from this the USA market holds the largest spirulina market with a market value of 570-million-dollar (Silva, 2020).

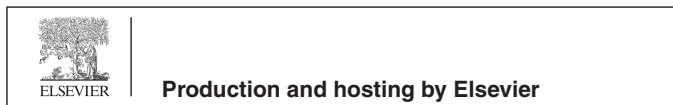
Spirulina is sourced both from the wild natural waters and manmade indoor and outdoor ponds. Spirulina considered as a super miracles food, functional food in health perspective and food additives in food industry and popular in health and aquaculture areas (Koukouraki et al., 2020; Paula da Silva et al., 2021; Soni et al., 2017). Spirulina has a valuable high amount of macro and micronutrients including high amount of protein, carbohydrate, different vitamins like beta-carotene, minerals including Iron, calcium, magnesium, essential fatty acids like gamma-linolenic fatty acids and other bioactive compounds (Carcea et al., 2015; Soni et al., 2017; Ye et al., 2018).

According to the United States Food and Drug Administration (FDA) (Lafarga et al., 2020) and the European Union (EU) (European Union, 2015; Lafarga et al., 2020), Spirulina is accepted as a novel and safe food for human consumption. In Brazil, the culture industry and human consumption of Spirulina LEB-18 can also be practicable within the framework of globally accepted biomass production under the guidelines of food safety standards (de Jesus

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et al., 2018). Spirulina is also efficient in treating wastewater including effluent water from fish farms and if integrated in aquaculture it could be beneficial and added advantage to fish farmer as additives and supplemental fish diets (Zhang et al., 2020). Supporting study report also Spirulina bioremediation function in aquaculture industry and in producing high value added biomass and in reducing production cost (Cardoso et al., 2021). Also spirulina help in making of good animal feed formulation and supplement including in broilers (Khan et al., 2020).

Additionally, some of the bio-active compounds of Spirulina are actively function as anti-inflammatory, antibacterial, and anti-cancer therapy/medicine in human health. Besides, Spirulina together with its bio-active compounds plays a vital role in human health, for treating several diseases associated with metabolic disease and other conditions (Jimenez-Lopez et al., 2021; Koukouraki et al., 2020; Lafarga et al., 2020; Pina-Pérez et al., 2017). Another supporting studies also reported that Spirulina function to human health includes antiallergic, antihypertensive, antitumor, and immunomodulatory (Anahite et al., 2018), liver protector caused by toxicants (Al-qahtani and Binobead, 2019), control virus reproduction, cure from the disease and reduces mortality (El-sheekh and Abomohra, 2020).

Phenolic compounds are bioactive secondary metabolites from Spirulina, providing a natural and sustainable source of food preservatives through combating the activity of microorganisms that are known to spoil food products. In light of this, research findings have indicated that phenolic compounds isolated from Spirulina were found to possess antimicrobial activity against various drug-resistant foodborne pathogens (Alshuniaber et al., 2021; Christ-Ribeiro et al., 2019).

Now a days, the artificial neural network (ANN) based models has been used in evaluating the process and interaction of different input and output variables on certain productions system.

Artificial Neural Network (ANN) is a discipline in the field of Artificial Intelligence and data processing technology which involves connecting neurons to one another to develop complex non-linear input-output relations. It is specifically described by networking topology, testing, or training algorithms, and activation functions and contains input and output functions (Tongal and Booi, 2018). There are different ANN models including the multi-layer perceptron (MLP), Levenberg-Marquart (LM), Conjugate gradient, Quasineutron and Brodyen-Flecher-Goldfarb-Shanno are the best and effective algorithms in every data driven systems (Nourani et al., 2021).

Therefore, in this study the effect of the spirulina growth mediums on total phenolic compounds was modeled using Artificial intelligence-based models including Adaptive - Neuro Fuzzy Inference System (ANFIS) and Multi-layer perceptron (MLP) neural network as well as the Step-Wise-Linear Regression (SWLR) models.

2. Material and methods

2.1. Proposed methodology

AI developed models was used as a methodology to accomplish this study including Adaptive - Neuro Fuzzy Inference System (ANFIS), Multi-layer perceptron (MLP) neural network and Step-Wise-Linear Regression (SWLR) were applied to predict the effect of spirulina algae growth mediums on the production of spirulina total phenolic compound (TPC). The data was adopted from the previous experimental study (Abd El-Baky et al., 2009). Spirulina maximum growth rate (μ max day⁻¹), productivity (mg L⁻¹ day⁻¹), extraction yield (%), total flavonoids (mg g⁻¹) was taken as an input variable and the amount of total phenolic compounds (TPC) (mg g⁻¹) was taken as an output variable.

2.2. Adaptive-Neuro fuzzy Inference system (ANFIS)

In artificial intelligence the Adaptive-Neuro Fuzzy Inference System (ANFIS) is taken as a universal, wide ranging and multipurpose model to estimate all kinds of problems. ANFIS is built by two important layers; that are adaptive multi-layer and feed forward networks. Feed forward networks again comprises input-output variables using fuzzy instruction of the Takagi - Sugeno type. The Fuzzier and defuzzifier are the key parts of the arrangement in the fuzzy data-base system. The fuzzy-logic comprises the change of input values into fuzzy data through a bid of membership functions. As a membership functions node work and allow in modelling of the relationship between input and outputs.

Therefore, node work as a connection function, permits the modelling of the relation between the input and outputs scheme. Connection functions are different and many, for example triangular, sigmoid, Gaussian and trapezoidal (Abba et al., 2020a). In the procedure there are two basic considerations that should be taken into account both from the input and output arrangements, firstly the two variables of the FIS 'x' and 'y' inputs data and one output 'f', a first-order Sugeno fuzzy and as a rule it follows the following formula.

$$\text{Procedure1 : if } \mu(x) \text{ is } A_1 \text{ and } \mu(y) \text{ is } B_1 \text{ then } f_1 = p_1x + q_1y + r_1 \quad (1)$$

$$\text{Procedure2 : if } \mu(x) \text{ is } A_2 \text{ and } \mu(y) \text{ is } B_2 \text{ then } f_2 = p_2x + q_2y + r_2 \quad (2)$$

where A_1, B_1, A_2, B_2 constraints are membership functions for x and y , and inputs $p_1, q_1, r_1, p_2, q_2, r_2$ are outlet function parameters. The building and design of ANFIS follows a five - layer neural network arrangement. Regarding the ANFIS preparation more details are presented by Lu et al., (LU et al., 2018).

2.3. Multilayer perceptron (MLP) neural network

The Multilayer perceptron (MLP) neural network is one of the communal illustrations of ANN, that help us to run and solve non-linear systems. Several scholars considered as a universally accepted estimator as compare with the other classes of ANNs (Choubin et al., 2016). Alike the other classical models of ANNs, the Multilayer perceptron (MLP) neural network is also built up using an input and output layers where an input layer is a hidden one (Abba, Pham, et al., 2020). Usually, the input layer nodes are linked to those of the hidden layer and then, the output layer. The program is motivated and then transmitted from the input to output layer using the help of the weight and biases by sequential mathematical processes. The Levenberg-Marquardt algorithm is commonly used as a learning algorithm to adjust and improve the error amongst the measured values and projected values. The training algorithms are iteratively repeated until the required outcomes are found. Just like the conventional ANN, MLP is also hold an input, as well as one or more hidden layers and output layers in its structure (Fig. 1) (Kim and Singh, 2014).

$$y_i = \sum_{j=1}^N w_{ji}x_j + w_{i0} \quad (3)$$

where N is the total number of nodes in the top layer of the node; w_{ji} is the weight between the nodes i and j in the upper layer; x_j defines the output derived from node j ; w_{i0} is the bias in node i , and y_i describes the input signal of node i which crosses via the transfer function.

2.4. Step-Wise-Linear regression (SWLR)

Commonly, linear regression (LR) is one of the most important methods in modeling several variables i.e., input and output vari-

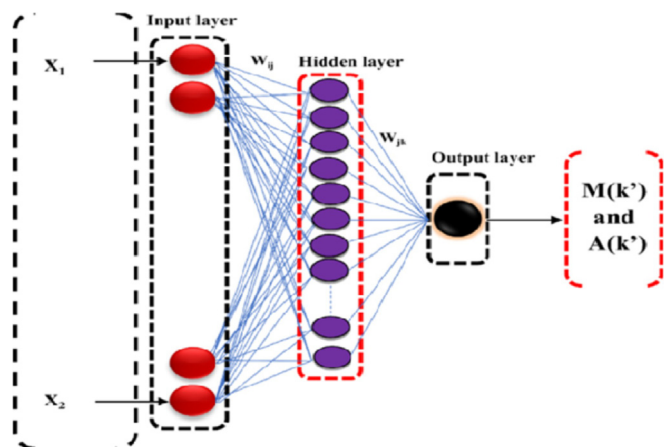


Fig. 1. Three-layer multilayer perceptron structure.

ables. Its key importance and position are shown during the correlation which exists between single and numerous variables in finding the best set of the parameters, which gives the highest prediction efficiency that is accompanying to the output variables (Yasar et al., 2012). According to Çevik, (2007) described the systematic regression as an advancing selection technique that took the best set of the input variables by deleting or adding the variables through the influence of the residual sum of the squares. Step-Wise-Linear Regression (SWLR) follows systematic modification of the variables through checking the effect of each variable on another. Every single variable that does not contribute and satisfy the base tool of the model, then that variable will be deleted step wise until its influences it's no longer present (Yasar et al., 2012). The concept of SWLR can be demonstrated through MLR (Wu et al., 2020). Systematic regression is taken during the process of input variable addition and deletion in the LR method of analysis (Hong et al., 2020).

2.5. Evaluation criteria for data - driven models

Most of the time for any type of data driven studies the performance accuracy is estimated by comparing the projected values with the measured values. In this work, the determination coefficient (DC) as a goodness of fit, correlation coefficient (CC) and two statistical error, including root mean-squared error (RMSE) and mean - squared error (MSE) were applied to estimate the models:

$$DC = 1 - \frac{\sum_{j=1}^N [(Y)_{obs,j} - (Y)_{com,j}]^2}{\sum_{j=1}^N [(Y)_{obs,j} - \bar{(Y)}_{obs,j}]^2} \tag{4}$$

$$CC = \frac{\sum_{i=1}^N (Y_{obs} - \bar{Y}_{obs})(Y_{com} - \bar{Y}_{com})}{\sqrt{\sum_{i=1}^N (Y_{obs} - \bar{Y}_{obs})^2 \sum_{i=1}^N (Y_{com} - \bar{Y}_{com})^2}} \tag{5}$$

$$RMSE = \sqrt{\frac{\sum_{i=1}^N (Y_{obs,i} - Y_{com,i})^2}{N}} \tag{6}$$

$$MSE = \frac{1}{N} \sum_{i=1}^N (Y_{obs,i} - Y_{com,i})^2 \tag{7}$$

where; N, $Y_{obs,i}$, \bar{Y} and $Y_{com,i}$ are data number, observed data, average value of the observed data and computed values, respectively.

2.6. Data set description and validation of the models

The prime objective of data driven scheme is to make the data suitable for the models for a certain value set build on the bases of the working needles, so that we can make reliable and consistent prediction of the unknown data sets. In this procedure issues such as overfitting values, reasonable working activities are not always taken into account. So, in the endorsement stage, different types of checking, cross-validation and proof were applied like k-fold cross-validation, others are holdout; leave one out, and so on. The most important rewards of the k fold proof tool are that in everyone single pointed, the verification and the working sets are self-determining. As indicated above, the data is further distributed into two groups 75% for the training and 25 % for the testing stage and also taking the k-fold cross-validation is important. Another important remark for this methodology is the validation methods that we applied to the data set (Abba et al., 2020b), in which the data set composed of 27 occurrences for every of the variables.

3. Results

Data-based approaches (ANFIS, MLP and SWLR) were applied to model total phenolic compounds based on the result of the different spirulina growth mediums. Before the standardization of the model, the data were analyzed statistically as shown in Table 1.

The result indicated that all the models (ANFIS, MLP and SWLR) have shown good prediction, as shown in the Table 3 below.

Additional comparisons of the analysis are produced in scattered plot (see, Fig. 3). From the Fig. 3. ANFIS-TPC and SWLR-TPC are stronger than MLP-TPC model. Even if there is a slight difference between the models but overall, the result showed that all models tell the strong relation between the observed and predicted values with the ideal models (ANFIS, SWLR and MLP).

4. Discussion

In Spirulina (A. platensis) production, the interaction of different factors, including nutrients and light intensity and salt concentration affect the photosynthetic efficiency, growth, productivity and the bioactive compounds of the blue-green algae. In a study the process of photosynthesis in the spirulina was found to be negatively affected by the increase in a concentration of salt from 2.5 to 5 and 10 % (V/V), while a decrease in growth and productivity of the blue-green algae was simultaneously observed (Markou et al., 2021). On the other hand, other research findings revealed that the amount of phenolic compound in the Spirulina was increased eight times through the application of light intensity treatment, while at the same time an increment was seen in on the important nutrients, such as protein, carotenoids, carbohydrates, phycocyanin and antioxidant activities (Aysun et al., 2012). The growth of Spirulina maxima in Zarrouks medium supplemented with different concentration of sodium nitrate and phenylalanine had positive effects on the production of biomass (Abd El-Baky et al., 2009), whereas the turbidness of the growing mediums influences the spirulina yield and its bioactive compounds. Thus, the varying turbidness in the growing mediums is associated with the availability and/or addition of the different nutrients. So, a balance between the nutrients and light availability is an important parameter, with considerable variations of digestate concentrations (Markou et al., 2021).

Statistical analysis is generally used to understand the science of the data to navigate the common problems that can lead to incorrect results as well as a proper decision making based on the raw data. Spearman Pearson correlation describes how well

Table 1
Statistical and Spearman Pearson Correlation Analysis.

Statistical Analysis		P	E Y	TF	% F	%P	TPC	
Mean	0.163741	50.57741	13.22926	2.611852	0.257778	0.873333	8.751852	
Standard Deviation	0.046338	8.22757	1.870134	1.369436	0.13687	0.397374	4.004735	
Minimum	0.096	37.39	10.14	1.29	0.1261	0.3	4.28	
Maximum	0.255	65.53	16.35	5.34	0.5181	1.717	18.2	
Spearman Pearson Correlation Analysis		MGR	P	E Y	TF	% F	%P	TPC
MGR		1						
P		0.966042	1					
E Y		0.960457	0.938316	1				
TF		0.897094	0.901528	0.896418	1			
% F		0.897881	0.903637	0.898931	0.998802	1		
%P		0.948397	0.930937	0.933104	0.974398	0.975856	1	
TPC		0.950116	0.930721	0.929665	0.978256	0.976224	0.991862	1

Table 2
The amount of Total phenolic compound (TPC) prediction using ANFIS, MLP and SWLR models both in the training and testing stages (milligram per gram of daily weight (mg g-1) DW).

Training Stage			Testing stage		
ANFIS-TP	MLP-TP	SWLR-TP	ANFIS-TP	MLP-TP	SWLR-TP
4.7401	4.7462	4.871	10.9503	10.4464	10.9125
4.5098	4.5124	4.5351	10.48	9.4767	10.4999
4.2801	4.3346	4.3643	7.0852	6.793	6.6896
6.0104	6.2503	5.7019	6.5281	6.553	6.5287
5.68	5.9517	5.5349	6.0067	6.318	6.3816
5.3397	5.3591	5.5555	13.8723	12.652	13.759
7.7184	7.5458	7.4952	12.9353	12.747	12.9499
7.3643	7.3032	7.2532	12.0124	12.9451	12.182
6.9973	7.0528	7.0271	18.2001	16.4157	18.0691
5.5379	5.6304	5.2395	16.9598	16.4957	16.9363
5.1929	5.367	5.1486	15.7201	16.6593	15.844
4.8391	5.135	5.0859			
8.9064	9.1625	9.3665			
8.6467	8.7615	8.7828			
8.3668	8.3285	8.2443			
11.4198	12.1433	11.3417			

Table 3
Results on ANFIS, MLP and SWLR models.

Models	Training			
	DC	CC	MSE	RMSE
ANFIS-TPC	0.999998	0.999999	6.9E-06	0.002627
MLP-TPC	0.984993	0.992468	0.056328	0.237335
SWLR-TPC	0.989124	0.994547	0.040824	0.20205
	Testing			
ANFIS-TPC	0.999999	0.999999	1.54E-05	0.003928
MLP-TPC	0.953476	0.976461	0.507541	0.712419
SWLR-TPC	0.997851	0.998925	0.02344	0.1531

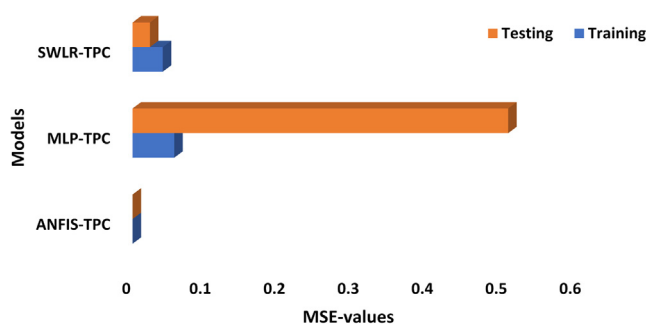


Fig. 2. Measure square errors (MSE) of the models in both the training and testing stages.

the relationship between the variables can be described using a linear function. The strength of the correlation is not dependent on the direction or sign. A positive coefficient indicates that increase in the first parameter would correspond to an increase in the second parameter, while a negative correlation indicates an inverse relationship whereby one parameter increases and the second parameter decreases (Eisinga et al., 2012). As indicated in Table 1 the spirulina total phenolic compound (TPC) has a high positive correlation with the spirulina productivity (P), extraction yield (EY), total flavonoids (TF), percent of flavonoid (%F), percent of phenols (%P) with R = 1 as shown in Table 1 above.

In the development of the data driven models of the ANFIS, MLP and SWLR models MATLAB 9.3 (R2017a) were applied. In any arti-

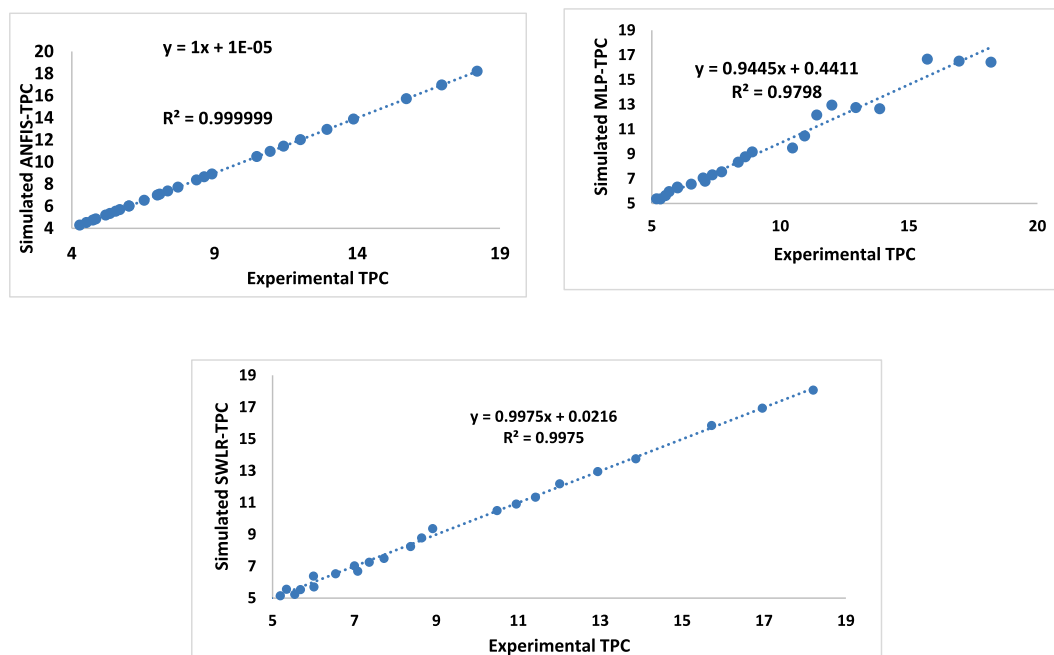


Fig. 3. Scatter plots for ANFIS, SWLR and MLP of TPC.

ficial neural network (ANN) modeling, getting appropriate hidden nodes is a key aspect to solve overfitting problems caused by different factors (Bao Pham et al., 2019; Elkiran et al., 2019). Many scholars agreed that there is no specific procedure to estimate the appropriate number for hidden neurons. According to Usman et al. (Usman et al., 2020), the proper number of nodes in the hidden layer ranges from $(2n1/2 + m)$ to $(2n + 1)$ for the identification of the optimum number of hidden layers, where n is the number of input neurons and m is the number of output neurons. Hence, 3–27 was found to be the range of the hidden neurons of the models for the simulation development.

From the simulated predictive result of the three models as shown in (Table 2 and 3), it can be observed clearly that the artificial intelligence-based models (ANFIS and MLP) and SWLR model gives an excellent result which is supported by other artificial intelligence based studies (Dahmoune et al., 2015; García Nieto et al., 2016; Sen et al., 2018; Uysal et al., 2019). The total phenolic compound (TP) prediction both in the training and testing stages using ANFIS ranged from 4.28 – 18.2 mg per gram of daily weight (mg g⁻¹) DW where us MLP predicted from 4.34 to 16.659 (mg g⁻¹) DW and SWLR ranged from 4.36 to 18.07 (mg g⁻¹) DW, please look the detail prediction of each model at Table 2.

Similarly, Table 3 equally shows the ANFIS specifies a superior ability over the other two models for the prediction of TPC and increases their performance accuracy up to 2% and 1% for MLP and SWLR respectively based on the determination co-efficient (R^2) in the training stage; where us the performance accuracy of the MLP and SWLR in the testing stage is up to 5% and 0.2% respectively. According to Table 2 and 3, both ANFIS and SWLR can work as reliable tool in the modeling of TPC. The result in Table 2 can be further discussed reasonably based on their corresponding mean squared error (MSE) by using bar chart as indicated in Fig. 2 below.

Based on the simulated outcome, it can be seen that the AI-based model i.e., ANFIS and SWLR developed as an excellent and reliable model. In addition, the correlation coefficient (R) as shown in Table 2 validates the advantages of these models over MLP model. Fig. 4 depicts the performance of the models using a radar chart, which shows the scale of R from 0 to 1 in the training, and

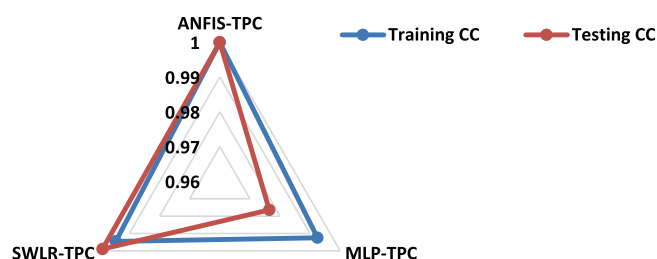


Fig. 4. Radar chart of ANFIS, SWLR and MLP of TPC in both the training and testing modeling.

testing stages. ANN models can be used in the different modeling of spirulina algae production system.

For example in a study, in the extraction and recovery of phenolic compounds from photosynthetic organisms were modeled using central composite design (CCD) and artificial neural networks (ANNs) in order to estimate ideal values and standards for the process; Dahmoune et al. (2015) studied the optimum standards of total phenolic compounds production using ultrasound green extraction method from *Pistacia lentiscus* (*P. lentiscus*) leaves, the models were helped in the forecast of the total phenolic compound (TPC) (Dahmoune et al., 2015). In another supporting study, Momordica charantia leaves phenolic compound extraction were made using response surface methodology (RSM) and ANN models; using three by three levels and variables arrangement i.e., extraction temperature, solvent concentration and extraction time (Uysal et al., 2019). In another experiment of spirulina platensis algae production, practical swarm optimization (PSO) with support vector sector machines (SVMs) models were applied; in this process adjusting kernel variables in the SVM process which determine and influence the accuracy of the regression is a key issue, and the PSO-SVM model of goodness values were fitted with the experimental values of Chlorophyll-a concentration which was a key bioactive compound that determine photosynthesis and

Chlorophyll-a, an ideal estimator for the algal biomass production (García Nieto et al., 2016).

Therefore, this displayed that the AI-based models are an excellent method to predict and developed a system to set the parameters in spirulina culture system and total phenolic compound production, supporting studies were reported (Dahmoune et al., 2015; García-Pérez et al., 2020; García Nieto et al., 2016; Yew et al., 2020).

5. Conclusion

In conclusion, the ANFIS and SWLR gives superior result in the testing phase and increased its accuracy by 2% compared to MLP model in the prediction of TPC. Thus, all the three models increase the prediction efficiency and helps in the relative comparisons of the result. Finally, the overall comparisons of the results showed that ANFIS and SWLR established outstanding performance and improved the accuracy of the model prediction accuracy for TPC by 2% compared to MLP model prediction.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- Abba, S.I., Pham, Q.B., Usman, A.G., Linh, N.T.T., Aliyu, D.S., Nguyen, Q., Bach, Q.-V., 2020a. Emerging evolutionary algorithm integrated with kernel principal component analysis for modeling the performance of a water treatment plant. *J. Water Process Eng.* 33, 101081. <https://doi.org/10.1016/j.jwpe.2019.101081>.
- Abba, S.I., Usman, A.G., Işık, S., 2020b. Simulation for response surface in the HPLC optimization method development using artificial intelligence models: A data-driven approach. *Chemom. Intell. Lab. Syst.* 201, 104007. <https://doi.org/10.1016/j.chemolab.2020.104007>.
- Abd El-Baky, H.H., El Baz, F.K., El-Baroty, G.S., 2009. Production of phenolic compounds from *Spirulina maxima* microalgae and its protective effects in vitro toward hepatotoxicity model. *African J. Pharm. Pharmacol.* 3, 133–139.
- Al-Qahtani, W.H., Binobeid, M.A., 2019. Saudi Journal of Biological Sciences Anti-inflammatory, antioxidant and antihepatotoxic effects of *Spirulina platensis* against D-galactosamine induced hepatotoxicity in rats. *Saudi J. Biol. Sci.* 26 (4), 647–652. <https://doi.org/10.1016/j.sjbs.2018.01.003>.
- Alshuniaber, M.A., Krishnamoorthy, R., AlQhtani, W.H., 2021. Antimicrobial activity of polyphenolic compounds from *Spirulina* against food-borne bacterial pathogens. *Saudi J. Biol. Sci.* 28 (1), 459–464. <https://doi.org/10.1016/j.sjbs.2020.10.029>.
- Anahite, C., Cesar, J., Carvalho, D., Vinícius, G., Pereira, D.M., 2018. Functional properties and health benefits of bioactive peptides derived from *Spirulina*: A review. *Food Rev. Int.* 34, 34–51. <https://doi.org/10.1080/87559129.2016.1210632>.
- Bao Pham, Q., Abba, S.I., Garba Usman, A., Thi Thuy Linh, N., Gupta, V., Malik, A., Costache, R., Duong Vo, N., Quang Tri, D., 2019. Potential of Hybrid Data-Intelligence Algorithms for Multi-Station Modelling of Rainfall. <https://doi.org/10.1007/s11269-019-02408-3>
- Belay, A., 2008. *Spirulina* (Arthrospira): production and quality assurance. *Spirulina Hum. Nutr. Heal.* 1, 1–23.
- Carcea, M., Sorto, M., Batello, C., Narducci, V., Aguzzi, A., Azzini, E., Fantauzzi, P., Finotti, E., Gabrielli, P., Galli, V., Gambelli, L., Maintha, K.M., Namba, F., Ruggeri, S., Turfani, V., 2015. Nutritional characterization of traditional and improved dihé, alimentary blue-green algae from the lake Chad region in Africa. *LWT - Food Sci. Technol.* 62 (1), 753–763. <https://doi.org/10.1016/j.lwt.2014.10.039>.
- Cardoso, L.G., Duarte, J.H., Costa, J.A.V., de Jesus Assis, D., Lemos, P.V.F., Druzian, J.I., de Souza, C.O., Nunes, I.L., Chinalia, F.A., 2021. *Spirulina* sp. as a Bioremediation Agent for Aquaculture Wastewater: Production of High Added Value Compounds and Estimation of Theoretical Biodiesel. *BioEnergy Res.* 14 (1), 254–264.
- Choubin, B., Khalighi-Sigaroodi, S., Malekian, A., Kişi, Ö., 2016. Multiple linear regression, multi-layer perceptron network and adaptive neuro-fuzzy inference system for forecasting precipitation based on large-scale climate signals. *Sci. J.* 61 (6), 1001–1009. <https://doi.org/10.1080/02626667.2014.966721>.
- Christ-Ribeiro, A., Graça, C.S., Kupski, L., Badiale-Furlong, E., de Souza-Soares, L.A., 2019. Cytotoxicity, antifungal and anti mycotoxins effects of phenolic compounds from fermented rice bran and *Spirulina* sp. *Process Biochem.* 80, 190–196. <https://doi.org/10.1016/j.procbio.2019.02.007>.
- Costa, J.A.V., Freitas, B.C.B., Rosa, G.M., Moraes, L., Moraes, M.G., Mitchell, B.G., 2019. Operational and economic aspects of *Spirulina*-based biorefinery. *Bioresour. Technol.* 292, 121946. <https://doi.org/10.1016/j.biortech.2019.121946>.
- Dahmoune, F., Remini, H., Dairi, S., Aoun, O., Moussi, K., Bouaoudia-Madi, N., Adjeroud, N., Kadri, N., Lefsih, K., Boughani, L., Mouni, L., Nayak, B., Madani, K., 2015. Ultrasound assisted extraction of phenolic compounds from *P. lentiscus* L. leaves: Comparative study of artificial neural network (ANN) versus degree of experiment for prediction ability of phenolic compounds recovery. *Ind. Crops Prod.* 77, 251–261. <https://doi.org/10.1016/j.indcrop.2015.08.062>.
- de Jesus, C.S., da Silva Uebel, L., Costa, S.S., Miranda, A.L., de Moraes, E.G., de Moraes, M.G., Costa, J.A.V., Nunes, I.L., de Souza Ferreira, E., Druzian, J.I., 2018. Outdoor pilot-scale cultivation of *Spirulina* sp. LEB-18 in different geographic locations for evaluating its growth and chemical composition. *Bioresour. Technol.* 256, 86–94. <https://doi.org/10.1016/j.biortech.2018.01.149>.
- Eisinga, R., Te Grotenhuis, M., Pelzer, B., 2012. The reliability of a two-item scale: Pearson, Cronbach, or Spearman-Brown? *Ó Swiss Sch. Public Heal.* <https://doi.org/10.1007/s00038-012-0416-3>
- El-sheekh, M., Abomohra, A.E., 2020. *Mini Review* 43 (60), 605–609.
- Elkiran, G., Nourani, V., Abba, S.I., 2019. Multi-step ahead modelling of river water quality parameters using ensemble artificial intelligence-based approach. *J. Hydrol.* 577, 123962. <https://doi.org/10.1016/j.jhydrol.2019.123962>.
- European Union, 2015. REGULATION (EU) 2015/ 2283 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL - of 25 November 2015 - on novel foods, amending Regulation (EU) No 1169/ 2011 of the European Parliament and of the Council and repealing Regula.
- García-Pérez, P., Lozano-Milo, E., Landín, M., Gallego, P.P., 2020. Combining Medicinal Plant In Vitro Culture with Machine Learning Technologies for Maximizing the Production of Phenolic Compounds. *Antioxidants* 9, 210. <https://doi.org/10.3390/antiox9030210>.
- García Nieto, P.J., García-Gonzalo, E., Alonso Fernández, J.R., Díaz Muñoz, C., 2016. A hybrid PSO optimized SVM-based model for predicting a successful growth cycle of the *Spirulina platensis* from raceway experiments data. *J. Comput. Appl. Math.* 291, 293–303. <https://doi.org/10.1016/j.cam.2015.01.009>.
- Hong, H., Zhang, Z., Guo, A., Shen, L., Sun, H., Liang, Y., Wu, F., Lin, H., 2020. Radial basis function artificial neural network (RBF ANN) as well as the hybrid method of RBF ANN and grey relational analysis able to well predict trihalomethanes levels in tap water. *J. Hydrol.* 591, 125574. <https://doi.org/10.1016/j.jhydrol.2020.125574>.
- Jimenez-Lopez, C., Pereira, A.G., Lourenço-Lopes, C., Garcia-Oliveira, P., Cassani, L., Fraga-Corral, M., Prieto, M.A., Simal-Gandara, J., 2021. Main bioactive phenolic compounds in marine algae and their mechanisms of action supporting potential health benefits. *Food Chem.* 341, 128262. <https://doi.org/10.1016/j.foodchem.2020.128262>.
- Khan, S., Mobashar, M., Mahsood, F.K., Javaid, S., 2020. *Spirulina* inclusion levels in a broiler ration : evaluation of growth performance , gut integrity , and immunity 3233–3240.
- Kim, S., Singh, V.P., 2014. Modeling daily soil temperature using data-driven models and spatial distribution. *Theor. Appl. Climatol.* 118 (3), 465–479. <https://doi.org/10.1007/s00704-013-1065-z>.
- Koukouraki, P., Tsoupras, A., Sotiroidis, G., Demopoulos, C.A., Sotiroidis, T.G., 2020. Antithrombotic properties of *Spirulina* extracts against platelet-activating factor and thrombin. *Food Biosci.* 37, 100686. <https://doi.org/10.1016/j.fbio.2020.100686>.
- Lafarga, T., Fernández-Sevilla, J.M., González-López, C., Acien-Fernández, F.G., 2020. *Spirulina* for the food and functional food industries. *Food Res. Int.* 137, 109356. <https://doi.org/10.1016/j.foodres.2020.109356>.
- LU, J., WANG, M.-M., WANG, Q., LI, H.-P., YANG, Z.-G., 2018. Determination of Benzotriazole and Its Derivatives in Aqueous Sample with Air-assisted Liquid-Liquid Microextraction Followed by High-performance Liquid Chromatography. *Chinese J. Anal. Chem.* 46 (4), e1817–e1825. [https://doi.org/10.1016/S1872-2040\(17\)61082-X](https://doi.org/10.1016/S1872-2040(17)61082-X).
- Markou, G., Diamantis, A., Arapoglou, D., Mitrogiannis, D., González-Fernández, C., Unc, A., 2021. Growing *Spirulina* (*Arthrospira platensis*) in seawater supplemented with digestate: Trade-offs between increased salinity, nutrient and light availability. *Biochem. Eng. J.* 165, 107815. <https://doi.org/10.1016/j.bej.2020.107815>.
- Nourani, V., Gökçekuş, H.& Gichamo, T., 2021. Ensemble data-driven rainfall-runoff modeling using multi-source satellite and gauge rainfall data input fusion. *Earth Sci. Inform.* <https://doi.org/10.1007/s12145-021-00615-4>.
- Paula da Silva, S., Ferreira do Valle, A., Perrone, D., 2021. Microencapsulated *Spirulina maxima* biomass as an ingredient for the production of nutritionally enriched and sensorially well-accepted vegan biscuits. *LWT* 142, 110997. <https://doi.org/10.1016/j.lwt.2021.110997>.
- Pina-Pérez, M.C., Rivas, A., Martínez, A., Rodrigo, D., 2017. Antimicrobial potential of macro and microalgae against pathogenic and spoilage microorganisms in food. *Food Chem.* 235, 34–44. <https://doi.org/10.1016/j.foodchem.2017.05.033>.
- Sen, S., Nandi, S., Dutta, S., 2018. Application of RSM and ANN for optimization and modeling of biosorption of chromium(VI) using cyanobacterial biomass. *Appl. Water Sci.* 8, 148. <https://doi.org/10.1007/s13201-018-0790-y>.
- Silva, R., 2020. Book of Proceedings esdAveiro2020 Online.

- Soni, R.A., Sudhakar, K., Rana, R.S., 2017. Spirulina – From growth to nutritional product: A review. *Trends Food Sci. Technol.* 69, 157–171. <https://doi.org/10.1016/j.tifs.2017.09.010>.
- Tongal, H., Booi, M.J., 2018. Simulation and forecasting of streamflows using machine learning models coupled with base flow separation. *J. Hydrol.* 564, 266–282.
- Usman, A.G., Işık, S., Abba, S.I., 2020. A Novel Multi-model Data-Driven Ensemble Technique for the Prediction of Retention Factor in HPLC Method Development. *Chromatographia* 83, 933–945. <https://doi.org/10.1007/s10337-020-03912-0>
- Uysal, S., Cvetanović, A., Zengin, G., Zeković, Z., Mahomoodally, M.F., Bera, O., 2019. Optimization of Maceration Conditions for Improving the Extraction of Phenolic Compounds and Antioxidant Effects of *Momordica Charantia* L. Leaves Through Response Surface Methodology (RSM) and Artificial Neural Networks (ANNs). *Anal. Lett.* 52 (13), 2150–2163. <https://doi.org/10.1080/00032719.2019.1599007>.
- Wu, X.J., Dong, Y., Zhang, Y.N., Liu, J., 2020. River runoff influence factors recognition using stepwise regression analysis: The case of a northern Chinese coal mining area. *Polish J. Environ. Stud.* 29, 893–900. <https://doi.org/10.15244/pjoes/103360>.
- Yasar, A., Bilgili, Simsek, Erdogan, Yasar, A, Bilgili, M, Simsek, E, Bilgili, M., Simsek, E, M., 2012. Water Demand Forecasting Based on Stepwise Multiple Nonlinear Regression Analysis. *Arab. J. Sci. Eng.* 37, 2333–2341. <https://doi.org/10.1007/s13369-012-0309-z>.
- Ye, C., Mu, D., Horowitz, N., Xue, Z., Chen, J., Xue, M., Zhou, Y., Klutts, M., Zhou, W., 2018. Life cycle assessment of industrial scale production of spirulina tablets. *Algal Res.* 34, 154–163. <https://doi.org/10.1016/j.algal.2018.07.013>.
- Yew, G.Y., Puah, B.K., Chew, K.W., Teng, S.Y., Show, P.L., Nguyen, T.H.P., 2020. *Chlorella vulgaris* FSP-E cultivation in waste molasses: Photo-to-property estimation by artificial intelligence. *Chem. Eng. J.* 402, 126230. <https://doi.org/10.1016/j.cej.2020.126230>.
- Zhang, F., Man, Y.B., Mo, W.Y., Wong, M.H., 2020. Application of Spirulina in aquaculture: a review on wastewater treatment and fish growth. *Rev. Aquac.* 12 (2), 582–599.