

Morus alba-Mediated Green Synthesis of ZnO Nanoparticles

Coupled with Augmented ANN Modeling for Process Optimization and Predictive Design

Abstract

A sustainable and environmentally benign route for the synthesis of zinc oxide (ZnO) nanoparticles was developed using *Morus alba* leaf extract as a natural reducing and stabilizing agent. Multiple green synthesis approaches were systematically investigated in order to evaluate the influence of processing conditions on the physicochemical properties of the resulting nanoparticles. Key synthesis parameters, including reaction strategy and operating conditions, were analyzed with respect to their effects on crystallinity, particle size, and surface characteristics. The results revealed that the synthesis pathway plays a decisive role in governing the structural quality of ZnO nanoparticles, and an optimal operating window was identified that produces particles with enhanced crystallinity and favorable surface features. To further support process optimization, a data-augmented artificial neural network (ANN) model was developed to establish predictive relationships between synthesis parameters and nanoparticle properties. The ANN exhibited superior generalization capability and predictive accuracy compared with conventional statistical modeling approaches. Overall, this study provides both experimental insight and data-driven tools for the rational design and optimization of green ZnO nanoparticle synthesis, offering a reliable framework for scalable and eco-friendly nanomaterial production.

Keywords: Artificial neural network, Green synthesis, Predictive modeling, Process optimization, Zinc oxide nanoparticles.

1. Introduction

In recent decades, the development of green and sustainable technologies has emerged as one of the main priorities in the fields of nanotechnology and advanced materials [1, 2]. Nanoparticles, defined as particles within the nanometer scale, play a vital role in diverse applications such as medicine, environmental protection, electronics, and catalysis, owing to their unique physical, chemical, and biological properties [3, 4]. Among these, zinc oxide (ZnO) nanoparticles have attracted particular attention due to their distinctive features, including semiconducting behavior, optical permeability, low toxicity, and versatile applicability across different industries, granting them a prominent position in scientific research [5-7].

Nevertheless, nanoparticle production must be carried out with strict consideration of environmental and safety concerns to prevent biological and ecological hazards [8]. In this context, green synthesis methods, which utilize natural resources and bio-based materials, have gained recognition as efficient and eco-friendly alternatives [9]. Green synthesis, based on the use of plant extracts as rich sources of bioactive compounds, offers environmentally friendly pathways by reducing the use of toxic chemicals and energy consumption while effectively facilitating solid-phase reactions [10, 11]. One notable plant in this domain is the (Morus alba), whose leaves contain valuable active constituents such as phenols, flavonoids, and other antioxidants, making them suitable for nanoparticle synthesis [12].

The leaves of the white mulberry tree are known to contain a wide range of natural compounds that act as reducing agents and play a crucial role in green nanoparticle synthesis. These compounds, including phenols, flavonoids, phenolic acids, tetrapeptides, and antioxidants, possess hydroxyl and other functional groups capable of electron transfer, thus enabling the reduction of metal ions such as zinc, copper, and others [13]. By reducing metal ions to their

oxide or pure metallic states, these natural compounds serve as safe, natural, and environmentally compatible reducing agents [14]. Their involvement not only decreases the use of hazardous starting materials but also enhances control over the size, shape, and structure of nanoparticles, which in turn directly influences the physicochemical properties of the synthesized products [15]. The reducing agents present in mulberry leaves therefore provide a sustainable alternative to conventional synthetic chemicals. They also contribute positively to biological and ecological processes, supporting the advancement of safe and sustainable nanotechnology approaches [16, 17]. Such comparisons can be based on criteria including nanoparticle formation efficiency, size and shape control, process yield, and scalability [18]. Moreover, the influence of physicochemical parameters, such as temperature and thermal conditions, must be carefully assessed as they play a significant role in optimizing production processes [19].

In this study, not only are different synthesis methods compared in terms of efficiency and compliance with biological and environmental principles, but also the final properties of the nanoparticles, such as particle size, morphology, crystal structure, as well as optical and biological characteristics, are evaluated according to the synthesis approach employed. The ultimate objective is to identify an optimal and effective method for the green and environmentally friendly production of ZnO nanoparticles that can be utilized in a wide range of scientific and industrial fields, including pharmaceuticals, water treatment, and the development of smart materials.

Consequently, this research is expected to play an important role in advancing green and sustainable technologies in the field of nanomaterials. The findings promise to improve nanoparticle synthesis strategies by minimizing negative environmental impacts while enhancing process efficiency. Furthermore, careful control of process parameters, combined with the use of natural and plant-based resources, paves the way for an industrial-scale,

sustainable future for green nanoparticles. Ultimately, this work not only contributes to the advancement of green technologies but also deepens understanding of parameter influences, creating new opportunities in nanoscience and nanotechnology.

In this regard, four commonly employed methods for nanoparticle synthesis, ambient temperature processing, oven-assisted synthesis, water bath (Bain-Marie), and heated magnetic stirring, are investigated. Ambient temperature synthesis, being the simplest and most cost-effective method, is particularly suited for assessing the feasibility of green synthesis at the laboratory scale. Conversely, oven-assisted synthesis provides a controlled environment at elevated temperatures, allowing improved regulation of nanoparticle morphology, size, and dispersion. The water bath method, which employs indirect heating and drying, is typically applied to achieve finer control over chemical processes and nanoparticle formation in aqueous media without direct heating. Additionally, magnetic stirrer heating, which enables simultaneous control of both temperature and solution agitation, is considered an effective method for improving synthesis efficiency and precisely tailoring nanoparticle structure.

2. Materials and Methods

2.1. Materials

White mulberry (*Morus alba*) leaves were collected from park trees in Sanandaj (Iran). Deionized water (Morvarid Pars Co., Iran) was used as the solvent for extract preparation. Zinc nitrate hexahydrate ($\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$), the precursor salt for ZnO nanoparticle synthesis, was purchased from Sigma-Aldrich.

2.2. Experimental Methods

2.2.1. Preparation of white mulberry leaf extract

A total of 300 g of white mulberry leaves were dried at ambient temperature for 5 days. After drying, 10 g of the leaves were ground and added to 100 mL of boiling deionized water; extraction was performed for 10 min. The mixture was then filtered through filter paper. The resulting extract was transferred to a dark, tightly sealed bottle and stored at 4 °C until ZnO nanoparticle synthesis.

2.2.2. Experimental design and statistical analysis; mechanistic overview

Green synthesis of ZnO nanoparticles was adopted, recognizing that numerous parameters could influence the properties of the resulting nanoparticles [30]. The overall formation mechanism is a coordinated, multi-stage process involving chemical and bio-chemical reactions: (1) Preparation of the reaction solution: $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ is dissolved in water to release Zn^{2+} ions. (2) Reduction of metal ions: concurrently, the mulberry leaf extract, containing reducing constituents such as hydroxyl-bearing compounds, phenols, flavonoids, and other antioxidants, transfers electrons to the Zn^{2+} ions, generating neutral Zn species (Zn^0). (3) Nucleation and growth: primary particles aggregate and grow into nanometric structures; bioactive species in the extract act as both reducing and capping/stabilizing agents, thereby controlling particle size and dispersion. (4) Oxidation to ZnO: the initially formed Zn^0 particles are oxidized in a furnace, yielding crystalline ZnO nanoparticles.

To systematically evaluate the effects of operating conditions and to accelerate steps (2) and (3), a full factorial design was employed across four synthesis methods (categorical factor): (i) ambient-temperature processing, (ii) hotplate–magnetic stirring (heated stirring), (iii) oven, and (iv) water bath (Bain-Marie).

For each synthesis method, two quantitative factors, temperature (30° , 35° , and 40° °C) and synthesis time (10 , 15 , and 20 min), were examined at three levels. Accordingly, the total number of experimental runs was calculated using Eq. (1):

$$N = n_c \times L^{n_q} \quad (1)$$

where N is the total number of experiments, n_c is the number of categorical parameters (ξ methods), L is the number of levels for each quantitative parameter (τ), and n_q is the number of quantitative parameters (γ). Thus:

$$N = \xi \times \tau^\gamma = 3^6$$

For every run (all 3^6 conditions), γ g of $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ were added to 10 mL of the prepared mulberry leaf extract in an individual vessel. After complete mixing, green synthesis of ZnO nanoparticles was carried out under the designed temperature–time settings. Upon completion of all reactions, the products were calcined in a furnace at 400° °C for τ h to effect calcination and convert the prepared suspensions into powders. A schematic illustration of the experimental workflow and representative photographs of the synthesized ZnO nanoparticle powders are presented in the Supplementary Material (Figure S1).

2.3. Characterization and property analysis

The specific surface area of the synthesized ZnO nanoparticles was measured by BET using a JW-BK134F instrument. The average crystallite size was determined from X-ray diffraction (XRD) patterns ($D5000$, Siemens Co., Karlsruhe, Germany) recorded with a wavelength of 1.54 Å over a 2θ range of 10 – 90° . Crystallite size D was calculated using the Scherrer equation as follows [16,17]:

$$D = \frac{\lambda \times 10^4}{\beta \cos \theta} \quad (2)$$

where D is the crystallite size, λ is the X-ray tube wavelength, β is the full width at half maximum (FWHM) of the diffraction peak, and θ is the Bragg diffraction angle.

The effects of the selected variables on the average particle (crystallite) size and specific surface area were analyzed to compare outcomes among the different synthesis methods.

2.4. Artificial Neural Network Modeling

In this study, a multilayer perceptron (MLP) neural network was employed to predict both the crystal size and the specific surface area of iron oxide nanoparticles. The network consists of an input layer, a single hidden layer, and an output layer, with the number of hidden neurons optimized through multiple trials. The number of neurons in the hidden layer was varied from 1 to 10, and for each configuration, the training was repeated 10 times with randomized train/validation/test splits to ensure robustness and avoid potential local minima. The best number of hidden neurons was selected based on the network yielding the lowest Mean Relative Error (MRE) on the test set.

Hidden layer activation was implemented using the hyperbolic tangent sigmoid (tansig) function to introduce nonlinearity and enable the network to capture complex relationships between input and output variables. The output layer employed a linear (purelin) activation function, allowing the network to produce continuous numerical predictions suitable for regression tasks. Network weights were optimized using the Levenberg–Marquardt (trainlm) algorithm, which provides fast convergence and stability for medium-sized networks in nonlinear regression problems.

The dataset was divided into training, validation, and test subsets with proportions of 70%, 10%, and 10%, respectively. The training set was used for updating network weights, the validation set for monitoring the training process and preventing overfitting, and the test set for evaluating final network performance. All input variables were normalized to comparable scales to improve convergence and stability. Continuous variables such as Temperature and Time were scaled, while the categorical variable representing experimental methods was encoded using binary (0/1) indicators.

Network performance was quantitatively assessed using Mean Relative Error (MRE, %), Mean Squared Error (MSE), Root Mean Squared Error (RMSE), Mean Absolute Error (MAE), and the Coefficient of Determination (R^2). The best-performing network for each output was selected based on the lowest MRE observed on the test dataset, ensuring reliable predictive capability. To further enhance robustness, 20 independent training runs were conducted for each hidden neuron configuration, minimizing the influence of random weight initialization and data splitting on the final model selection. The mapping between the input variables and the network output can be expressed as:

$$y = \sum_{k=1}^{N_h} w_k f \left(\sum_{j=1}^{N_i} w_{jk} x_j + b_k \right) + b \quad (3)$$

where x_j represents the j -th input variable, w_{jk} and b_k denote the weights and bias of the hidden layer, f is the hidden layer activation function (tansig), w_k and b are the weights and bias connecting the hidden layer to the output neuron, N_h is the total number of hidden neurons, and N_i is the number of input variables. This formulation illustrates how the multilayer perceptron transforms the inputs through a nonlinear hidden layer to produce continuous outputs suitable for regression tasks. The optimal network configuration, including the number of hidden neurons, was determined based on minimizing the Mean Relative Error (MRE) on the test set.

2.4.1. Data Preparation and Augmentation for Neural Network Training

To enhance the dataset for robust MLP modeling, both data preparation and augmentation were performed. The original experimental dataset consisted of 36 measurements with four main factors: Method, Temperature, Time, and two output variables: Particle size and Specific surface area.

For numerical modeling, the categorical feature “Method” (Oven, Bain-Marie, Room Temperature, Heater) was transformed into one-hot encoding, producing four binary input columns (Method_Oven, Method_BainMarie, Method_RoomTemp, Method_Heater), where only the active method is coded as 1 and the others as 0. This resulted in a total of six input features: Temperature, Time, and the four method columns.

To increase dataset size and variability, a dual-phase data augmentation strategy was applied:

1. Gaussian noise injection: Noise was added to each continuous input and output feature (Temperature, Time, Particle size, Specific surface area) from a normal distribution with zero mean and standard deviation equal to 5% of the feature-wise standard deviation. This generated 36 noise-augmented samples while maintaining the original statistical properties.
2. Linear interpolation: Intermediate samples were created between consecutive original samples using weighted averaging (x_1, y_1, x_2, y_2) , resulting in 36 additional interpolated samples. Notably, the binary method columns were kept unchanged during augmentation.

The final augmented dataset therefore consists of 104 samples: 36 original, 36 noise-perturbed, and 32 interpolated samples. This structured dataset ensures broader coverage of the feature space, allowing the MLP to better capture nonlinear relationships and improve generalization.

3. Results and Discussion

3.1. Factorial Analysis of Experimental Results

According to the factorial design, a total of 36 experiments were performed, and the mean particle size and specific surface area were considered as the responses. The obtained results, together with the predicted values generated by the Minitab software using the factorial method, are reported in Table 1.

Table 1. Experimental design and the measured/predicted responses for each set of independent variables.

Predicted Specific Area (m ² /g)	Predicted Mean Particle Size (nm)	Experimental Specific Area (m ² /g)	Experimental Mean Particle Size (nm)	Time (min)	Temperature (°C)	Method
29,91	76	28,23	71	10	30	Oven
31,44	79	29,21	77	40	30	
28,66	76	29,64	76	70	30	
31,67	71	30,44	79	10	30	
37,66	73	30,48	77	40	30	
28,31	71	34,88	73	70	30	
30,04	60	31,44	74	10	40	
32,33	73	32,96	71	40	40	
31,19	00	32,64	07	70	40	
28,49	79	29,32	78	10	30	Bain-Marie
32,36	71	30,21	74	40	30	
32,91	60	30,66	73	70	30	
33,66	72	31,02	77	10	30	
34,46	77	33,47	76	40	30	
31,49	60	32,79	71	70	30	
31,19	73	32,42	73	10	40	
33,40	71	32,99	60	40	40	
33,02	09	31,74	08	70	40	
16,14	78	18,33	79	10	30	Room Temperature
17,66	74	19,60	70	40	30	
21,03	70	20,06	73	70	30	
17,03	73	18,69	78	10	30	
21,61	71	20,74	74	40	30	
24,69	73	21,06	70	70	30	
17,62	78	19,99	76	10	40	

۲۲,۸۴	۷۵	۲۱,۶۹	۷۲	۴۵	۴۰	
۲۳,۴۷	۶۸	۲۲,۸۱	۶۸	۷۵	۴۰	
۲۷,۲۴	۴۹	۲۶,۶۱	۴۳	۱۵	۳۰	Heater-Stirrer
۲۹,۱۴	۳۷	۲۷,۰۴	۳۴	۴۵	۳۰	
۲۹,۹۳	۴۰	۲۸,۶۶	۳۹	۷۵	۳۰	
۲۵,۴۷	۴۳	۲۷,۶۴	۴۱	۱۵	۳۵	
۲۷,۲۱	۳۶	۲۸,۴۱	۳۳	۴۵	۳۵	
۲۹,۴۷	۳۸	۲۸,۸۷	۳۶	۷۵	۳۵	
۲۵,۱۱	۳۹	۲۶,۴۴	۳۸	۱۵	۴۰	
۲۶,۴۷	۳۴	۲۷,۳۴	۳۱	۴۵	۴۰	
۲۸,۹۱	۳۶	۲۷,۸۴	۳۴	۷۵	۴۰	

After conducting experiments with two variables at three levels each and for four synthesis methods, a total of ۳۶ runs were obtained. The responses (mean particle size and BET surface area) were then analyzed, and the effect of each parameter at the defined levels was evaluated. The results are presented in Fig. ۱ (a and b).

As shown in Fig. ۱a, the response related to mean particle size is plotted against two-way interactions (method–temperature, method–time, and time–temperature) across all considered levels. The clearer and more detailed representation is shown in Fig. ۱b. Based on this figure, comparison of the synthesis methods indicates that the heater-stirrer method was the most efficient, yielding an average particle size of less than ۴۰ nm. In contrast, the room-temperature method resulted in the largest average particle size, representing the least favorable synthesis condition. The oven and bain-marie methods showed intermediate performance.

These differences can be attributed to the effect and type of heat transfer and its role in accelerating nanoparticle synthesis. For example, one critical factor is the uniformity and rate of heat transfer. In methods such as heater-stirrer, heat is delivered more rapidly and uniformly to the reaction medium, ensuring a homogeneous sublimation and nucleation process throughout the system. This leads to the formation of smaller and more uniform nanoparticles. On the other hand, under room-temperature conditions, heat transfer occurs naturally without precise control, which can result in non-uniform nucleation and uncontrolled growth,

ultimately producing larger and more heterogeneous particles. Another factor is the controlled heating rate in thermal methods, which stabilizes the temperature and enhances the precision of the precipitation and growth process. This reduces growth time and restricts final particle size. By contrast, under room-temperature synthesis, temperature gradients and fluctuations dominate, favoring the growth of larger and irregular particles.

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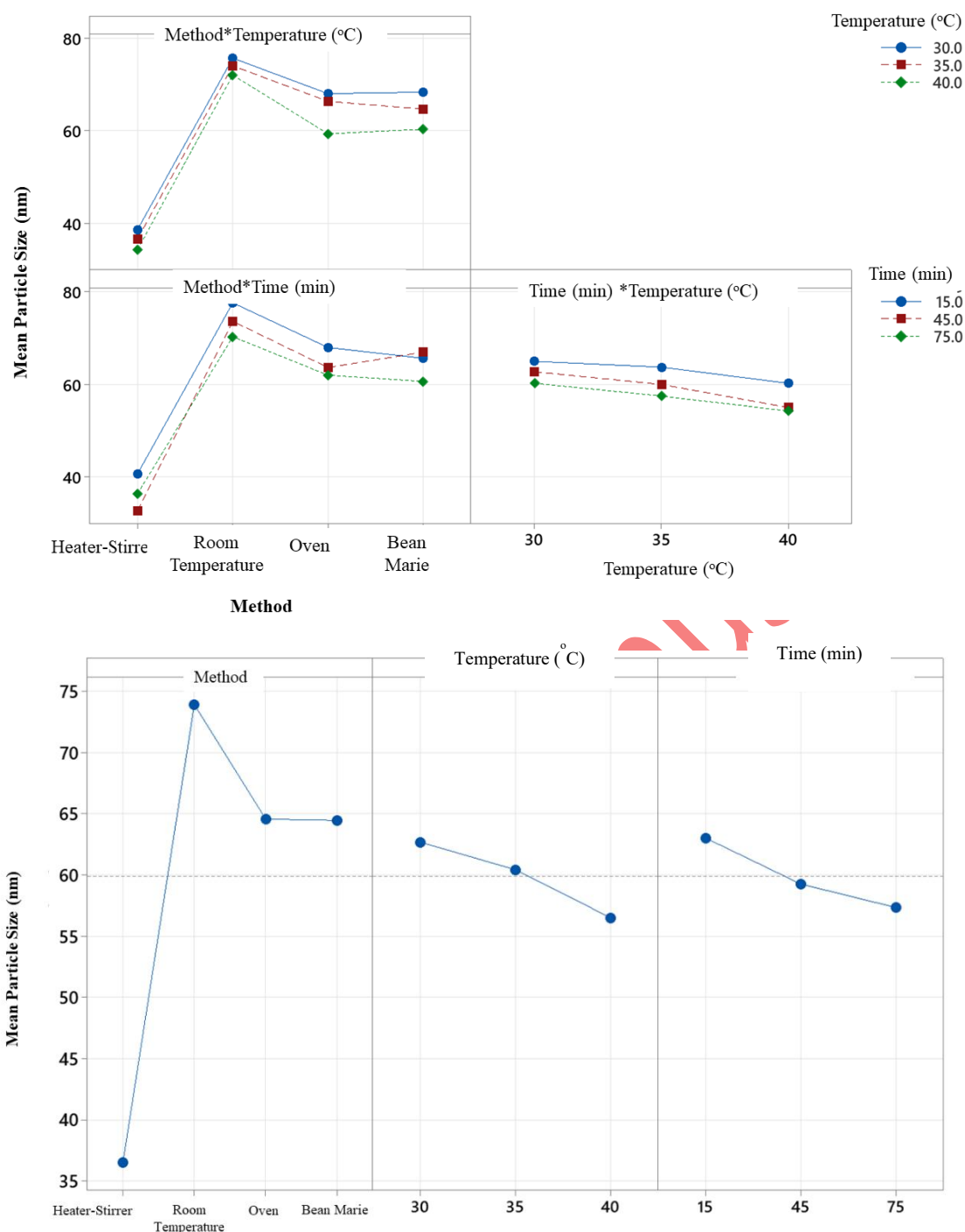


Fig. 1. (a) Interaction plots of mean particle size vs. process factors; (b) detailed response plots.

Further evaluation of the effects of time and temperature on mean particle size revealed that in both cases, increasing temperature and synthesis time generally reduced the average particle size. This can be explained by their influence on nucleation and growth processes. At higher temperatures, the system provides greater thermal energy, which accelerates the nucleation rate

and shortens the growth time of each nucleus. As a result, numerous smaller nuclei are formed, limiting particle growth and yielding smaller, more compact nanoparticles. Similarly, prolonging the synthesis time increases the opportunity for nucleation and stabilization of particles. With proper control, this prevents uncontrolled growth and favors the formation of smaller, more uniform nanoparticles. In longer reaction times, the system tends to reach more stable, low-energy states, which are typically associated with smaller and more crystalline particles. Therefore, increasing both temperature and time enhances nucleation, limits excessive growth, and ultimately decreases the mean nanoparticle size. This highlights the crucial role of thermal conditions in controlling the final particle size during synthesis.

As shown in Fig. 5a, the response related to the specific surface area of synthesized ZnO nanoparticles is plotted against two-way interactions (method–temperature, method–time, and time–temperature) across all levels, with a clearer representation in Fig. 5b. According to Fig. 5b, comparison of different synthesis methods indicates that the oven method yielded the highest surface area ($32 \text{ m}^2/\text{g}$), whereas the room-temperature method resulted in the lowest value ($\sim 20 \text{ m}^2/\text{g}$). The heater-stirrer and bain-marie methods exhibited intermediate results.

These differences can be attributed to multiple scientific factors. In thermal processes, higher temperatures provide sufficient energy for nucleation and crystallization, producing more homogeneous and ordered nanoparticles. This enhances control over particle size, leading to smaller particles with a higher surface-to-volume ratio, and therefore, higher specific surface area. Conversely, under room-temperature conditions, the synthesis occurs without precise control. The reaction and growth processes are slower and less ordered, resulting in larger, irregular particles with reduced surface area. Furthermore, thermal methods promote better crystallinity and ordered structures, which allow the formation of nanoparticles with higher active surface area. In contrast, the lack of temperature control in room-temperature synthesis results in less crystalline and irregular structures, reducing the active surface area.

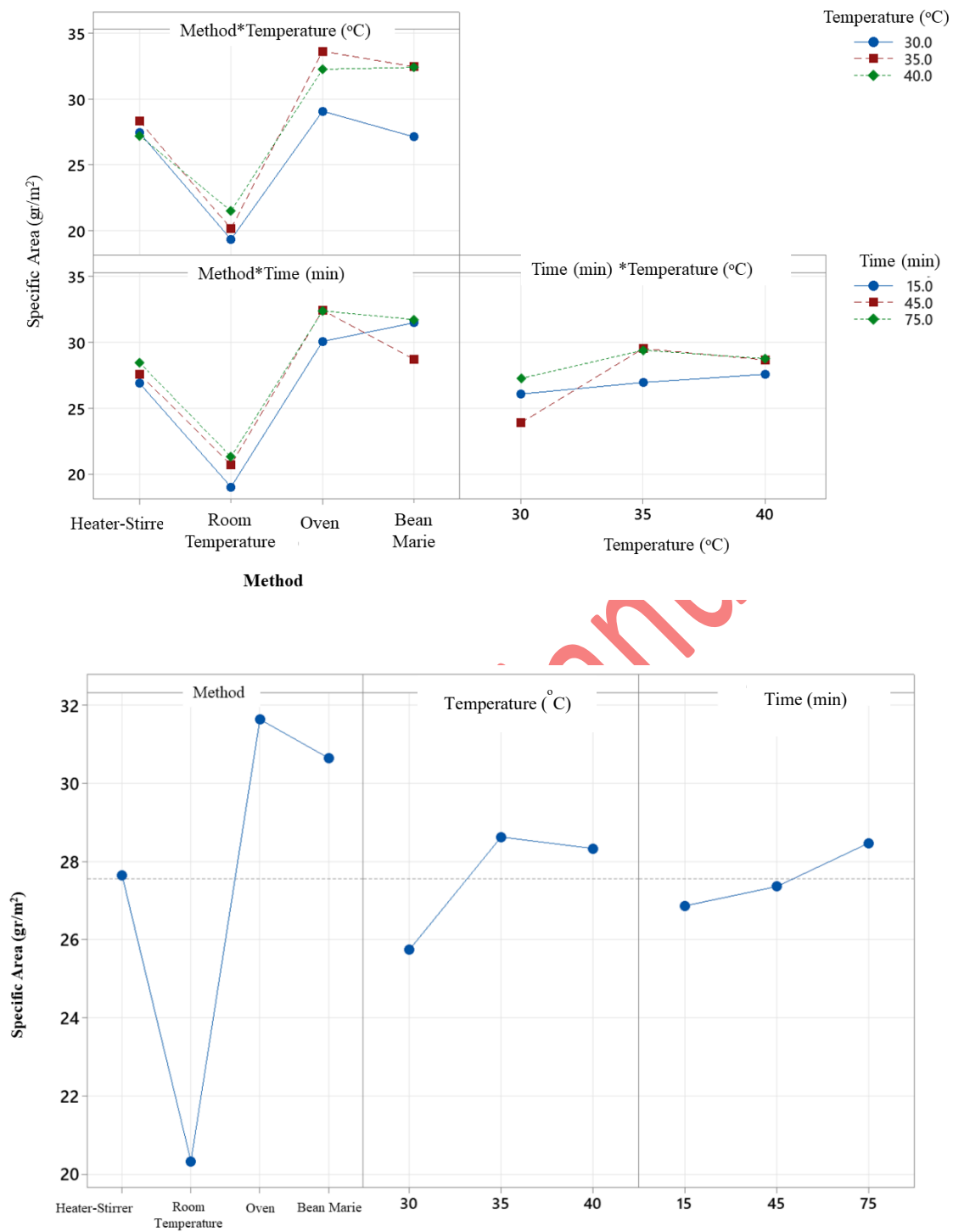


Fig. 9. (a) Interaction plots of BET surface area vs. process factors; (b) detailed response plots.

The effect of temperature on surface area shows that intermediate temperatures ($\sim 30^{\circ}\text{C}$) provide the best condition for producing nanoparticles with high surface area. At this level, nucleation and crystallization occur optimally, yielding small, uniform nanoparticles with large external surface area relative to their volume. Increasing the temperature from 30°C to 35°C enhanced the nucleation rate and formation of smaller, more ordered nanoparticles, thereby increasing surface area. However, further temperature increase to 40°C reversed this trend. At higher temperatures, additional energy promotes particle growth and aggregation (Ostwald ripening), causing smaller particles to merge into larger ones [21, 22]. This reduces the surface-to-volume ratio and consequently decreases the surface area. Therefore, $\sim 35^{\circ}\text{C}$ is the optimal condition, while higher temperatures favor growth and reduce the surface area of ZnO nanoparticles.

The effect of synthesis time was consistently positive: longer synthesis times led to an increase in specific surface area. Extended reaction duration allows more complete nucleation and crystallization, yielding a larger number of smaller, compact nanoparticles with high surface-to-volume ratios. In longer processes, fewer particles undergo secondary growth, as the conditions stabilize toward uniform crystallization, resulting in more homogeneous structures with greater active surface area. Thus, increasing synthesis time provides more opportunity for the formation and stabilization of small, uniform nanoparticles, directly enhancing the specific surface area of ZnO nanoparticles.

3.2. Optimization of the Factorial Design Results

Based on the factorial design outcomes and the analysis of the effects of the selected variables, synthesis method, temperature, and synthesis time, on the chosen responses (mean particle size

and specific surface area), a final optimization was performed. The corresponding optimization results are presented in Fig. 3.

As shown in Fig. 3, the optimal settings to achieve the minimum mean particle size (33 nm) and the maximum specific surface area (28.41 m²/g) were identified for the heater–stirrer method at 35 °C and 45 min. These findings can reliably guide the production of nanoparticles with desirable properties. Following determination of the optimal points from the optimization analysis, confirmatory experiments were conducted under the design-identified conditions to validate the results. To provide additional morphological evidence of the synthesized ZnO nanoparticles, an SEM image of the sample obtained under the optimized synthesis conditions is provided in the Supplementary Information (Figure S3).

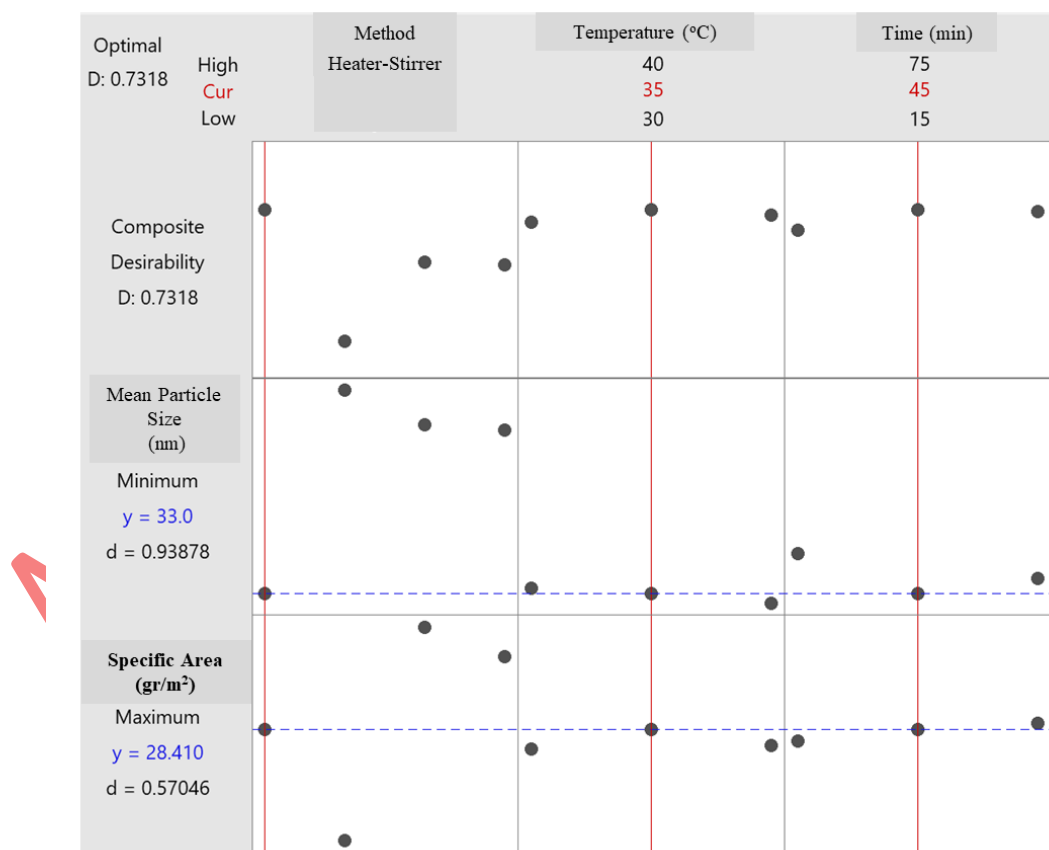


Fig. 3. Final optimization obtained from the factorial design.

3.3. Artificial neural network modeling results

Following data preparation and augmentation (as described in Section 2.4.1), the final dataset consisted of 104 samples, including 36 original experimental points, 36 Gaussian noise-augmented samples, and 32 linearly interpolated samples. Each sample included six input features: Temperature, Time, and four one-hot encoded method columns (Oven, Bain-Marie, Room Temperature, Heater-Stirrer), with two output variables: Mean Particle Size and Specific Surface Area.

Table 2 presents a portion of the dataset, highlighting the original experimental measurements alongside the augmented intermediate values. For instance, Data No. 1–36 correspond to the original factorial design experiments with combinations of the four synthesis methods, three temperatures (30, 35, 40 °C), and three reaction times (10, 40, 70 min). Data No. 37–104 show intermediate samples generated via Gaussian noise and linear interpolation, extending coverage of the input space. This augmentation strategy ensured broader exploration of the feature space, allowing the MLP model to better capture nonlinear dependencies between synthesis conditions and nanoparticle characteristics.

Table 2. The original and augmented dataset used for ANN modeling.

Data no.	Temperature (°C)	Time (min)	Oven	Bain Marie	Room Temperature	Heater Stirrer	Mean Particle Size (nm)	Specific Area (m ² /gr)
1	30	10	1	0	0	0	71	28,33
2	30	40	1	0	0	0	67	29,21
3	30	70	1	0	0	0	66	29,64
4	35	10	1	0	0	0	69	30,44
5	35	40	1	0	0	0	67	30,48
6	35	70	1	0	0	0	63	34,88
7	40	10	1	0	0	0	64	31,44
8	40	40	1	0	0	0	61	33,96
9	40	70	1	0	0	0	57	32,64
10	30	10	0	1	0	0	68	29,32
11	30	40	0	1	0	0	64	30,21
12	30	70	0	1	0	0	63	30,66
13	35	10	0	1	0	0	67	31,02

14	30	40	.	1	.	.	66	33,47
15	30	70	.	1	.	.	61	32,79
16	40	10	.	1	.	.	63	32,42
17	40	40	.	1	.	.	60	32,99
18	40	70	.	1	.	.	58	31,74
19	30	10	.	.	1	.	79	18,33
20	30	40	.	.	1	.	70	19,60
21	30	70	.	.	1	.	73	20,06
22	30	10	.	.	1	.	78	18,69
23	30	40	.	.	1	.	74	20,74
24	30	70	.	.	1	.	70	21,06
25	40	10	.	.	1	.	76	19,99
26	40	40	.	.	1	.	72	21,69
27	40	70	.	.	1	.	68	22,81
28	30	10	.	.	.	1	43	26,61
29	30	40	.	.	.	1	34	27,04
30	30	70	.	.	.	1	39	28,66
31	30	10	.	.	.	1	41	27,64
32	30	40	.	.	.	1	33	28,41
33	30	70	.	.	.	1	36	28,87
34	40	10	.	.	.	1	38	26,44
35	40	40	.	.	.	1	31	27,34
36	40	70	.	.	.	1	34	27,84
37	32,1	30,0	1	.	.	.	70,2	29,70
38	31,0	44	1	.	.	.	66,0	30,18
39	30	16	1	.	.	.	68	30,8
40	36,0	46	1	.	.	.	60,0	33,2
41	39	62	1	.	.	.	60,0	32,9
42	34,0	10	.	1	.	.	67,0	30,6
43	36	43	.	1	.	.	60	32,8
44	40	40,0	.	1	.	.	61,0	33
45	33	16	.	.	1	.	70,0	19,8
46	36	40	.	.	1	.	72,0	21,3
47	31	44,0	.	.	.	1	30,0	27,0
48	39	70	.	.	.	1	37	27,8
49	34,0	33,0	.	.	1	.	73,0	21
50	32	34	.	1	.	.	66	30,9
51	30,0	50	1	.	.	.	66	34,1
52	36,0	40	.	.	1	.	71	21,8
53	33,0	20	.	1	.	.	60	30,70
54	36	52	.	.	1	.	71	21,8
55	32	32	.	.	.	1	39	28,20
56	34	46	1	.	.	.	67	32,1
57	37	50	1	.	.	.	64	33
58	33,0	22,0	.	1	.	.	60,0	30,0
59	30	42	.	.	1	.	70	21,0

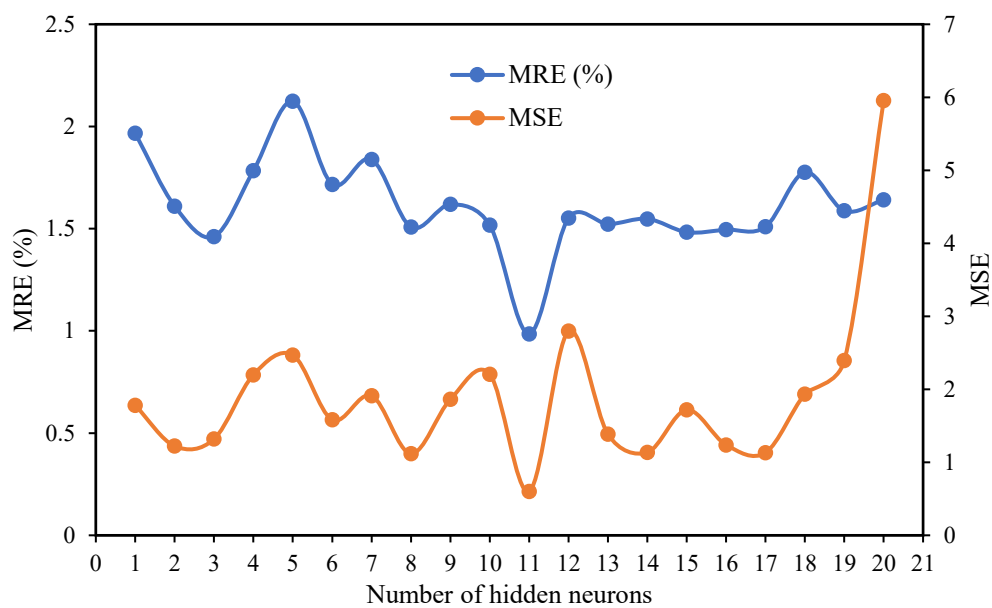
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٧٣	٣٤	٤٥	.	١	.	.	٦٦	٣٢
٧٤	٣٥	٥٠	.	.	١	.	٧٠	٢١,٥
٧٥	٣٦	٦٠	١	.	.	.	٦٤	٣٣
٧٦	٣٧	٥٥	.	.	.	١	٣٦	٢٨,٥
٧٧	٣٢,٥	٣٥	.	.	١	.	٧٢	٢١,٥
٧٨	٣٤,٥	٤٠	.	١	.	.	٦٦	٣١,٥
٧٩	٣٣,٥	٣٨	.	.	.	١	٣٧,٥	٢٨
٨٠	٣٥,٥	٤٢	.	.	١	.	٧١	٢١,٨
٨١	٣٦,٥	٤٨	١	.	.	.	٦٥	٣٣,٥
٨٢	٣٤	٤٤	.	١	.	.	٦٦	٣٢,٨
٨٣	٣٣	٣٦	.	.	١	.	٧٠	٢١,٥
٨٤	٣٥	٥٠	١	.	.	.	٦٧	٣٤
٨٥	٣٦	٤٥	.	.	١	.	٧١	٢١,٨
٨٦	٣٨	٦٠	١	.	.	.	٦٢	٣٢,٥
٨٧	٣٧	٥٥	.	.	.	١	٣٦	٢٨,٥
٨٨	٣٤	٤٨	.	.	١	.	٧٢	٢١,٥
٨٩	٣٣,٥	٤٠	.	١	.	.	٦٦,٥	٣١,٦
٩٠	٣٢,٥	٣٧	.	.	.	١	٣٧,٥	٢٨,٢
٩١	٣٥	٤٤	١	.	.	.	٦٦	٣٣
٩٢	٣٦,٥	٥٠	.	.	١	.	٧١	٢١,٨
٩٣	٣٧	٥٢	١	.	.	.	٦٣	٣٣,١
٩٤	٣٤,٥	٤٦	.	١	.	.	٦٦	٣٢,٨
٩٥	٣٣,٥	٣٨	.	.	١	.	٧٠	٢١,٥
٩٦	٣٥,٥	٤٢	.	.	.	١	٣٧,٥	٢٨
٩٧	٣٦	٤٩	١	.	.	.	٦٥	٣٣,٥
٩٨	٣٤	٤٤	.	.	١	.	٧١	٢١,٨
٩٩	٣٥	٥٠	١	.	.	.	٦٧	٣٤
١٠٠	٣٣,٥	٤١	.	١	.	.	٦٦,٥	٣٢,٢
١٠١	٣٦,٥	٥٣	.	.	١	.	٧١	٢١,٩
١٠٢	٣٤,٥	٤٧	.	.	.	١	٣٧	٢٨,٢
١٠٣	٣٣	٣٩	.	١	.	.	٦٦	٣٢,٨
١٠٤	٣٢,٥	٣٦	.	.	.	١	٣٧,٥	٢٨,١

The augmented dataset allowed the MLP model to train effectively and generalize beyond the original 36 experimental points. Initial visual inspection of the dataset confirms that the augmentation maintained realistic distributions for both particle size and specific surface area while introducing variability sufficient for robust learning.

The performance curves for different numbers of hidden neurons are shown in Fig. 4. The figures show the changes in MRE (%) and MSE values for the test dataset as a function of hidden neurons. These plots indicate that the optimal number of hidden neurons for both outputs balances prediction accuracy and network complexity, avoiding overfitting while minimizing error. Accordingly, neural networks with 11 and 9 hidden neurons were selected to estimate mean particle size and surface area, respectively.

The performance of the MLP models for predicting mean particle size and surface area was evaluated using multiple metrics, including Mean Relative Error (MRE), Mean Squared Error (MSE), Root Mean Squared Error (RMSE), Mean Absolute Error (MAE), and the coefficient of determination (R^2). Table 3 summarizes the results for the optimized networks, compared with the RSM model.

(a)



(b)

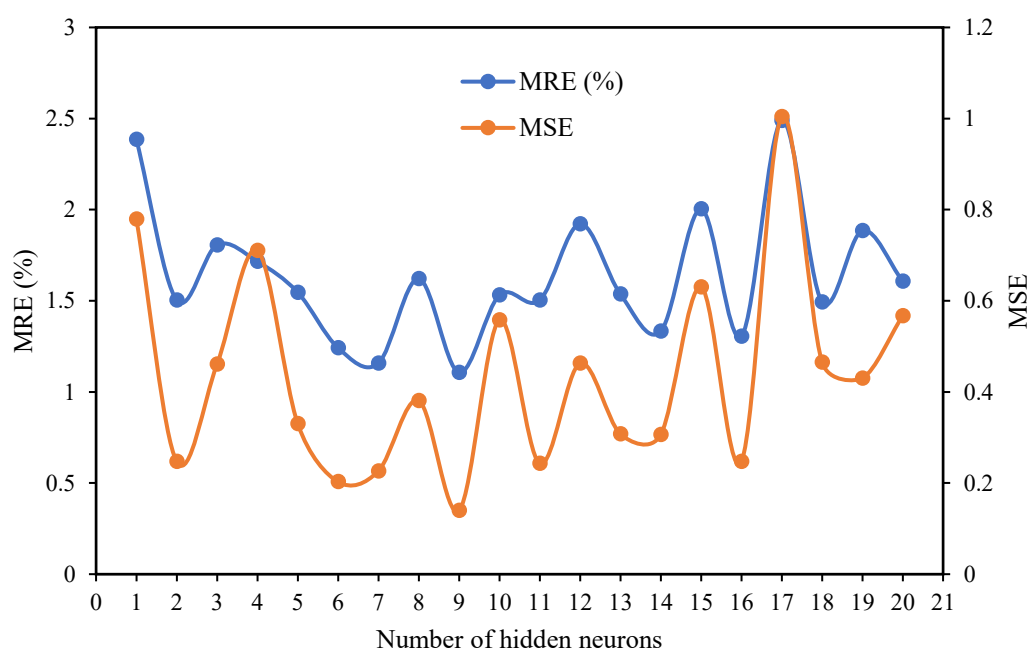


Fig. 4. MRE (%) and MSE values vs. number of hidden neurons for (a) mean particle size and (b) surface area.

Table 3. Performance metrics of the optimized MLP models for particle size and specific surface area prediction.

Output	Stage	Data points	MRE (%)	MSE	RMSE	MAE	R ²
Mean Particle Size	Training	70	1.031	0.774	0.881	0.719	0.9960
	Validating	10	1.450	1.216	1.103	0.717	0.9912
	Testing	14	2.100	3.100	1.761	1.037	0.9802
	Overall	104	1.230	1.079	0.988	0.790	0.9939
	RSM	36	4.074	7.006	2.606	2.222	0.9760
Specific Area	Training	70	1.133	0.192	0.438	0.322	0.9911
	Validating	10	1.994	0.016	0.718	0.037	0.9999
	Testing	14	2.031	0.020	0.721	0.404	0.9990
	Overall	104	1.378	0.283	0.016	0.371	0.9879
	RSM	36	0.840	2.970	1.723	1.000	0.8768

Tables 4 and 5 present the optimized weights and biases of the trained neural networks corresponding to particle size and specific surface area prediction, respectively. These numerical parameters define the internal structure of the best-performing MLP models and can be directly applied in Eq. (3) to reproduce the network outputs. By substituting the tabulated weights and biases into the general MLP formulation, the predictive model becomes explicitly available in an analytical form, which enables independent verification, replication, and practical implementation of the ANN models beyond the training environment.

Table 4. Optimized weights and biases of the trained MLP network for particle size prediction.

Neuron	W _{ji}						b _j	b _k =-0.7477
	Temperature (°C)	Time (min)	Oven	BainMarie	RoomTemp	Heater		W _{kj}
1	0.2839	1.7690	1.1609	1.0204	-1.0807	-1.7042	1.8682	0.2080
2	1.3710	-0.7792	0.2217	-1.9072	-1.7214	2.2030	-1.2106	0.1700
3	-0.8221	1.4083	0.0908	2.2446	-1.0030	-0.3803	0.2290	-0.7810
4	-1.9136	-0.1289	0.3661	-0.0149	1.7810	-1.3101	0.7998	-0.1490
5	0.9078	0.0201	0.1131	1.2626	-0.9188	-0.2627	-0.3306	-0.7067
6	-0.9696	0.7488	1.0241	0.8920	-1.0849	-0.7019	0.7841	0.2270
7	0.2687	-1.0266	-0.0246	0.3688	-1.3939	-1.3113	-0.4624	0.3110
8	-0.4963	0.7110	0.2444	-1.0697	0.1478	-0.7431	-1.1730	-0.2206
9	0.3741	0.4420	-0.7349	1.2200	0.4482	-0.8266	1.7432	0.0342
10	-0.9608	1.3246	-0.0628	1.1409	1.2879	-1.8762	1.7290	0.7022
11	-0.0321	-0.4017	-0.3284	-0.4217	-1.2480	-1.2874	-1.0094	0.0196

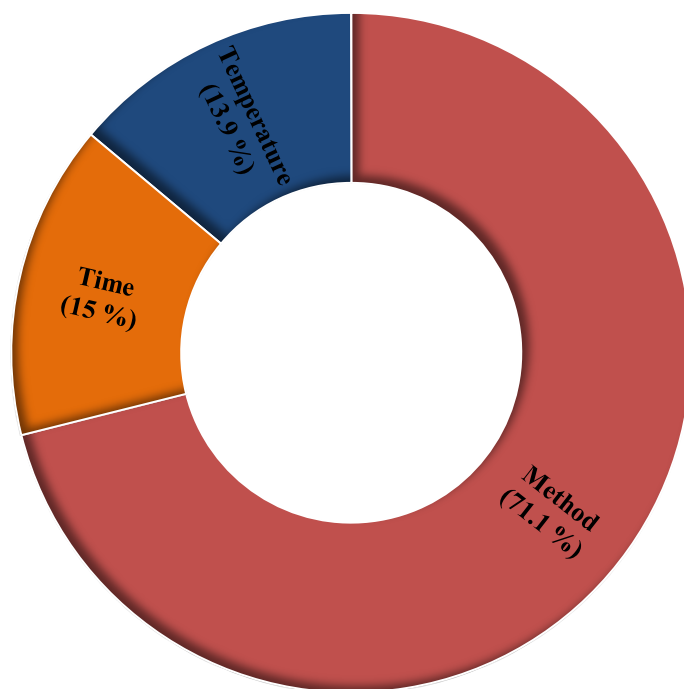
Table 9. Optimized weights and biases of the trained MLP network for specific surface area prediction.

Neuron	W _{ji}						b _j	b _k =0.2262
	Temperature (°C)	Time (min)	Oven	BainMarie	RoomTemp	Heater		
1	-0.1798	-0.1007	-0.0012	2.1231	-1.0370	0.0439	1.3301	0.2487
2	-0.1070	2.0323	-0.7028	0.7862	0.4016	2.4202	-2.7031	0.1266
3	-2.3028	8.1878	0.1300	0.4889	0.7000	0.0934	-1.4389	-0.0832
4	3.0120	0.8109	-0.4443	1.1208	-4.0829	1.1232	-0.3134	0.3301
5	0.3904	-0.4786	-2.4960	-0.7181	-0.7701	-0.0307	0.0932	-0.3910
6	2.2676	1.2246	-0.0944	2.1074	1.8882	-0.4481	-0.8370	0.1030
7	-0.9919	1.1469	2.2392	1.3831	-0.0890	-4.8278	-0.1096	0.1639
8	-2.0081	1.4049	0.9810	-1.7271	-2.0400	1.3061	1.6042	0.0408
9	2.0320	-1.4930	-0.0768	1.0768	0.7780	1.8147	-3.4063	-0.0870

Feature importance analysis, based on the trained MLP weights, revealed that the synthesis method contributed the most to the predictive performance of both models, accounting for approximately 71.1% of the total influence. In contrast, reaction temperature and time exhibited considerably lower contributions, with values of 13.9% and 10.0% for particle size (Fig. 9a), and 13.94% and 14.96% for specific surface area (Fig. 9b), respectively.

These results highlight that the choice of synthesis method is the dominant factor governing nanoparticle properties, while temperature and reaction time play supportive but less significant roles. Such findings are consistent with experimental observations, where the applied synthesis technique strongly dictates the nucleation and growth environment, whereas thermal and temporal parameters mainly fine-tune the resulting particle morphology and surface characteristics.

(a)



(b)

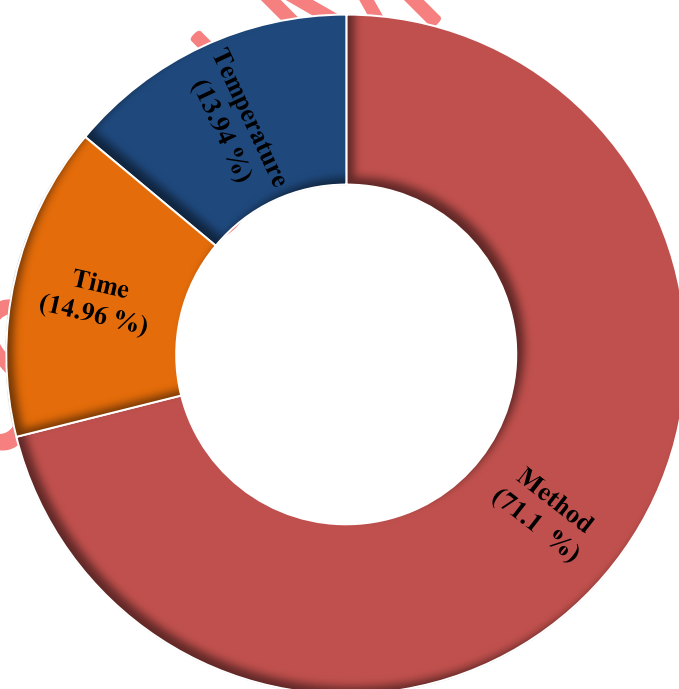


Fig. 9. Relative importance of input variables for the ANN models: (a) mean particle size, and (b) specific surface area prediction.

Overall, the MLP networks trained on the augmented dataset provide highly accurate predictions for both particle size and specific surface area, outperforming the original RSM models. The dual-phase data augmentation strategy contributed to improved generalization and robustness, enabling reliable mapping of experimental conditions to nanoparticle properties.

4. Conclusions

1. Four green synthesis methods were systematically compared under identical factorial conditions. Heated magnetic stirring consistently produced the smallest crystallites (range: 31–43 nm, mean: 36.06 nm), while oven and bain-marie achieved higher surface areas (mean 31.78 m²/g and 31.62 m²/g) than room-temperature synthesis (mean 20.34 m²/g).
2. Multi-response desirability optimization identified 30 °C and 40 min under heated magnetic stirring as the balanced optimum, delivering a crystallite size of 33 nm and a specific surface area of 28.41 m²/g, experimentally validated in confirmatory trials.
3. ANN models trained on 104 samples achieved excellent accuracy, with R² = 0.9939 (particle size) and 0.9879 (specific area), and test MRE of 2.1 % and 2.3 %. These results clearly outperformed the RSM baseline (R² = 0.9660 and 0.8768).
4. Feature importance analysis highlighted the dominant role of synthesis method (71.1 %), with temperature (13.9–13.94 %) and time (14.96–10 %) acting as secondary factors.
5. For obtaining small-sized ZnO nanoparticles under mild green conditions, heated magnetic stirring around 30 °C and 40 min is recommended. The ANN model provides a reliable predictive tool to reduce experimental trial-and-error.

7. Expanding the factor space (e.g., precursor concentration, extract dosage, or pH), testing alternative extracts, and coupling ANN with multi-objective optimization could further enhance scalability and performance in sustainable ZnO production.

Nomenclature

Symbol	Description	Unit
b	Bias of the output neuron in the ANN model	-
b_k	Bias of the k -th hidden neuron in the ANN model	-
D	Crystallite size	nm
f	Hidden layer activation function (tansig)	-
L	Number of levels for each quantitative parameter	-
N	Total number of experiments	-
N_i	Number of input variables in the ANN	-
n_c	Number of categorical parameters	-
n_q	Number of quantitative parameters	-
w_{jk}	Weight connecting the j -th input to the k -th hidden neuron	-
w_k	Weight connecting the k -th hidden neuron to the output neuron	-
x_j	The j -th input variable to the ANN	-
y	Output of the ANN model	-

Greek Symbols

β	Full Width at Half Maximum of XRD peak	rad
θ	Bragg diffraction angle	°
λ	X-ray wavelength	Å

Abbreviations

ANN	Artificial Neural Network
BET	Brunauer-Emmett-Teller method
MAE	Mean Absolute Error
MRE	Mean Relative Error
MSE	Mean Squared Error
MLP	Multilayer Perceptron
RMSE	Root Mean Squared Error
RSM	Response Surface Methodology
XRD	X-Ray Diffraction
ZnO	Zinc Oxide

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

During the preparation of this work, the authors used ChatGPT to improve readability and language editing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Figure captions:

Fig. ١. (a) Interaction plots of mean particle size vs. process factors; (b) detailed response plots.

Fig. ٢. (a) Interaction plots of BET surface area vs. process factors; (b) detailed response plots.

Fig. ٣. Final optimization obtained from the factorial design.

Fig. ٤. MRE (%) and MSE values vs. number of hidden neurons for (a) mean particle size and (b) surface area.

Fig. ٥. Relative importance of input variables for the ANN models: (a) mean particle size, and (b) specific surface area prediction.

Table captions:

Table ١. Experimental design and the measured/predicted responses for each set of independent variables.

Table ٢. The original and augmented dataset used for ANN modeling.

Table ٣. Performance metrics of the optimized MLP models for particle size and specific surface area prediction.

Table ٤. Optimized weights and biases of the trained MLP network for particle size prediction.

Table ٥. Optimized weights and biases of the trained MLP network for specific surface area prediction.