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Review

Optimizing Recovery of High-Added-Value Compounds from Complex Food Matrices Using Multivariate Methods

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Abstract: In today's food industry, optimizing the recovery of high-value compounds is crucial for enhancing quality and yield. Multivariate methods like Response Surface Methodology (RSM) and Artificial Neural Networks (ANNs) play key roles in achieving this. This review compares their technical strengths and examines their sustainability impacts, highlighting how these methods support greener food processing by optimizing resources and reducing waste. RSM is valued for its structured approach to modeling complex processes, while ANNs excel in handling nonlinear relationships and large datasets. Combining RSM and ANNs offers a powerful, synergistic approach to improving predictive models, helping to preserve nutrients and extend shelf life. The review emphasizes the potential of RSM and ANNs to drive innovation and sustainability in the food industry, with further exploration needed for scalability and integration with emerging technologies.

Keywords: optimization; high-added-value compounds; food industry; ANN; RSM

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1. Introduction

As science and technology continue to advance, consumer expectations for food product quality have reached new heights. This has prompted the exploration of artificial intelligence (AI) as a means to enhance predictive capabilities and meet the diverse needs of customers [1]. In tandem with scientific progress, technological advancements, and economic prosperity, there has been a growing emphasis on consumer health and food safety [2]. Previous research efforts have made significant contributions to food science. Prominent solutions encompass the utilization of response surface methodology (RSM) with both linear models and artificial neural networks (ANNs) [3]. These methods involve designing, modeling, and establishing quadratic equations to assess the responses of multiple variables, their quadratic terms, and their possible interactions. Within the extensive body of existing literature [1], there is growing interest in applying backpropagation in feedforward NNs for the optimization and modeling of various processes within the food industry.

RSM is a comprehensive toolkit that combines mathematical techniques and advanced statistics; thus, it holds a prominent position in both prediction and optimization. Its application involves a series of critical steps, encompassing the design of experiments,

statistical analysis, and the optimization of variables, as outlined in detail elsewhere [4]. Researchers have predominantly relied on RSM to model complex multivariate processes, enabling the optimization of outcomes influenced by multiple variables [5]. It not only assesses the individual effects of independent variables but also accounts for their interactive responses. RSM, while useful for preliminary understanding, often relies on polynomial models that may lack physical or chemical significance, particularly when applied to factors like temperature or duration that might exhibit nonlinear responses. Therefore, RSM should be seen as a tool for initial exploration rather than a definitive optimization method. In the pursuit of achieving higher accuracy prediction models in agronomy and the food industry, a range of advanced techniques have been employed, including Partial Least Squares (PLSR), Gradient-Boosted Decision Trees (GBDT), K-Nearest Neighbors (KNN), and Random Forest (RF) [6]. Inspired by the biological neural systems of humans and guided by accumulated experiences, the ANN serves as a mathematical tool equipped with distributed, parallel, and adaptive data processing capabilities to model nonlinear systems in the pursuit of regression and/or classification/discrimination [7]. There are many architectures in ANNs, and feedforward backpropagation is one of the most common ones. A feedforward backpropagation ANN consists of three types of layers: an input layer, one or more hidden layers, and an output layer, each comprised of so-called neurons [8]. The versatile application of ANNs in food processing spans various domains, including food quality assessment, food extraction, food fermentation, food safety, food drying, and both thermal and non-thermal food processing operations [9]. In comparative studies evaluating prediction models for their overall acceptability in cooking rice, both linear modeling approaches (such as Multiple Linear Regression Analysis (MLR), Principal Component Regression, and PLSR) or other approaches more focused on a nonlinear modeling approach (ANNs, GBDT, KNN, and RF) were employed.

The computational functioning of ANNs closely emulates the biological operations of the human brain. This surge in interest arises from the pressing need for heightened accuracy and more comprehensive statistical capabilities compared to traditional food analysis methods [10]. The complementary combination of ANNs in the RSM umbrella processes serves a vital purpose in addressing the challenge of achieving higher extraction yields for high-added-value compounds. These methods excel in handling numerous variable nonlinear interactions, providing robust and over-determined interpretations, enhancing abstraction capabilities, mitigating interference, compensating for statistical deficiencies, and enhancing observational insights [11].

This combination emerges as a powerful and efficient tool for predicting and optimizing complex process models [12]. Moreover, it has been observed that ANNs consistently outperform RSM in the development of superior predictive models [13]. Building upon these insights, our present review was undertaken to predict and optimize responses in food processing.

Until now, there has been limited research that directly compares the optimization of high-added-value compounds' recovery using RSM with an ANN. This gap in research is primarily due to the prevailing focus on exploring the optimal extraction conditions for independent variables and validating the resulting optimized parameters [14]. Various statistical parameters were employed to compare estimation capabilities and modeling performance. Notably, the coefficient of determination (R^2) and root mean square error (RMSE) were among the critical metrics examined [14]. While both RSM and ANNs have been extensively studied independently, their combined application in optimizing the recovery of high-value compounds in the food industry remains underexplored. This study provides a novel approach by integrating these two methodologies, offering a more robust and accurate optimization framework. We provide a scalable optimization strategy that can be adapted to various food processing scenarios, potentially leading to significant improvements in yield and quality.

2. Materials and Methods Selection for RSM and ANNs

Box and Wilson proposed RSM in 1951 [15], and it has since gained significant attention for its strong empirical performance in modeling. RSM is particularly effective in providing well-fitting models to describe the relationship between input parameters and responses. The flow chart of an RSM is illustrated in Figure 1. RSM employs two primary sampling methods: Box–Behnken Design (BBD) and Central Composite Design (CCD). BBD is a three-level design that avoids placing points at the vertices of a cubic region defined by the upper and lower limits of each variable. In contrast, CCD incorporates a full or fractional factorial design with center points, augmented by a group of axial points, which enables the estimation of the curvature in the model [16].

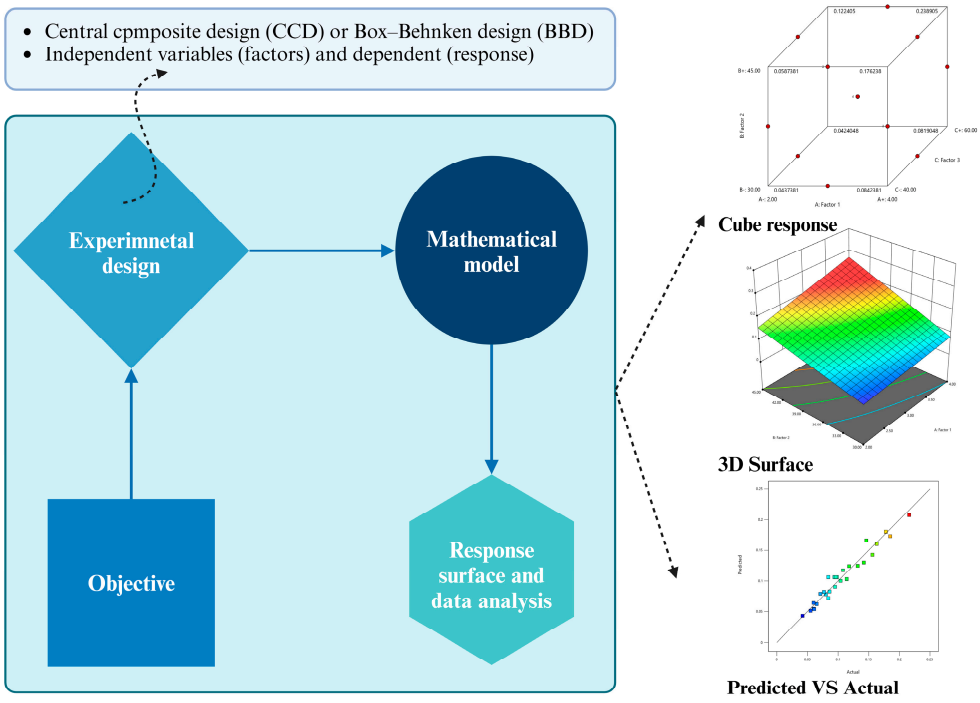


Figure 1. Flow chart of RSM (Created in BioRender.com).

RSM is well-suited for modeling and optimizing linear and low-order nonlinear relationships, such as quadratic nonlinearity. However, its reliance on simple model assumptions, local approximation, and traditional experimental designs makes it less effective for complex nonlinear systems. For such cases, more advanced modeling approaches, such as artificial neural networks or machine learning models, are often necessary.

Artificial Neural Networks (ANNs) are a mathematical modeling approach that utilize neural network structures to simulate physical systems [17]. The foundational theory of ANNs was first introduced by McCulloch and Pitts in 1943 [18]. The flow chart of an ANNs is illustrated in Figure 2. ANNs are simplified representations of biological nervous systems, capable of mapping nonlinear relationships and predicting outcomes even with incomplete data. Through the use of connection weights that link inputs, hidden layers, and outputs, ANNs achieve accurate predictions. The parallel architecture of ANNs ensures rapid responses and low computation times, making them particularly suitable for real-time food processing applications [19]. A commonly employed supervised learning algorithm for training multilayer perceptron (MLP) neural networks in solving nonlinear food-engineering problems is the backpropagation algorithm [20]. Consequently, ANNs are highly recommended for modeling nonlinear systems in food engineering.

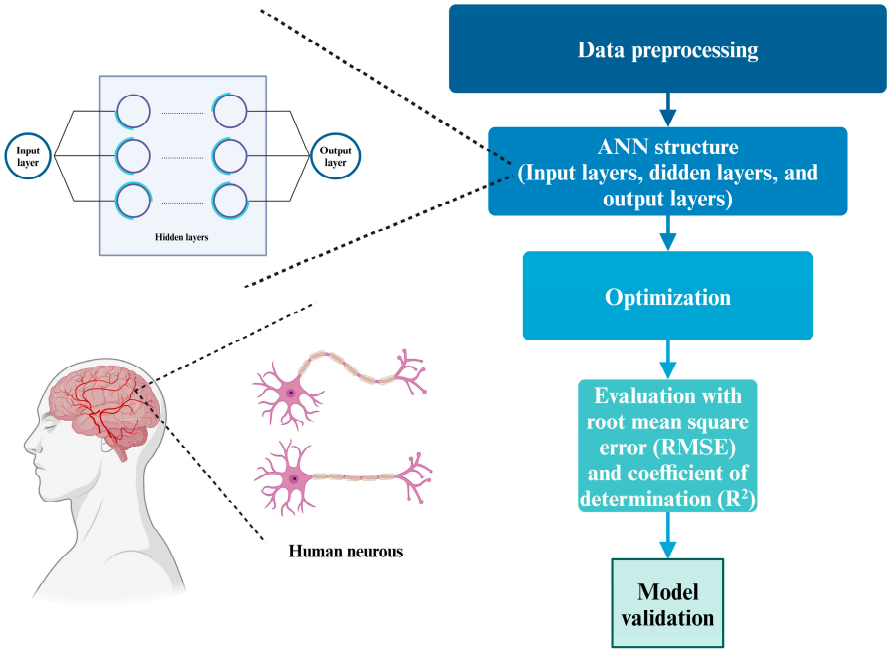


Figure 2. Flow chart of ANN (Created in BioRender.com).

A recent study simplifies the understanding of the materials and methods for RSM and ANNs by investigating a hybrid RSM–ANN–Genetic Algorithm (GA) approach to optimize extraction conditions for bioactive component-rich laver (*Porphyra dentata*) extracts [4]. This research compares and optimizes infusion extraction and ultrasound-assisted extraction using both RSM and the hybrid RSM–ANN–GA methods. The optimization focused on the total phenolic, flavonoid, and amino acid contents, as well as the color value and R-phycoerythrin content. The experimental variables included temperatures (60, 80, and 100 °C) and times (10, 15, and 20 min), and were designed to optimize these parameters in the laver extract. Modeling began with RSM using a three-level factorial design, where the response variables were analyzed based on experimental runs generated by the RSM model. Subsequently, the experimental data from the RSM design points were used to develop the ANN–GA model, identifying the optimal neural network architecture. The extraction conditions were then optimized using statistical analyses based on the RSM and ANN–GA calculations. Similarly, a recent study demonstrated that ANN–GA predictions yield a higher accuracy and align more closely with experimental data compared to RSM-predicted values [5].

3. Optimization Based on Nutrients (Carbohydrates, Proteins, Lipids, and Fatty Acids)

3.1. Carbohydrates

Carbohydrates, being natural organic molecules, primarily consist of carbon, hydrogen, and oxygen, and play a pivotal role in the human body due to their biocompatibility and biodegradability [21]. A better understanding of the relationship between nutrient recovery and ANNs or RSM is summarized in Figure 3. Consequently, carbohydrates and polysaccharides offer several advantages, including their chemical stability, resistance to protein interactions, well-defined chemical structures, ease of formation, water solubility, and compatibility with various cell receptors. These attributes make them highly proficient components in delivery systems [21]. Polysaccharides, widely found among animals, microorganisms, and plants, are well-recognized for their diverse resources [22]. These macromolecules exhibit significant variability in their chemical structures, influenced by factors such as the types of monosaccharide units, their linkages, molecular weights, and the presence of other substituents. Polysaccharides, characterized by their glycosidic bonds linking monosaccharide units, typically possess higher molecular weights, along with diverse structural arrangements. These attributes, like their monosaccharide compositions,

linkages below sugar residues, and solution conformations, contribute to their pivotal roles in numerous physiological activities [23]. In recent years, there has been a growing focus on exploring the biological activities of polysaccharides. These include their immunomodulatory and anti-diabetic properties [22], as well as their anti-tumor, antioxidant, hypotensive, cardioprotective, and prebiotic activities [24]. Furthermore, polysaccharides have found applications in biomaterials, biofuels, and pharmaceuticals over the past few decades [25].

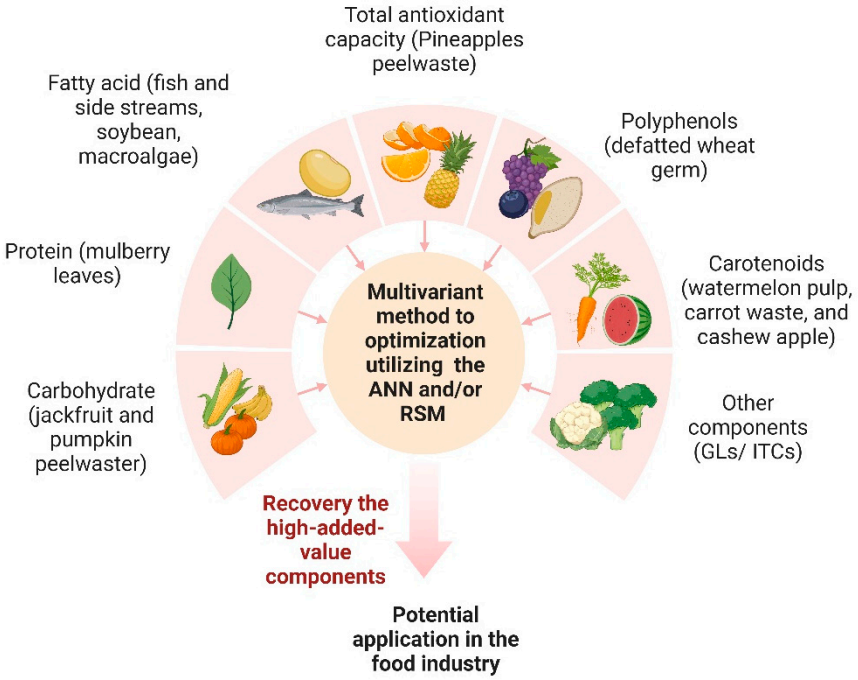


Figure 3. Recovery of high-added-value components from the food industry using the ANNs or RSM optimization method (Created with BioRender.com).

Starch, one of the most abundant polysaccharides, finds global utility in the food industry. RSM with an ANN has been employed to enhance starch extraction processes. Following a comparative analysis, it was found that the RSM exhibited superior efficiency, as evidenced by a higher R^2 and lower average absolute deviation (AAD) during both the design and validation stages [26]. This resulted in a remarkable improvement in the starch yield from *Amorphophallus paeoniifolius* corms, with a yield of 51.76 g/100 g of corm dry weight, representing an increase of 7.61–27.24-fold over previous methods [26]. In another application, the ultrasound-assisted extraction of *Ginkgo biloba* leaves polysaccharides (GBLPs) underwent optimization using RSM, resulting in an optimized GBLP yield of 5.37%. This was achieved with the ultrasonic power set at 340 W, a liquid-to-material ratio of 30 mL/g, and an extraction time of 50 min [27]. Pectin, a naturally occurring biopolymer, holds significant importance in biotechnology and the food industry. It is known for its contributions to enhancing stability, as well as its role as a carrier for protecting the targeted delivery of bioactive compounds [28]. Recent research efforts combined pulsed electric fields (PEFs) with microwave-assisted extraction for pectin polysaccharide extraction from jackfruit waste. This process was optimized and analyzed using both Box–Behnken Design (BBD) and an ANN. The optimized treatment conditions obtained by BBD included 11.99 kV/cm of PEF strength, 4.00 min of PEF treatment time, 647.30 W/g of MAE power density, and 5.00 min of MAE exposure time. Notably, the ANN (R^2 between 0.95 and 0.99, and mean squared error between 0.008 and 0.1) model outperformed the BBD (R^2 between 0.89 and 0.98, and sum of squared error between 0.076 and 0.781) in terms of performance and accuracy [29].

3.2. Proteins

Protein, a vital macronutrient, is witnessing a rapid shift in demand for new sources. Notably, nutrient deficiencies in dairy diets have affected over two billion people, particularly in developing and underdeveloped countries facing challenging circumstances due to such deficiencies [30].

Traditional methods for vegetable protein extraction typically involve alkaline extraction. This process enhances protein solubility in aqueous solutions by disrupting the hydrogen bonds and unfolding the protein matrix under alkaline conditions [3]. However, challenges arise when proteins are bound with substances like cellulose in green-leaved plants, limiting the protein extraction yield [31]. Extraction processes assisted by various novel methods hold significant potential for improving the yield of target products. Ultrasound, for instance, has found extensive applications in food physical processing, particularly for the extraction of macromolecular substances, including proteins [32]. Ultrasound primarily modifies proteins by disrupting water and hydrogen bonds through ultrasonic cavitation and mechanical effects. It also induces alterations in secondary protein structures, leading to increased protein solubility by enhancing protein repulsion [33].

The ultrasound-assisted cellulase degradation (UACD) method was used to extract mulberry leaf protein, and the process parameters were optimized to maximize the protein dissolution amount (PDA) from mulberry leaves. This optimization process combined single-factor experimentation and RSM [34]. Fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM) were employed by previous researchers to analyze the extracted mulberry leaf protein. The results demonstrated that under the optimized conditions (a pH value of 7.2, an ultrasound temperature of 35.0 °C with an enzyme dosage of 4.2%, and an ultrasound time of 10.0 min), the experimentally verified PDA value was 13.87 mg/mL, closely aligning with the predicted value of 13.5 mg/mL [34].

3.3. Lipids and Fatty Acids

Previous studies have collectively provided valuable insights into lipid oxidation, which encompasses autoxidation, thermal oxidation, enzymatic oxidation, and photo-oxidation. These processes typically involve the utilization of free radicals or reactive species as intermediates. A better understanding of the relationship between nutrient recovery and ANNs or RSM is summarized in Table 1.

In a prior study, lipids were comprehensively classified and defined, resulting in their categorization into eight representative groups. These include fatty acids (FAs), glycerolipids (GLs), glycerophospholipids (GPs), sphingolipids (SPs), sterol lipids (STs), prenol lipids (PRs), saccharolipids (SLs), and polyketides (PKs). The classification of lipids has expanded to encompass over 47,000 variations, posing significant challenges in the analysis of these diverse lipid types and complex lipid structures [35]. In general, oils extracted from sources such as fish, shellfish, microalgae, and plants are characterized by exceptionally high levels of polyunsaturated fatty acids, rendering them prone to instability [36]. Lipid oxidation, as elucidated in prior studies, is a multifaceted process. Unsaturated fatty acids generate unstable products during reactions, which subsequently decompose and polymerize into secondary products [36]. Furthermore, to enhance the mechanical and barrier properties of soybean aqueous extract-based films, process parameters were optimized using RSM, and film properties were predicted using an ANN. The resulting film exhibited outstanding antioxidant properties and a superior morphology [37]. The ANN approach was also employed to determine the optimum culture conditions for biodiesel production. This optimization yielded optimal conditions, including a pH of 7 after 16 days of cultivation, resulting in total lipid, unsaturated lipid, and biomass concentrations of 1266.33 mg/L, 1072.058 mg/L, and 2663.34 mg/L, respectively [38].

Table 1. Nutrient recovery from food processing using ANN or RSM as multifactorial decision tools for optimization.

Target Compounds Are Taken Into Account	Type of Multifactorial Design	Source	Optimal Conditions	Reference
Bioactive polysaccharides	RSM; the genetic algorithm–artificial neural networks (GA–ANN)	*Bletilla striata*	52 °C, 167 min, and 0.01 mol/L NaOH (alkali-assisted extraction)	[39]
Carbohydrate	RSM	Folium Ginkgo	Water/solid ratio of 4, extraction of 95 °C for 120 min	[40]
Maximum reducing sugar	ANN; RSM	Pumpkin peel waster	Hydrolysis time of 120 min, loading substrate of 17.5 g/L, α-amylase concentration of 7.5 U/g, amylglucosidase concentration of 56.40 U/mL, fermentation temperature of 45 °C, pH of 5.06, shaking speed of 188.5 rpm, and yeast concentration of 1.95 g/L	[41]
Polysaccharides	RSM	Zagros oak leaf	Ultrasonic power of 205.8 W, extraction temperature of 81.9 °C, extraction time of 55.6 min, and ratio of water to raw material of 23.4 (ultrasonic-assisted extraction).	[42]
The optimization of microwave-assisted phosphorylation modification of MBP and its effect on functional and structural characterizations	RSM	Mung bean protein (MBP)	STP/protein ratio of 0.063 g/g, microwave power of 590 W, microwave time of 155 s, and pH of 7.8.	[43]
Higher biomass productivity, lipid content, and productivity	RSM	Dunaliella parva (marine microalga)	Optimized medium containing 0.63 g/L of nitrogen, 0.02 g/L of phosphorus, and 1.61 M of NaCl	[44]
Algal lipids	RSM	Marine macroalgae	Extraction temperature of 72 °C, solvent-to-algae ratio of 5:1, algal particle size of 0.16 mm, and extraction time of 134 min.	[45]
Methyl esters yield from Anacardium occidentale kernel oil	RSM and ANN	Anacardium occidentale kernel oil	At modeling conditions, including temperature of 65 °C, mole ratio of 7:1, catalyst concentration of 2.5 wt %, stirring speed of 600 rpm, and time of 150 min, RSM-predicted and validated methyl ester yields were 94.82%, and 94.70%, respectively. In contrast, ANN-predicted and validated yields were 93.21% and 93.33%, respectively.	[46]
n-3 Long-chain polyunsaturated fatty acids (LC-PUFAs)	RSM	Tuna oil	Optimal conditions for hydrolysis reactions were reaction temperature of 54 °C, enzyme load of 3%, reaction time of 6 h, and mass ratio of water to tuna oil of 1.5:1.	[47]

Table 1. *Cont.*

Target Compounds Are Taken Into Account	Type of Multifactorial Design	Source	Optimal Conditions	Reference
Higher retention of bioactive compounds	Artificial neural network–particle swarm optimization (ANN–PSO) and RSM	Finger mille (*Eleusine coracana*)	ANN–PSO modeling outperformed RSM in process prediction, and optimization conditions for ANN–PSO were a 76% amplitude, water-to-grain ratio (W:G) of 3.5:1, and 17.5 min treatment time at 40 kHz.	[48]
Monitoring the lipid oxidation and fatty acid profile of oil using algorithm-assisted surface-enhanced Raman spectroscopy	ANN and principal component analysis (PCA)	Sunflower oil (SO)	Developed Raman and SERS methods could detect low levels of 2% trans fats with a sensitivity of 94% and 97%, respectively.	[49]
Fatty acid and tocopherol content	ANN and random forest regression (RFR)	Rapeseed (*Brassica napus* L.) oil	RFR and ANNs are prosperous for modelling rapeseed seed quality, and the ANN model predicted erucic acid with highest accuracy.	[50]

4. Optimization Based on Antioxidant Response (Total Antioxidant Capacity, Polyphenols, Carotenoids)

4.1. Total Antioxidant Capacity (TAC)

It is widely accepted that natural antioxidants, including carotenoids (such as carotenes and xanthophylls), polyphenols (including flavonoids, phenolic acids, and anthocyanins), and vitamins (such as vitamin C and E), play a pivotal role in various biological functions. Notably, these compounds exhibit properties such as antifungal, antibacterial, and anti-inflammatory effects [51]. The antioxidant capacity of natural compounds can be evaluated based on five key characteristics: their reduction potential, the fate of the resultant antioxidant-derived radical compound, their capacity for the stabilization and delocalization of unpaired electrons, their reactivity with other antioxidant compounds, and their potential for chelating transition metals. These factors collectively determine their antioxidant effectiveness [52]. Previously published peer-reviewed research data have laid the foundation for assessing the antioxidant potential of natural products. This assessment forms the basis for recommendations regarding the best antioxidant-rich foods and the ranking of antioxidant-rich plants. Contrary to becoming reactive free radicals, antioxidants mitigate reactivity by donating electrons to free radicals, a process considered beneficial for human health. The antioxidant activity can be quantified using assays such as the oxygen radical absorbance capacity (ORAC) assay. This method relies on the changes in fluorescence during the reaction between fluorescein sodium and peroxyl radicals ($ROO^{\cdot}$), with a decrease in fluorescence indicating the extent of antioxidant activity [53].

A comparative assessment of the performance of the ANN and RSM was conducted to optimize microwave-assisted extraction (MAE) and evaluate the antioxidant capacity of extracts obtained from *Vernonia cinerea* leaves. The ANN models exhibited superior performances, as evidenced by higher R^2, lower RMSE, and absolute average deviation (AAD) values. It is worth noting that both the ANN (0.9912 for yield, 0.9928 for DPPH, 0.9928 for DPPH, and 0.9944 for ABTS in R^2, respectively) and RSM (0.9590 for yield, 0.9888 for DPPH, 0.9891 for DPPH, and 0.9944 for ABTS in R^2, respectively) demonstrated commendable estimation capabilities [54]. Similarly, the impact of ultrasound-assisted extraction (UAE) parameters, including the extraction time, acetone concentration, and solvent-to-solid ratio, on kidney bean extraction was investigated and optimized using RSM and ANNs (ANN–radial basis function (RBF) and ANN–multi-layer perception (MLP)). The optimization process resulted in the attainment of maximum values for two

output parameters, namely, 917.2 mg GAE/100 g DW of total phenolic content (TPC) and 56.03 µmol Trolox/g DW of ABTS (2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)) antioxidant activity. These optimal conditions were determined to be a solvent-to-solid ratio of 37 mL/g, an acetone concentration of 53%, and an extraction time of 70 min [55]. Furthermore, it is noteworthy that the ANN model outperformed the RSM model in optimizing kidney bean antioxidants, with estimative values demonstrating a hierarchy of prediction accuracy: ANN–RBF (TPC: 0.9950 for R^2, 8.530 for RMSE, and 0.436 for AAD (%); and ABTS: 0.9885 for R^2, 1.010 for RMSE, and 0.119 for AAD (%) > ANN–MLP (TPC: 0.9851 for R^2, 14.82 for RMSE, and 1.499 for AAD (%); and ABTS: 0.9764 for R^2, 1.195 for RMSE, and 0.139 for AAD (%) > RSM (TPC: 0.9791 for R^2, 17.10 for RMSE, and 1.862 for AAD (%); and ABTS: 0.9666 for R^2, 1.275 for RMSE, and 0.153 for AAD (%).

4.2. Polyphenols

Non-enzymatic antioxidants, including phenolics, tocopherols, carotenoids, and vitamin C, alongside the body's enzymatic systems, such as catalase, superoxide dismutase, and glutathione peroxidase, collectively safeguard the human body against oxidative damage. Numerous studies have explored the close association between the total phenolic content (or individual phenolics) and overall antioxidant activity [56]. The research presented thus far offers compelling evidence that polyphenols derived from grains have a beneficial impact on the proliferation of beneficial intestinal bacteria. Moreover, plant polyphenols have demonstrated their potential as quorum-sensing inhibitors, effectively regulating the expression of virulence factors in harmful intestinal bacteria [57].

Polyphenols are characterized by the presence of one or more aromatic rings linked to one or more hydroxyl groups. These compounds are produced as secondary metabolites in plants, boasting a diverse array of over 800 structures, which include phenolic acids, flavonoids, tannins, and stilbenes [58]. Polyphenols exhibit a wide range of functionalities, encompassing antioxidant properties, anticancer activities, and anti-inflammatory effects. Furthermore, they can modulate transcription factors such as Nrf-2 and NF-kB, thereby amplifying their bioactive effects and mitigating oxidative stress [59].

Due to the intricate nature of phenolic compounds, the efficacy of complete extraction processes is influenced by the preparation methods. As a result, there is no universally accepted protocol for phenolic extraction processes [60]. The studies presented thus far underscore the importance of establishing an optimization process for phenolic extraction. This optimization should take into account factors such as the availability of techniques, the specific analysis objectives, the targeted compounds, and the nature of the sample, all of which should be considered comprehensively [60].

Previous research has harnessed the RSM to optimize the extraction of polyphenolic compounds from tomatoes, successfully predicting the optimal extraction conditions [61]. Similarly, RSM design and analyses were employed in the investigation of ultrasound-assisted extraction (UAE) for antioxidant compounds, total phenolics, and soluble proteins from bitter gourd (*Momordica charantia*) [62]. The pulsed-mode sonication approach yielded optimal bioactive compound extraction, resulting in an antioxidant activity of 77.9%, a total soluble protein content of 42.1 mg/1000 mL, and a total polyphenol content of 104.5 mg GAE/g. These optimal conditions included an extraction time of 12 min, a temperature of 68.4 °C, and a bitter gourd to water ratio of 0.25 g/mL. To assess the predictive capabilities of the developed models from RSM and ANN, various statistical parameters, including R^2, AAD, and RMSE, were considered regarding phenolic compounds and antioxidant activity [63]. In a separate study, the correlation between RSM and ANNs in predicting bioactive compounds from unripe *Musa acuminata* peel was explored. The ANN model demonstrated a superior predictive potential, as indicated by its higher R^2 (R^2_{RSM} = 0.9742, R^2_{ANN} = 0.9803), lower AAD (AAD_{RSM} = 5.64%, AAD_{ANN} = 3.38%), and lower RMSE ($DMSE_{RSM}$ = 3.07, $DMSE_{ANN}$ = 2.69) [63].

4.3. Carotenoids

Carotenoids are recognized as pigments accumulated in the chloroplasts and chromoplasts of various organisms, including plants, bacteria, fungi, photosynthetic algae, animals, and shellfish [64]. These lipid-soluble tetraterpenoids consist of 40 carbon atoms with multiple double bonds and are predominantly categorized into two groups: carotenes. Notable examples include β-carotene and lycopene [64]. Carotenoids play pivotal roles in the physiology of animals, encompassing functions such as cancer prevention, immune system modulation, regulation of growth factors and intracellular signaling pathways, control of metabolic activity in cells, offering photoprotection against UV radiation, and serving as precursors for the visual pigment retinol.

The optimization of microwave-assisted carotenoid extraction was achieved through the application of RSM. The study focused on determining the ideal microwave power, extraction time, and oil-to-waste ratio for maximizing carotenoid recovery. The optimized conditions were identified as 165 W of microwave power, 9.39 min of extraction time, and an oil-to-waste ratio of 8.06:1 g/g, resulting in a carotenoid recovery rate of 77.48% [65]. In another investigation, the valorization of waste apricot flesh (WAF) was explored, with the extraction conditions optimized using the Box–Behnken design. This approach led to the attainment of a total carotenoid content (TCC) of 42.75 mg/100 g of dried weight under the following optimized conditions: 60 min of extraction time, a temperature of 41.53 °C, 200 W of power, and a liquid-to-solid ratio of 0.10 g/mL [66]. The comparison of the extraction yield of chlorophylls and carotenoids from the wet and heat-dried isolated microalgal (*Chlorella thermophila*) biomass using ethanol has been optimized with ANN, and the result found that chlorophyll extraction yield was observed to be 2.7 fold higher from wet biomass than dry biomass while carotenoid yield was 6.7 fold higher and the highest chlorophyll yield (∼60 mg/g-dry biomass) was observed at 6 min of homogenization time, 10,000 rpm, 1 mg/mL of solid solvent ratio, and 58 °C of solvent temperature from wet biomass with extraction efficiency of approximately 94% [67].

While certain methods have been developed for carotenoid extraction, they are often associated with drawbacks such as high costs, extended extraction times, and the use of organic solvents, which can impose limitations on the efficiency of carotenoid extraction [68]. In this context, the valorization of food side streams offers a promising solution to address both environmental and economic challenges while meeting the demand for natural carotenoids. A better understanding of the relationship between the antioxidant compounds of the ANN and RSM is summarized in Table 2.

Table 2. Antioxidant compounds are used to optimize antioxidant properties from food processing using the Artificial Neural Networks (ANNs) or Response Surface Methodology (RSM).

Target Compounds	Type of Multifactorial Design	Source	Optimal Conditions	Reference
Antioxidant activity	RSM	Pineapple peel waste	Solvent to substrate ratio of 20:1 mL/g, microwave power of 600 W, and extraction time 40 min	[69]
Anthocyanins	RSM	*Purple-heart* Radish	Optimized conditions: 25.0 g/100 g cellulase dosage, 60 mL/100 mL ethanol concentration, pH of 4.0, temperature of 50 °C, extraction time of 7.15 min, 80 mesh particle size, and 60:1 mL/g liquid-to-material ratio	[70]
Total phenolic content, total flavonoid content, and antioxidant activity	RSM	Buckwheat (*Fagopyrum esculentum Moench*)	Sample to solvent ratio of 1:35, extraction time of 49.045 min	[71]

Table 2. *Cont.*

Target Compounds	Type of Multifactorial Design	Source	Optimal Conditions	Reference
Polyphenols extraction with ultrasound-assisted	RSM and ANN	Domestic garlic (*Allium sativum* L.)	Extraction time of 13.5 min, temperature of 59.0 °C, methanol concentration of 71.0% and solvent-to-solid ratio of 20.0 mL/g	[14]
Polyphenols	RSM and ANN	Defatted wheat germ	ANN showed minor advantage in fitting quality; RSM provided further insights via influence analysis. Optimization conditions for RSM were ethanol concentration of 58.0%, extraction time of 14.5 min, liquid-solid ratio of 25 mL/g, and irradiation power of 800 W; optimization conditions for ANN were ethanol concentration of 50.0%, extraction time of 15 min, liquid-solid ratio of 25 mL/g, and irradiation power of 400 W.	[72]
Polysaccharides and polyphenols	RSM and ANN	*Schisandra Chinensis*	ANN displayed better prediction capability than RSM. Optimal high-pressure conditions in ANN were liquid-to-material ratio of 87.1 mL/g, pressure of 4.8 MPa, temperature of 60.9 °C, and time of 16.0 min.	[73]
Carotenoid compounds	RSM	Watermelon pulp	6.025 g/g of Span 20/pulp sample-(S), 8.827 of glycerol/S, temperature of 38.75 °C, and time of 18.75 min (Extraction-1); 1.13 g/g of SMP/S, 7.53 g/g of Salt/S, 66.25 °C and 46.3 min (Extraction-2).	[74]
Carotenoids recovery	RSM	Carrot waste	Ultrasonic power of 213 W, extraction time of 36.0 min, and temperature of 44.6 °C	[75]
Carotenoid extraction	RSM	Cashew apple	38% acetone, 30% ethanol, and 32% petroleum ether for conventional extraction (CE); 44% acetone and 56% methanol for ultrasonic-assisted extraction (UAE)	[76]
Carotenoid composition	RSM	Paprika oleoresin	Static time of 28 min, extraction temperature of 78 °C, and 2 cycles for accelerated solvent extraction (ASE)	[77]

5. Optimization Based on Other Compounds (Glucosinolates (GLSs)/ Isothiocyanates (ITCs)

Glucosinolates (GLSs), well-recognized as a significant group of sulfur-rich anionic secondary metabolites, are prevalent in plants belonging to the *Brassicaceae* family [78–80]. Among these plants, the *Brassicaceae* family is renowned for having the highest concentrations of GLSs, with examples including horseradish, broccoli, wasabi, and various other species [81]. Prior studies have delved into optimizing the hydrolysis of GLSs found in Brassica vegetables to produce isothiocyanates [82]. Furthermore, efforts have been made to enhance the myrosinase activity sourced from select Brassica vegetable varieties. In this regard, an optimal myrosinase extract was achieved to facilitate the production of sulforaphane from glucoraphanin. Notably, the highest myrosinase activity was attained

under specific conditions, including a vacuum pressure of 40 mbar and a temperature of 40 °C, with a duration of 90 min, as identified in this research [83].

Previous studies collectively offer valuable insights into the fermentation products generated through microbial activity, specifically the conversion of sugar into lactic acid. Cruciferous vegetables have a long history of being utilized as fermented products, and the complete fermentation of GLSs occurs during this process [81]. A comparison between ANNs and RSM for optimizing fermentation media in the production of the biopolymer scleroglucan has been explored. The yield of scleroglucan (g/L) was modeled and optimized based on four independent variables, namely sucrose, yeast extract, K_2HPO_4, and $MgSO_4$ concentrations (g/L). The ANN approach demonstrated superior accuracy, with an average error of 6.5% compared to 20.0% for RSM. Furthermore, the correlation coefficient values were 0.98 for the ANN and 0.89 for RSM, highlighting the enhanced precision of the ANN in this context [84]. Additionally, the degradation products of GLSs possess bioactive properties. These hydrolysis products encompass isothiocyanates (ITCs), thiocyanates, oxazolidinethiones, epithionitriles, and nitriles, each exhibiting distinct bioactive attributes [85,86].

The hydrolysis of sinalbin to produce 4-hydroxy benzyl-isothiocyanate (4-OH-ITC) from yellow mustard seeds (*Sinapis alba*) was systematically optimized based on myrosinase activity utilizing RSM. The highest hydrolysis conversion of sinalbin to 4-OH-ITC, reaching 20.1 mg/g of seeds, was achieved under optimal hydrolysis conditions. These conditions included homogenization for 5 min at a pH of 5.8, adding 4.5 mM of ascorbic acid, and incubating at 51.0 °C for approximately 15.8 min [87]. RSM, with its establishment of mathematical models and consideration of variable parameters, emerged as an efficient optimization methodology for this process. In another application of RSM, the optimization of folate extraction from date palm fruits involved enzymatic de-pectinization. The highest extraction yield was attained under optimized conditions, which included 47.7 U of pectinase, an incubation temperature of 40 °C, and an incubation time of 38 min [88].

The optimization of the fermentation process for xylitol production from areca nut husk involved the utilization of both ANNs and RSM. This optimization considered five variable parameters: agitation (rpm), pH, temperature (°C), time (h), and xylose concentration (g/L). The outcomes from the ANN model demonstrated a significantly higher level of robustness and precision in estimating the dependent variables when compared to the RSM model, and the maximum concentration of xylitol achieved was approximately 9.96 g/L under the designed conditions [89]. The studies conducted thus far shed light on the enhanced accuracy in modeling and prediction offered by ANN models when compared with the use of RSM models. Researchers have attributed this phenomenon to the ANN's capacity for sensitivity analysis and the absence of a need for the prior specification of a suitable fitting function. In contrast, RSM is structured and valuable for estimating the likelihood of interactions among different components [89].

6. Application for Conventional and Innovative Extraction Approaches

6.1. Conventional Extraction Approaches

Traditionally, the extraction technique often deviates from the ideal, resulting in the use of conventional extraction programs that rely on a multitude of solvents and, at times, manual procedures that vary depending on the investigator and company's preferences [90]. To illustrate this, when extracting polyphenols, one can choose from a range of conventional methods such as Soxhlet extraction, maceration, infusion, serial exhaustive extraction, percolation, and decoction [91]. Typically, organic solvents like water, methanol, n-hexane, ethanol, acetone, chloroform, propanol, and ethyl acetate are employed due to their ease of mixing and high extraction yields.

Normally, the technique is not consistent with the ideal, as a consequence of the fact that the traditional extraction program is designed with a large number of solvents and some accidental manual procedures depend on the investigator and the company decision maker [90]. As an illustration, in the extraction of polyphenols, there are various choices for

conventional methods, including Soxhlet extraction, maceration, infusion, serial exhaustive extraction, percolation, and decoction [91]. Generally, water, methanol, n-hexane, ethanol, acetone, chloroform, propanol, and ethyl acetate are used as the solvent for extracting, as those organic solvents have the advantage of easily mixing easily and have a high extraction yield.

A previous research article has identified several conventional plant extraction methods, including maceration extraction (ME), infusion, digestion, decoction, percolation, and Soxhlet extraction [92]. Over the last few decades, it has become widely acknowledged that these traditional extraction techniques offer high yields without requiring complex instrumentation, such as magnetic stirring extraction or advanced maceration and Soxhlet extraction methods [93]. However, it is important to recognize that there are significant drawbacks associated with prolonged extraction times, substantial organic solvent usage, and potential environmental impacts [93]. As a result, there is a growing need for more sustainable and environmentally friendly extraction practices. While the extraction of high-added-value compounds using organic solvents showcases remarkable efficiency without the need for advanced equipment, its application in food products is constrained by the challenges of its high costs, potential toxicity, and the risk of residual contamination in the final products.

6.2. Innovation Processing Extraction Approaches

These novel extraction technologies have great potential for optimized extractions in the food industry. For instance, previous studies have demonstrated that subcritical water (SW) has a miraculous characteristic where it can remain in the liquid state under the boiling-point temperature (100.0 °C) and the critical-point temperature (374.0 °C) [94]. The SWE technology has the advantage of being chemical-free, as well as having shorter times and lower costs, and is characterized by associated advancements in extracting bioactive compounds [95]. Additionally, supercritical fluid extraction (SFE) exhibits an extraordinary solvating capability akin to hexane. This property finds applications in the recovery of high-purity, thermo-labile compounds, which are exemplified by carotenoid extracts [96].

Despite the existence of various parameters or independent variables, such as the solvent composition, extraction temperature, solvent-to-solid ratio, and particle size, which can influence the extraction process and its dependent variables, the predicted responses obtained from the ANN model demonstrate a high level of accuracy. This is evidenced by a lower relative deviation and RMSE, as well as a higher R^2 value [19]. The utilization of conventional methods for extracting high-value compounds from foods and food by-products presents several drawbacks. Some of the most common issues include a low extraction efficiency, extended extraction times, chemical consumption, and environmental hazards. However, innovative and eco-friendly technologies have emerged to overcome these limitations. These include enzyme-assisted extraction (EAE), pulsed electric field (PEF), SFE, accelerated solvent extraction (ASE), high-pressure processing (HPP), ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), subcritical water extraction (SWE), and pressurized liquid extraction (PLE) [95]. As an example of the application of such innovative techniques, UAE was employed to recover phytocompounds from dragon fruit peel, and the optimization process combined an ANN with genetic algorithms (GAs). The optimized conditions included an ultrasonic temperature of 60.0 °C, a solvent-to-sample ratio of 25:1 mL/g, a solvent concentration of 60%, and an ultrasonic treatment time of 20.0 min. These conditions are suitable for industrial implementation and offer accurate predictions and estimations for operational purposes [97].

While both RSM and ANNs offer specific advantages in terms of structured experimentation and handling complex datasets, other methods, such as genetic algorithms, may provide more flexibility in exploring a wider parameter space without relying on predetermined models. A comparative analysis suggests that a hybrid approach, integrating these different methods, may offer the most robust solutions for optimizing food processing

operations. A better understanding of the application of ANNs and RSM for conventional and innovative extraction approaches is illustrated in Figure 4.

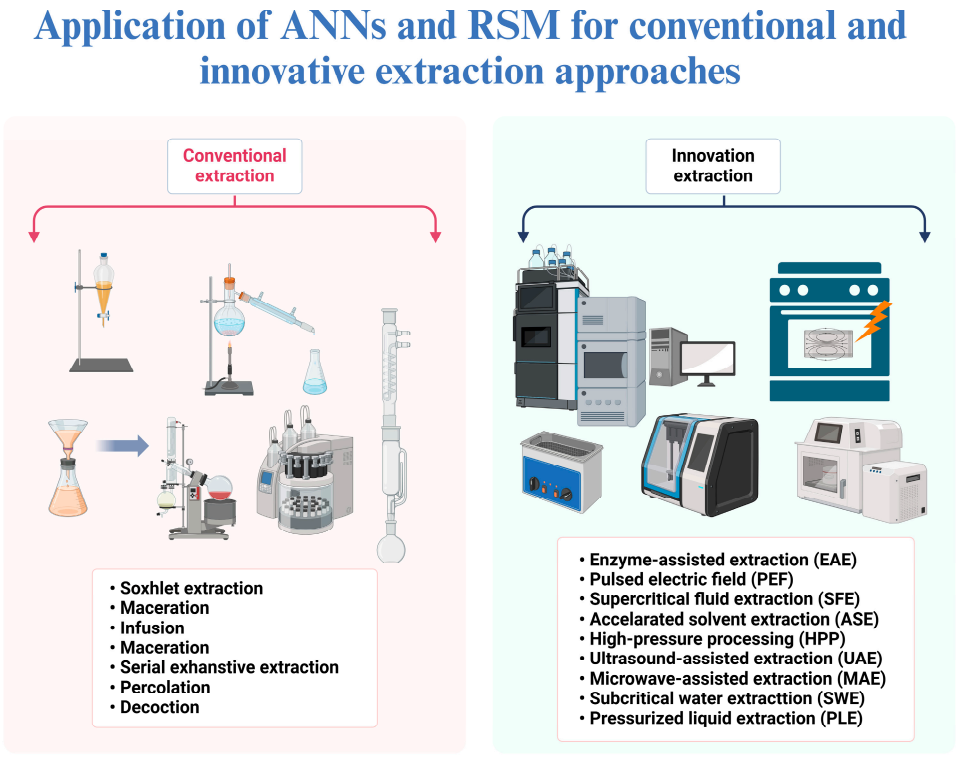


Figure 4. Application of Artificial Neural Networks (ANNs) and Response Surface Methodology (RSM) for conventional and innovative extraction approaches (Created with BioRender.com).

7. Advantages and Drawbacks

7.1. Advantages

ANNs offer a distinct advantage by exhaustively exploring all potential scenarios and selecting optimal parameters, eliminating the need for repetitive experimentation when testing new processing conditions [19]. In contrast to many traditional chemometric methods that struggle to accommodate nonlinear trends in data, ANNs excel in effectively addressing and navigating these nonlinear patterns in experimental data, consistently yielding highly favorable results [19,98]. This adaptability sets ANNs apart from other modeling approaches. When compared to conventional regression or classification analyses, ANNs demonstrate remarkable precision in predicting response variables, optimizing processes, and requiring fewer experimental trials to achieve reliable outcomes [54,99].

In the realm of food processing, while RSM has historically been a widely adopted modeling tool, ANNs have emerged as an alternative method with superior performance, exceptional predictive capabilities, and the ability to model complex nonlinear problems [100]. While RSM and ANNs have been widely used for optimizing various extraction processes, a critical analysis reveals that the effectiveness of these methods can vary significantly depending on the context, such as the type of raw material, solvent, and processing conditions. The reviewed studies demonstrate a consistent trend, with RSM providing a structured approach for initial experimentation, whereas ANNs excel in handling more complex, nonlinear relationships.

7.2. Drawbacks

It is widely acknowledged that certain key parameters, namely temperature, pH, solvent selection, and duration, hold significant importance in conventional extraction processes [101]. In the context of protein extraction, suboptimal heating conditions can lead to excessive protein denaturation, resulting in proteins with compromised functional

and nutritional properties. Similarly, high pH conditions may induce multiple protein aggregations, further affecting the quality of the extracted proteins [102].

While the SC-CO_2 technique eliminates the need for chemical solvents in carotenoid extraction, it has been observed that this method tends to recover more chlorophylls than carotenoids, ultimately impacting the purity of the extract [103]. Remarkably, recent research has highlighted a significant drawback of ANN modeling: the "black box" nature of the model, which makes it challenging to discern the exact reasons behind specific outputs [19]. Furthermore, it is worth mentioning that ANNs consume a multitude of statistics, potentially numbering in the thousands or millions, during the overfitting process, setting them apart from traditional machine learning algorithms [19]. Many of the studies reviewed have limitations related to their specificity with respect to local conditions, such as the particular raw materials, solvents, and equipment in the studies, which may not be directly transferable to other contexts. This raises concerns about the generalizability of the findings, highlighting the need for further research to validate these optimization methods across different scenarios.

8. Potential Scale-Up and Industrial Applications

8.1. Potential Application of RSM and ANNs in the Food Process Industry

Some attempts have been made to introduce mechanization into the continuous food industry. In one such endeavor, the Box–Behnken (BBD) design and ANNs were employed to optimize the cocoa pod breaking and bean extraction process across various parameters. The results indicate the superior performance of the ANN design over the BBD approach [11]. Under the optimized conditions, which included a roller speed of 360 rpm, a pod size of 160 mm, and an inclination angle of 45°, remarkable outcomes were achieved. These included a maximal capacity (636.8 kg/h), outstanding beans separation efficiency (86.4%), high shelling efficiency (96.3%), excellent machine efficiency (96.78%), minimal energy consumption (10.54 kJ), and a negligible percentage of beans damaged (<1%) [11].

ANNs have found applications in various aspects of food processing [1], including drying, extraction, separation techniques, extrusion, fermentation, high-pressure processing (HPP), and power technology. Moreover, ANNs have been effectively employed to assess and predict food quality and properties, encompassing their chemical composition, nutrient analysis, texture and rheology, color evaluation, thermal conductivity measurement, classification, and quality control, as extensively documented in prior research [1].

An experimental and theoretical investigation was conducted to study shelled corn drying in a microwave-assisted fluidized bed dryer. The study involved four levels of air temperature (30.0, 40.0, 50.0, and 60.0 °C) and six levels of microwave power (0, 180.0, 360.0, 540.0, 720.0, and 900.0 W) using a ANN for prediction. The research also assessed the impact of uncertainties in output experimental data and ANN prediction values on the RMSE, which resulted from minor random errors within a range of ±5.0% [104]. In another study, plum pomace lyophilizate (PPL) at concentrations of 2.0–10.0%, sugar (sucrose) at concentrations of 10.0–15.0%, and amidated low-methoxy pectin (LMA) at concentrations of 0–0.2% were considered as independent variables for the optimization of product formulations. The optimal quality parameters were achieved with 10.0% PPL, 15.0% sucrose, and 0.0% LMA [105]. The findings from these studies have significant implications for the food industry. By optimizing the recovery of high-value compounds through the integrated use of RSM and ANNs, these studies not only enhance efficiency and yield but also contribute to more sustainable processing practices. These advancements align with the growing demand for environmentally responsible food production methods.

The optimization methods discussed in this review, while useful for practical applications, also provide valuable insights for food process engineering. The ability to optimize extraction processes is not only relevant to production efficiency but also to the design of new processes and equipment, making these findings applicable to both academic research and industrial practice.

8.2. Potential Application of RSM and ANNs in Addition to the Food Process

In addition to their applications in food processing, both RSM and ANNs have found potential applications in other areas of the food industry, including food quality, food safety, and food texture characteristics. Certifying the varieties and origins of extra virgin olive oil presents a significant challenge due to various factors influencing its properties, such as olive varieties, climatic conditions, and variations in production and storage methods. In a previous study, the application of an ANN successfully analyzed extensive datasets, achieving remarkable accuracy rates and exceeding 99% in certain instances [106]. Artificial intelligence (AI), when integrated with diverse data sources, is emerging as a transformative technology capable of swiftly addressing food safety concerns. Recent research has indicated that specific AI techniques may be more suitable for certain food safety applications than others [107]. The sensory attributes of apples, including their flavor, texture, color, and mouthfeel, are significantly affected by storage temperatures. To predict shelf life, prior research employed both the Partial Least Squares (PLS) and ANN techniques. The results demonstrate that lower storage temperatures are more effective in preserving apple color, pulp firmness, and the release of volatile compounds [108]. Furthermore, the ANN model, renowned for its nonlinear capabilities, proves to be a valuable and effective tool for predicting the shelf life of apples under both temperature settings. The results demonstrate that the integrated use of RSM and ANNs not only improves the accuracy of predictive models, as evidenced by higher R^2 and lower RMSE values, but also offers a more sustainable and efficient approach to food processing, which has not been previously documented in the literature.

9. Conclusions and Prospects

This review has extensively explored the application of multivariate methods, particularly Response Surface Methodology (RSM) and Artificial Neural Networks (ANNs), in optimizing the recovery of high-added-value compounds in the food industry. Our findings underscore these methods' significant role in enhancing the efficiency, accuracy, and sustainability of food processing techniques. The superior predictive capabilities of ANNs, as evidenced by higher R^2 and lower RMSE values compared to RSM, highlight its potential as a leading tool in complex, nonlinear problem-solving scenarios within the food industry. This advantage is critical in addressing the dynamic and multifaceted challenges of food processing, ranging from nutrient preservation to the optimization of sensory qualities.

Furthermore, the application of these methods extends beyond mere technical enhancements; they represent a significant step towards more sustainable food processing practices. By optimizing resource utilization and reducing waste, these methods contribute to a more eco-friendly and economically viable food industry. This aspect is particularly pertinent in the current global context, where sustainability is increasingly becoming a priority. Looking forward, the integration of these methods with emerging technologies like AI and machine learning presents exciting opportunities for further advancements in the field. However, this also brings forth challenges such as scalability, the need for extensive datasets, and the balance between technological innovation and environmental responsibility. This optimized approach can be applied to various sectors within the food industry, including the extraction of bioactive compounds, enhancing the nutritional profile of food products, and improving shelf life, ultimately leading to cost savings and better product quality.

In conclusion, our study reaffirms the relevance and potential of RSM and ANNs in the food industry, not only as tools for optimization but also as catalysts for innovation and sustainability. While these methods have shown promising results, there remains ample scope for future research that could explore the application of this integrated optimization approach to other food matrices or extend the methodology to scale-up studies, ensuring its applicability in industrial settings. Additionally, further experimentation could involve the integration of emerging technologies such as machine learning algorithms to further

enhance their predictive accuracy and process optimization. The future of food processing, guided by these advanced methodologies, looks toward a more efficient, sustainable, and health-conscious industry.

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References

1. Guiné, R.P.F.; Dets, C. The use of artificial neural networks (ANN) in food process engineering. *ETP Int. J. Food Eng.* **2019**, *5*, 15–21. [CrossRef]
2. da Costa, N.L.; da Costa, M.S.; Barbosa, R. A review on the application of chemometrics and machine learning algorithms to evaluate beer authentication. *Food Anal. Methods* **2021**, *14*, 136–155. [CrossRef]
3. Junttila, M.H. Extraction of brewers' spent grain in near subcritical conditions: A method to obtain high protein contents extracts. *J. Agric. Food Res.* **2022**, *10*, 100378. [CrossRef]
4. Aung, T.; Kim, S.-J.; Eun, J.-B. A hybrid RSM-ANN-GA approach on optimisation of extraction conditions for bioactive component-rich laver (*Porphyra dentata*) extract. *Food Chem.* **2022**, *366*, 130689. [CrossRef] [PubMed]
5. Yahya, H.S.M.; Abbas, T.; Amin, N.A.S. Optimization of hydrogen production via toluene steam reforming over Ni–Co supported modified-activated carbon using ANN coupled GA and RSM. *Int. J. Hydrogen Energy* **2021**, *46*, 24632–24651. [CrossRef]
6. Jiménez Carvelo, A.M.; Casado, A.G.; González, M.G.B.; Rodríguez, L.C. Alternative data mining/machine learning methods for the analytical evaluation of food quality and authenticity—A review. *Food Res. Int.* **2019**, *122*, 25–39. [CrossRef]
7. Moldes, O.A.; Mejuto, J.C.; Rial-Otero, R.; Simal-Gandara, J. A critical review on the applications of artificial neural networks in winemaking technology. *Crit. Rev. Food Sci. Nutr.* **2017**, *57*, 2896–2908. [CrossRef]
8. Deng, F.; Lu, H.; Yuan, Y.; Chen, H.; Li, Q.; Wang, L.; Tao, Y.; Zhou, W.; Cheng, H.; Chen, Y.; et al. Accurate prediction of the eating and cooking quality of rice using artificial neural networks and the texture properties of cooked rice. *Food Chem.* **2023**, *407*, 135176. [CrossRef]
9. Onyeaka, H.N.; Nwabor, O.F. Conventional preservation and preservatives. In *Food Preservation and Safety of Natural Products*; Onyeaka, H.N., Nwabor, O.F., Eds.; Academic Press: Cambridge, MA, USA, 2022; pp. 51–56.
10. Li, S.; Tian, Y.; Jiang, P.; Lin, Y.; Liu, X.; Yang, H. Recent advances in the application of metabolomics for food safety control and food quality analyses. *Crit. Rev. Food Sci. Nutr.* **2021**, *61*, 1448–1469. [CrossRef]
11. Srikanth, V.; Rajesh, G.K.; Kothakota, A.; Pandiselvam, R.; Sagarika, N.; Manikantan, M.R.; Sudheer, K.P. Modeling and optimization of developed cocoa beans extractor parameters using box behnken design and artificial neural network. *Comput. Electron. Agric.* **2020**, *177*, 105715. [CrossRef]
12. Ameer, K.; Bae, S.; Jo, Y.; Lee, H.; Ameer, A.; Kwon, J. Optimization of microwave-assisted extraction of total extract, stevioside and rebaudioside-A from *Stevia rebaudiana* (Bertoni) leaves, using response surface methodology (RSM) and artificial neural network (ANN) modelling. *Food Chem.* **2017**, *229*, 198–207. [CrossRef] [PubMed]

13. Khawas, P.; Dash, K.K.; Das, A.J.; Deka, S.C. Modeling and optimization of the process parameters in vacuum drying of culinary banana (Musa ABB) slices by application of artificial neural network and genetic algorithm. *Dry. Technol.* **2016**, *34*, 491–503. [CrossRef]
14. Ciric, A.; Krajnc, B.; Heath, D.; Ogrinc, N. Response surface methodology and artificial neural network approach for the optimization of ultrasound-assisted extraction of polyphenols from garlic. *Food Chem. Toxicol.* **2020**, *135*, 110976. [CrossRef] [PubMed]
15. Draper, N.R. Introduction to Box and Wilson (1951) on the experimental attainment of optimum conditions. In *Breakthroughs in Statistics: Methodology and Distribution*; Kotz, S., Johnson, N.L., Eds.; Springer: New York, NY, USA, 1992; pp. 267–269.
16. Fu, X.; Wang, Y.; Yu, C.; Zhang, H.; Wang, J.; Gao, B. Investigation on thermal-hydraulic performance prediction of a new parallel-flow shell and tube heat exchanger with different surrogate models. *Open Phys.* **2020**, *18*, 1136–1145. [CrossRef]
17. Xu, A.; Chang, H.; Xu, Y.; Li, R.; Li, X.; Zhao, Y. Applying artificial neural networks (ANNs) to solve solid waste-related issues: A critical review. *Waste Manag.* **2021**, *124*, 385–402. [CrossRef] [PubMed]
18. McCulloch, W.S.; Pitts, W. A logical calculus of the ideas immanent in nervous activity. *Bull. Math. Biophys.* **1943**, *5*, 115–133. [CrossRef]
19. Bhagya Raj, G.V.S.; Dash, K.K. Comprehensive study on applications of artificial neural network in food process modeling. *Crit. Rev. Food Sci. Nutr.* **2022**, *62*, 2756–2783. [CrossRef]
20. Huang, Y.; Kangas, L.J.; Rasco, B.A. Applications of artificial neural networks (ANNs) in food science. *Crit. Rev. Food Sci. Nutr.* **2007**, *47*, 113–126. [CrossRef]
21. Kakade, P.; Chatterjee, A.; Pandya, A.; Disouza, J.; Patravale, V. Carbohydrate anchored lipid nanoparticles. *Int. J. Pharm.* **2022**, *618*, 121681. [CrossRef]
22. Mohan, K.; Muralisankar, T.; Uthayakumar, V.; Chandirasekar, R.; Revathi, N.; Ganesan, A.R.; Velmurugan, K.; Sathishkumar, P.; Jayakumar, R.; Seedevi, P. Trends in the extraction, purification, characterisation and biological activities of polysaccharides from tropical and sub-tropical fruits–A comprehensive review. *Carbohydr. Polym.* **2020**, *238*, 116185. [CrossRef]
23. Xu, Y.; Wu, Y.; Sun, P.; Zhang, F.; Linhardt, R.J.; Zhang, A. Chemically modified polysaccharides: Synthesis, characterization, structure activity relationships of action. *Int. J. Biol. Macromol.* **2019**, *132*, 970–977. [CrossRef] [PubMed]
24. Kruchinin, A.G.; Savinova, O.S.; Glazunova, O.A.; Moiseenko, K.V.; Agarkova, E.Y.; Fedorova, T.V. Hypotensive and hepatoprotective properties of the polysaccharide-Stabilized foaming composition containing hydrolysate of whey proteins. *Nutrients* **2021**, *13*, 1031. [CrossRef] [PubMed]
25. Dedhia, N.; Marathe, S.J.; Singhal, R.S. Food polysaccharides: A review on emerging microbial sources, bioactivities, nanoformulations and safety considerations. *Carbohydr. Polym.* **2022**, *287*, 119355. [CrossRef] [PubMed]
26. Karmakar, B.; Saha, S.P.; Chakraborty, R.; Roy, S. Optimization of starch extraction from Amorphophallus paeoniifolius corms using response surface methodology (RSM) and artificial neural network (ANN) for improving yield with tenable chemical attributes. *Int. J. Biol. Macromol.* **2023**, *237*, 124183. [CrossRef] [PubMed]
27. Li, J.; Chen, Z.; Shi, H.; Yu, J.; Huang, G.; Huang, H. Ultrasound-assisted extraction and properties of polysaccharide from Ginkgo biloba leaves. *Ultrason. Sonochem.* **2023**, *93*, 106295. [CrossRef]
28. Rehman, A.; Ahmad, T.; Aadil, R.M.; Spotti, M.J.; Bakry, A.M.; Khan, I.M.; Zhao, L.; Riaz, T.; Tong, Q. Pectin polymers as wall materials for the nano-encapsulation of bioactive compounds. *Trends Food Sci. Technol.* **2019**, *90*, 35–46. [CrossRef]
29. Lal, A.M.N.; Prince, M.V.; Kothakota, A.; Pandiselvam, R.; Thirumdas, R.; Mahanti, N.K.; Sreeja, R. Pulsed electric field combined with microwave-assisted extraction of pectin polysaccharide from jackfruit waste. *Innov. Food Sci. Emerg. Technol.* **2021**, *74*, 102844. [CrossRef]
30. Kumar, M.; Tomar, M.; Potkule, J.; Verma, R.; Punia, S.; Mahapatra, A.; Belwal, T.; Dahuja, A.; Joshi, S.; Berwal, M.K.; et al. Advances in the plant protein extraction: Mechanism and recommendations. *Food Hydrocoll.* **2021**, *115*, 106595. [CrossRef]
31. Liu, J.; Yu, X.; Liu, Y. Effect of ultrasound on mill starch and protein in ultrasound-assisted laboratory-scale corn wet-milling. *J. Cereal Sci.* **2021**, *100*, 103264. [CrossRef]
32. Gani, A.; Ashraf, Z.U.; Noor, N.; Wani, I.A. Ultrasonication as an innovative approach to tailor the apple seed proteins into nanosize: Effect on protein structural and functional properties. *Ultrason. Sonochem.* **2022**, *86*, 106010. [CrossRef]
33. Chen, L.; Zhang, S.-B. Structural and functional properties of self-assembled peanut protein nanoparticles prepared by ultrasonic treatment: Effects of ultrasound intensity and protein concentration. *Food Chem.* **2023**, *413*, 135626. [CrossRef] [PubMed]
34. Fan, W.; Duan, H.; Ren, X.; Guo, X.; Zhang, Y.; Li, J.; Zhang, F.; Chen, J.; Yang, X. Optimization of ultrasound-assisted cellulase degradation method on the extraction of mulberry leaf protein and its effect on the functional characteristics. *Ultrason. Sonochem.* **2023**, *99*, 106561. [CrossRef] [PubMed]
35. Wang, D.; Xiao, H.; Lyu, X.; Chen, H.; Wei, F. Lipid oxidation in food science and nutritional health: A comprehensive review. *Oil Crop Sci.* **2023**, *8*, 35–44. [CrossRef]
36. Zhu, W.; Han, M.; Bu, Y.; Li, X.; Yi, S.; Xu, Y.; Li, J. Plant polyphenols regulating myoglobin oxidation and color stability in red meat and certain fish: A review. *Crit. Rev. Food Sci. Nutr.* **2022**, *64*, 2276–2288. [CrossRef] [PubMed]
37. Kumar, V.A.; Srivastav, P.P.; Pravitha, M.; Hasan, M.; Mangaraj, S.P.V.; Verma, D.K. Comparative study on the optimization and characterization of soybean aqueous extract based composite film using response surface methodology (RSM) and artificial neural network (ANN). *Food Packag. Shelf Life* **2022**, *31*, 100778.

38. Liyanaarachchi, V.C.; Nishshanka, G.K.S.H.; Sakarika, M.; Nimarshana, P.H.V.; Ariyadasa, T.U.; Kornaros, M. Artificial neural network (ANN) approach to optimize cultivation conditions of microalga Chlorella vulgaris in view of biodiesel production. *Biochem. Eng. J.* **2021**, *173*, 108072. [CrossRef]
39. Chen, H.; Wang, B.; Li, J.; Xu, J.; Zeng, J.; Gao, W.; Chen, K. Comparative study on the extraction efficiency, characterization, and bioactivities of Bletilla striata polysaccharides using response surface methodology (RSM) and genetic algorithm-artificial neural network (GA-ANN). *Int. J. Biol. Macromol.* **2023**, *226*, 982–995. [CrossRef]
40. Song, L.; Mei, A.; Hu, Y.; Zhang, J.; Chai, X. Response surface optimized extraction of carbohydrate compound from Folium Ginkgo and its bioactivity. *Carbohydr. Polym.* **2012**, *88*, 112–117. [CrossRef]
41. Chouaibi, M.; Daoued, K.B.; Riguane, K.; Rouissi, T.; Ferrari, G. Production of bioethanol from pumpkin peel wastes: Comparison between response surface methodology (RSM) and artificial neural networks (ANN). *Ind. Crops Prod.* **2020**, *155*, 112822. [CrossRef]
42. Tahmouzi, S. Optimization of polysaccharides from Zagros oak leaf using RSM: Antioxidant and antimicrobial activities. *Carbohydr. Polym.* **2014**, *106*, 238–246. [CrossRef]
43. Hadidi, M.; Jafarzadeh, S.; Ibarz, A. Modified mung bean protein: Optimization of microwave-assisted phosphorylation and its functional and structural characterizations. *LWT-Food Sci. Technol.* **2021**, *151*, 112119. [CrossRef]
44. Fawzy, M.A.; Alharthi, S. Use of response surface methodology in optimization of biomass, lipid productivity and fatty acid profiles of marine microalga Dunaliella parva for biodiesel production. *Environ. Technol. Innov.* **2021**, *22*, 101485. [CrossRef]
45. AlMohamadi, H.; Alamoudi, M.; Yameen, M.Z.; Naqvi, S.R. An integrated approach for the extraction of lipids from marine macroalgae consortium using RSM optimization and thermo-kinetic analysis. *Chemosphere* **2023**, *338*, 139623. [CrossRef] [PubMed]
46. Agu, C.M.; Orakwue, C.C.; Menkiti, M.C.; Agulanna, A.C.; Akaeme, F.C. RSM/ANN based modeling of methyl esters yield from Anacardium occidentale kernel oil by transesterification, for possible application as transformer fluid. *Curr. Res. Green Sustain. Chem.* **2022**, *5*, 100255. [CrossRef]
47. Sun, C.; Chen, Y.; Zhang, H.; Zhu, L.; Li, X.; Liang, S. Preparation of glycerides enriched with n-3 long-chain polyunsaturated fatty acids by Thermomyces lanuginosus lipase-catalyzed hydrolysis of tuna oil. *LWT-Food Sci. Technol.* **2023**, *182*, 114875. [CrossRef]
48. Dubey, A.; Tripathy, P.P. Ultrasound-Mediated hydration of finger millet: Effects on antinutrients, techno-functional and bioactive properties, with evaluation of ANN-PSO and RSM optimization methods. *Food Chem.* **2023**, *435*, 137516. [CrossRef]
49. Nagpal, T.; Yadav, V.; Khare, S.K.; Siddhanta, S.; Sahu, J.K. Monitoring the lipid oxidation and fatty acid profile of oil using algorithm-assisted surface-enhanced Raman spectroscopy. *Food Chem.* **2023**, *428*, 136746. [CrossRef]
50. Rajković, D.; Jeromela, A.M.; Pezo, L.; Lončar, B.; Grahovac, N.; Špika, A.K. Artificial neural network and random forest regression models for modelling fatty acid and tocopherol content in oil of winter rapeseed. *J. Food Compos. Anal.* **2023**, *115*, 105020. [CrossRef]
51. Martí-Quijal, F.J.; Khubber, S.; Remize, F.; Tomasevic, I.; Roselló-Soto, E.; Barba, F.J. Obtaining antioxidants and natural preservatives from Food by-products through fermentation: A review. *Fermentation* **2021**, *7*, 106. [CrossRef]
52. Rice Evans, C.; Miller, N.; Paganga, G. Antioxidant properties of phenolic compounds. *Trends Plant Sci.* **1997**, *2*, 152–159. [CrossRef]
53. Tristán, A.I.; Abreu, A.C.; Sáez, L.M.A.; Peña, A.; Bueno, A.C.; Fernández, I. Evaluation of ORAC, IR and NMR metabolomics for predicting ripening stage and variety in melon (*Cucumis melo* L.). *Food Chem.* **2022**, *372*, 131263. [CrossRef] [PubMed]
54. Alara, O.R.; Abdurahman, N.H.; Afolabi, H.K.; Olalere, O.A. Efficient extraction of antioxidants from Vernonia cinerea leaves: Comparing response surface methodology and artificial neural network. *Beni-Suef Univ. J. Basic Appl. Sci.* **2018**, *7*, 276–285. [CrossRef]
55. Yang, Q.; Gan, R.; Zhang, D.; Ge, Y.; Cheng, L.; Corke, H. Optimization of kidney bean antioxidants using RSM & ANN and characterization of antioxidant profile by UPLC-QTOF-MS. *LWT-Food Sci. Technol.* **2019**, *114*, 108321.
56. Nascimento, K.S.d.; Sattler, J.A.G.; Macedo, L.F.L.; González, C.V.S.; de Melo, I.L.P.; da Silva Araújo, E.; Granato, D.; Sattler, A.; de *Almeida-Muradian*, L.B. Phenolic compounds, antioxidant capacity and physicochemical properties of Brazilian Apis mellifera honeys. *LWT-Food Sci. Technol.* **2018**, *91*, 85–94. [CrossRef]
57. Zhou, Y.; Zhang, Y.; Zhou, M.; Wu, Y.; Guan, X. Study on the interaction between grain polyphenols and intestinal microorganisms: A review. *Food Biosci.* **2023**, *53*, 102536. [CrossRef]
58. Rubab, M.; Chelliah, R.; Saravanakumar, K.; Kim, J.-R.; Yoo, D.; Wang, M.-H.; Oh, D.-H. Phytochemical characterization, and antioxidant and antimicrobial activities of white cabbage extract on the quality and shelf life of raw beef during refrigerated storage. *RSC Adv.* **2020**, *10*, 41430–41442. [CrossRef]
59. Xia, T.; Zhang, Z.; Zhao, Y.; Kang, C.; Zhang, X.; Tian, Y.; Yu, J.; Cao, H.; Wang, M. The anti-diabetic activity of polyphenols-rich vinegar extract in mice via regulating gut microbiota and liver inflammation. *Food Chem.* **2022**, *393*, 133443. [CrossRef]
60. Alara, O.R.; Abdurahman, N.H.; Ukaegbu, C.I. Extraction of phenolic compounds: A review. *Curr. Res. Food Sci.* **2021**, *4*, 200–214. [CrossRef]
61. Li, H.; Deng, Z.; Wu, T.; Liu, R.; Loewen, S.; Tsao, R. Microwave-assisted extraction of phenolics with maximal antioxidant activities in tomatoes. *Food Chem.* **2012**, *130*, 928–936. [CrossRef]
62. Chakraborty, S.; Uppaluri, R.; Das, C. Optimization of ultrasound-assisted extraction (UAE) process for the recovery of bioactive compounds from bitter gourd using response surface methodology (RSM). *Food Bioprod. Process.* **2020**, *120*, 114–122. [CrossRef]
63. Said, F.M.; Gan, J.Y.; Sulaiman, J. Correlation between response surface methodology and artificial neural network in the prediction of bioactive compounds of unripe Musa acuminata peel. *Eng. Sci. Technol. Int. J.* **2020**, *23*, 781–787. [CrossRef]

64. Yu, J.; Liu, X.; Zhang, L.; Shao, P.; Wu, W.; Chen, Z.; Li, J.; Renard, C.M.G.C. An overview of carotenoid extractions using green solvents assisted by Z-isomerization. *Trends Food Sci. Technol.* **2022**, *123*, 145–160. [CrossRef]
65. Elik, A.; Yanık, D.K.; Göğüş, F. Microwave-assisted extraction of carotenoids from carrot juice processing waste using flaxseed oil as a solvent. *LWT-Food Sci. Technol.* **2020**, *123*, 109100. [CrossRef]
66. Suo, A.; Fan, G.; Wu, C.; Li, T.; Cong, K. Green extraction of carotenoids from apricot flesh by ultrasound assisted corn oil extraction: Optimization, identification, and application. *Food Chem.* **2023**, *420*, 136096. [CrossRef] [PubMed]
67. Sarkar, S.; Manna, M.S.; Bhowmick, T.K.; Gayen, K. Extraction of chlorophylls and carotenoids from dry and wet biomass of isolated Chlorella Thermophila: Optimization of process parameters and modelling by artificial neural network. *Process Biochem.* **2020**, *96*, 58–72. [CrossRef]
68. Liu, X.; Feng, W.; Bao, C.; Jia, Q. Determination of carbamate pesticides and phthalates in vegetables by a cloud point extraction process using tergitol 15-s-7 and high performance liquid chromatography. *Anal. Lett.* **2012**, *45*, 2663–2674. [CrossRef]
69. Bansod, S.P.; Parikh, J.K.; Sarangi, P.K. Pineapple peel waste valorization for extraction of bio-active compounds and protein: Microwave assisted method and Box Behnken design optimization. *Environ. Res.* **2023**, *221*, 115237. [CrossRef]
70. Chen, L.; Zhong, J.; Lin, Y.; Yuan, T.; Huang, J.; Gan, L.; Wang, L.; Lin, C.; Fan, H. Microwave and enzyme co-assisted extraction of anthocyanins from purple-heart radish: Process optimization, composition analysis and antioxidant activity. *LWT-Food Sci. Technol.* **2023**, *187*, 115312. [CrossRef]
71. Phull, T.; Gupta, M. Extraction process optimization for antioxidants, nutritional, physicochemical and functional properties in Fagopyrum esculentum Moench leaves of Himalayan region. *Food Humanit.* **2023**, *1*, 696–709. [CrossRef]
72. Teslić, N.; Bojanić, N.; Rakić, D.; Takači, A.; Zeković, Z.; Fišteš, A.; Bodroža-Solarov, M.; Pavlić, B. Defatted wheat germ as source of polyphenols—Optimization of microwave-assisted extraction by RSM and ANN approach. *Chem. Eng. Process. Process Intensif.* **2019**, *143*, 107634. [CrossRef]
73. Zhang, F.; Xu, Y.; Bu, X.; Wang, Z.; Qi, S.; Li, D.; Wang, L.; Bai, J.; Yang, Y. A novel procedure for simultaneous extraction of polysaccharides and polyphenols from Schisandra Chinensis: Modeling, characterization and biological properties. *Ind. Crops Prod.* **2023**, *193*, 116208. [CrossRef]
74. İnan-Çınkır, N.; Ağçam, E.; Altay, F.; Akyıldız, A. Extraction of carotenoid compounds from watermelon pulp with microemulsion based technique: Optimization studies. *Food Chem.* **2022**, *380*, 132169. [CrossRef] [PubMed]
75. Han, J.; Jia, W.; Wan, Y.; Sun, X.; Liang, M.; Wei, C.; Liu, W. Ultrasonic-assisted extraction of carotenoids using cottonseed oil: Optimization, physicochemical properties, and flavor studies. *J. Food Compos. Anal.* **2022**, *112*, 104663. [CrossRef]
76. Coelho, T.L.S.; Silva, D.S.N.; Junior, J.M.D.S.; Dantas, C.; Nogueira, A.R.D.A.; Júnior, C.A.L.; Vieira, E.C. Multivariate optimization and comparison between conventional extraction (CE) and ultrasonic-assisted extraction (UAE) of carotenoid extraction from cashew apple. *Ultrason. Sonochem.* **2022**, *84*, 105980. [CrossRef]
77. Huang, P.; Yu, Q.; Feng, X.; Ma, C.; Kan, J. Optimization of accelerated solvent extraction of paprika oleoresin and its effect on capsaicinoid and carotenoid composition. *J. Food Compos. Anal.* **2022**, *110*, 104589. [CrossRef]
78. Clarke, D.B. Glucosinolates, structures and analysis in food. *Anal. Methods* **2010**, *2*, 310–325. [CrossRef]
79. Maina, S.; Misinzo, G.; Bakari, G.; Kim, H.-Y. Human, animal and plant health benefits of glucosinolates and strategies for enhanced bioactivity: A systematic review. *Molecules* **2020**, *25*, 3682. [CrossRef]
80. Di Gioia, F.; Pinela, J.; de Haro Bailón, A.; Fereira, I.C.F.R.; Petropoulos, S.A. The dilemma of "good" and "bad" glucosinolates and the potential to regulate their content. In *Glucosinolates: Properties, Recovery, and Applications*; Galanakis, C.M., Ed.; Academic Press: Cambridge, MA, USA, 2020; pp. 1–45.
81. Dekker, M.; Hennig, K.; Verkerk, R. Differences in thermal stability of glucosinolates in five *Brassica* vegetables. *Czech J. Food Sci.* **2009**, *27*, S85–S88. [CrossRef]
82. Hanschen, F.S.; Klopsch, R.; Oliviero, T.; Schreiner, M.; Verkerk, R.; Dekker, M. Optimizing isothiocyanate formation during enzymatic glucosinolate breakdown by adjusting pH value, temperature and dilution in *Brassica* vegetables and *Arabidopsis thaliana*. *Sci. Rep.* **2017**, *7*, 40807. [CrossRef]
83. Sangkret, S.; Pongmalai, P.; Devahastin, S.; Chiewchan, N. Enhanced production of sulforaphane by exogenous glucoraphanin hydrolysis catalyzed by myrosinase extracted from Chinese flowering cabbage (*Brassica rapa* var. *parachinensis*). *Sci. Rep.* **2019**, *9*, 9882. [CrossRef]
84. Desai, K.M.; Survase, S.A.; Saudagar, P.S.; Lele, S.S.; Singhal, R.S. Comparison of artificial neural network (ANN) and response surface methodology (RSM) in fermentation media optimization: Case study of fermentative production of scleroglucan. *Biochem. Eng. J.* **2008**, *41*, 266–273. [CrossRef]
85. Barba, F.J.; Nikmaram, N.; Roohinejad, S.; Khelfa, A.; Zhu, Z.; Koubaa, M. Bioavailability of glucosinolates and their breakdown products: Impact of processing. *Front. Nutr.* **2016**, *3*, 24. [CrossRef] [PubMed]
86. Sikorska-Zimny, K.; Beneduce, L. The glucosinolates and their bioactive derivatives in Brassica: A review on classification, biosynthesis and content in plant tissues, fate during and after processing, effect on the human organism and interaction with the gut microbiota. *Crit. Rev. Food Sci. Nutr.* **2021**, *61*, 2544–2571. [CrossRef] [PubMed]
87. Pan, Z.; Meng, Z.; Tan, M.; Duan, H.; Ramaswamy, H.S.; Qiu, X.; Wang, C. Optimization the conversion of glucosinolate to isothiocyanate in yellow mustard seeds (*Sinapis alba*) by response surface methodology. *Appl. Food Res.* **2022**, *2*, 100207. [CrossRef]
88. Meng, Z.; Yi, L.; Hu, Q.; Lin, Z.; Ramaswamy, H.S.; Wang, C. Optimized extraction and characterization of folates from date palm fruits and their tracking during fruits wine fermentation. *Front. Nutr.* **2021**, *8*, 699555. [CrossRef]

89. Vardhan, H.; Sasamal, S.; Mohanty, K. Fermentation process optimisation based on ANN and RSM for xylitol production from areca nut husk followed by xylitol crystal characterisation. *Process Biochem.* **2022**, *122*, 146–159. [CrossRef]
90. Alara, O.R.; Abdurahman, N.H.; Ukaegbu, C.I.; Azhari, N.H. Vernonia cinerea leaves as the source of phenolic compounds, antioxidants, and anti-diabetic activity using microwave-assisted extraction technique. *Ind. Crops Prod.* **2018**, *122*, 533–544. [CrossRef]
91. Alara, O.R.; Abdurahman, N.H.; Ukaegbu, C.I. Soxhlet extraction of phenolic compounds from Vernonia cinerea leaves and its antioxidant activity. *J. Appl. Res. Med. Aromat. Plants* **2018**, *11*, 12–17. [CrossRef]
92. Abubakar, A.R.; Haque, M. Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. *J. Pharm. Bioallied Sci.* **2020**, *12*, 1–10. [CrossRef]
93. Saini, R.K.; Keum, Y.S. Carotenoid extraction methods: A review of recent developments. *Food Chem.* **2018**, *240*, 90–103. [CrossRef]
94. Ju, Z.; Howard, L.R. Subcritical water and sulfured water extraction of anthocyanins and other phenolics from dried red grape skin. *J. Food Sci.* **2005**, *70*, S270–S276. [CrossRef]
95. Hewage, A.; Olatunde, O.O.; Nimalaratne, C.; Malalgoda, M.; Aluko, R.E.; Bandara, N. Novel extraction technologies for developing plant protein ingredients with improved functionality. *Trends Food Sci. Technol.* **2022**, *129*, 492–511. [CrossRef]
96. Ahmadkelayeh, S.; Hawboldt, K. Extraction of lipids and astaxanthin from crustacean by-products: A review on supercritical CO_2 extraction. *Trends Food Sci. Technol.* **2020**, *103*, 94–108. [CrossRef]
97. Bhagya Raj, G.V.S.; Dash, K.K. Ultrasound-assisted extraction of phytocompounds from dragon fruit peel: Optimization, kinetics and thermodynamic studies. *Ultrason. Sonochem.* **2020**, *68*, 105180. [CrossRef]
98. Espinosa Sandoval, L.A.; Rivera, A.M.P.; Florez, L.C.; Figueroa, A.G. Application of artificial neural networks (ANN) for predicting the effect of processing on the digestibility of foods. In *Food Structure Engineering and Design for Improved Nutrition, Health and Well-Being*; Cerqueira, M.Â.P.R., Castro, L.M.P., Eds.; Academic Press: Cambridge, MA, USA, 2023; pp. 333–361.
99. Bellmann, S.; Krishnan, S.; de Graaf, A.; de Ligt, R.A.; Pasman, W.J.; Minekus, M.; Havenaar, R. Appetite ratings of foods are predictable with an in vitro advanced gastrointestinal model in combination with an in silico artificial neural network. *Food Res. Int.* **2019**, *122*, 77–86. [CrossRef]
100. Huang, S.; Kuo, C.; Chen, C.; Liu, Y.; Shieh, C. RSM and ANN modeling-based optimization approach for the development of ultrasound-assisted liposome encapsulation of piceid. *Ultrason. Sonochem.* **2017**, *36*, 112–122. [CrossRef]
101. Kolpakova, V.; Lukin, N.; Gaivoronskaya, I. Interrelation of functional properties of protein products from wheat with the composition and physicochemical characteristics of their proteins. In *Global Wheat Production*; IntechOpen: London, UK, 2018.
102. Gao, Z.; Shen, P.; Lan, Y.; Cui, L.; Ohm, J.-B.; Chen, B.; Rao, J. Effect of alkaline extraction pH on structure properties, solubility, and beany flavor of yellow pea protein isolate. *Food Res. Int.* **2020**, *131*, 109045. [CrossRef]
103. Rammuni, M.N.; Ariyadasa, T.U.; Nimarshana, P.H.V.; Attalage, R.A. Comparative assessment on the extraction of carotenoids from microalgal sources: Astaxanthin from H. pluvialis and β-carotene from D. salina. *Food Chem.* **2019**, *277*, 128–134. [CrossRef]
104. Momenzadeh, L.; Zomorodian, A.; Mowla, D. Experimental and theoretical investigation of shelled corn drying in a microwave-assisted fluidized bed dryer using Artificial Neural Network. *Food Bioprod. Process.* **2011**, *89*, 15–21. [CrossRef]
105. Bajić, A.; Pezo, L.L.; Stupar, A.; Filipčev, B.; Cvetković, B.R.; Horecki, A.T.; Mastilović, J. Application of lyophilized plum pomace as a functional ingredient in a plum spread: Optimizing texture, colour and phenol antioxidants by ANN modelling. *LWT-Food Sci. Technol.* **2020**, *130*, 109588. [CrossRef]
106. Binetti, G.; Del Coco, L.; Ragone, R.; Zelasco, S.; Perri, E.; Montemurro, C.; Valentini, R.; Naso, D.; Fanizzi, F.P.; Schena, F.P. Cultivar classification of Apulian olive oils: Use of artificial neural networks for comparing NMR, NIR and merceological data. *Food Chem.* **2017**, *219*, 131–138. [CrossRef] [PubMed]
107. O'Shea, N.; Greene, D.; Fenelon, M.A. Artificial intelligence in food safety. In *Reference Module in Food Science*; Elsevier: Amsterdam, The Netherlands, 2023.
108. Zhang, Y.; Zhu, D.; Ren, X.; Shen, Y.; Cao, X.; Liu, H.; Li, J. Quality changes and shelf-life prediction model of postharvest apples using partial least squares and artificial neural network analysis. *Food Chem.* **2022**, *394*, 133526. [CrossRef] [PubMed]

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